RANDOMISED TRIALS IN CHILD HEALTH IN DEVELOPING COUNTRIES

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SEARCH STRATEGY

Pubmed Hayne's strategy, search: ((Developing countries; Developing country; Countries, developing; Developed countries; Country, developing; Countries, developed; Developed country; Country, developed; Nations, developing; Developing nations OR India OR Africa OR Asia OR South America OR Papua New Guinea OR Asia-Pacific) and (Child*)) AND (randomized controlled trial[Publication Type] OR (randomized[Title/Abstract] AND controlled[Title/Abstract] AND trial[Title/Abstract])).

Introduction

This booklet is compiled annually to summarize the evidence on child health derived from randomized trials in developing countries over the previous year. The aim is to make this information widely available to paediatricians, nurses, other health workers and administrators in resource poor settings where up-to-date information is hard to find. It is hoped that such information will be helpful in reviewing treatment policies, clinical practice and public health strategies.

The method of searching for studies to include uses Pubmed, a search engine that is freely available and widely used in most countries throughout the world. The search strategy has been chosen to try to capture as many relevant studies as possible, although it is possible that some are missed. If you know of a relevant RCT that has not been included in this year's review, please let me know. The search strategy is reproducible by anyone with access to the Internet, through **http://www.ncbi.nlm.nih.gov/sites/entrez**

Randomized controlled trials (RCTs) are far from the only valuable scientific evidence, and some RCTs, because of problems with design or implementation have limited value. However the method of the Randomized Trial is the Gold Standard for determining attributable benefit or harm from clinical and public health interventions. When appropriately performed they eliminate bias and confounding. However their results should not be accepted uncritically and they should be evaluated for quality and validity. Before the result of an RCT can be generalized to another setting there must be consideration of the wider applicability, feasibility and potential for sustainability.

This year 200 studies were identified. These came from all regions of the world, mostly from developing country researchers. Several trials from 2010-11 will lead to significant changes in child health approaches or clinical recommendations.

We have included the web-link for papers that are freely available in full-text on the Internet. More importantly, through HINARI (**http://www.who.int/hinari/en/**) a program set up by WHO in collaboration with major publishers, the full-text version of over 7000 journal titles are now available to health institutions in 109 countries. If your health institution (medical school, teaching hospital, nursing school, government office) has not registered with HINARI, you can check your eligibility and register online.

Please feel free to distribute this booklet to any colleagues. Previous editions (2002-2010) are available at: **www.ichrc.org**

Four trials reported significant reductions in mortality (marked with *** in the booklet), **among these:**

- In Kenya, South Africa and Burkina Faso giving a combination of three antiretroviral (ARV) drugs to pregnant women who had HIV infection, from the last trimester through to six months of breastfeeding, reduced the risk of transmitting HIV to the baby and improves survival, compared to zidovudine in pregnancy and single dose nevirapine.
- In 11 centres in 9 African countries among more than 5000 children with severe malaria Artesunate substantially reduced mortality compared to quinine treatment.
- In rural China, micronutrient supplementation to pregnant women from the poorest households reduced neonatal mortality, and reduced low birth weight. Standard iron and

folic acid provided more protection against neonatal death than multiple micronutrient supplements.

- ❖ In Pakistan, in a trial involving over 46,000 households, a community-based program involving lady health workers who delivered antenatal care and maternal health education, clean delivery kits, promoted facility births, immediate newborn care, identification of danger signs, and care seeking, significantly reduced still-births and neonatal deaths.

Other important results in 2010-11

- In Rwanda paying primary health facilities for performance resulted in a 23% increase in the number of institutional deliveries and a significant increase in the number of preventive care visits by children
- In Bangladesh, day-case management of severe pneumonia in hospital was successful, as long as those with hypoxia were identified and managed as in-patients.
- A green banana-supplemented diet hastened recovery of acute and prolonged childhood diarrhoea managed at home in rural Bangladesh.
- There were several trials of zinc in India, Bangladesh and Pakistan this year. In a community-based effectiveness trial in India, educating caregivers to provide zinc supplementation to infants <6 months old reduced diarrhoea and acute lower respiratory infection. The extended protective effect of zinc when used as treatment for diarrhoea was the same whether zinc was given for 5 days or 10 days in Bangladesh; and in India there was no added effect of giving multivitamins or micronutrients on the treatment effect of zinc for diarrhoea. Although zinc supplementation in some populations seems to *prevent* acute respiratory infection, two trials this year from India showed no evidence that zinc was effective in the *treatment* of pneumonia.
- In a community-based trial in an urban slum in India probiotics given daily for 12 weeks, showed a 14% reduction in the occurrence of diarrhoea.
- Co-trimoxazole prophylaxis in HIV exposed children in rural Uganda provided 39% protection against malaria, when continued up to 2 years of age, and in a trial in South Africa, daily cotrimoxazole preventative therapy was associated with significantly lower risk of bacteraemia in HIV-infected children than intermittent prophylaxis given 3 times per week.
- In Zambia the use of rapid diagnostic tests (RDTs) for malaria by community health workers resulted in more rational prescribing of antimalarials, with significant decreases in inappropriate prescribing of artemether-lumefantrine, and a significant increase in the prescribing of amoxicillin for pneumonia. Community health workers adhered closely to simple guidelines based on RDTs (in contrast to some earlier studies where health workers treated with antimalarials regardless of the result).
- In phase II trials in Tanzania and Kenya, the lead candidate malaria vaccine RTS,S/AS01E provided sustained protective efficacy of 39% and 45% at 12 and 15 months respectively against the first episode of malaria, when given to young infants with other routine EPI vaccines.
- While there have been many trials in recent years showing the protective effect of intermittent preventative treatment for malaria, the effectiveness in communities using insecticide treated bed nets was not clear. This year two trials from Burkina Faso and Mali showed a strong protective effect (69% and 85% reduction in severe malaria

respectively; 46% reduction in hospitalisation in Burkina Faso; significant reductions in anaemia in both countries; and reduced malnutrition in Burkina Faso), among children who sleep under insecticide treated bed nets.

- Over a four year effectiveness trial in an urban area in Uganda, a multifaceted approach to malaria control using insecticide treated bed nets and artemisinin-based combination therapy, serious morbidity and deaths due to malaria were eliminated.
- To address treatment failure for visceral leishmaniasis with paramycin three studies investigated high doses or for longer duration or combination drug treatment with amphetericin B alone, or amphetericin B and miltefosine, or paramycin and miltefisine. Combination therapy provided in excess of 95% cure.
- A 23 year follow-up of a cohort of people in China involved in an early RCT of Hepatitis B vaccine showed sustained protective immunity, meaning that booster doses are unnecessary in fully vaccinated children for over 20 years
- In India, intranasal administration of lorazepam was not inferior to intravenous administration for termination of acute convulsive seizures in children, and daily oral folic acid decreased the incidence of phenytoin-induced gingival overgrowth in children with epilepsy.

Good trials should be designed and conducted not only to show benefit, but to demonstrate harm or adverse events where they occur. This year there were at least three trials that challenged conventional wisdom about the safety of commonly used interventions.

- In Tanzania, two trials showed Vitamin A – β carotene supplementation, when given to HIV-positive women in pregnancy and in the post-partum period, increased breast-milk transmission of HIV, possibly due to sub-clinical mastitis induced by β carotene.
- In Kenya, Uganda and Tanzania, fluid boluses with 0.9% sodium chloride or albumin in the emergency care of children with malaria and other common febrile illnesses, who have signs of poor peripheral perfusion, increased the risk of death.
- In Guinea-Bissau, when measles vaccine was combined with diphtheria-tetanus-pertussus and oral polio vaccines, there was a higher rate of infectious disease morbidity and poor growth at 12 months among girls, compared to girls who received only measles and oral polio vaccine. This effect was not seen in boys.

It is important to understand the context in which benefit (or harm) occurs in a trial. This context may include: individual or population characteristics, comorbidities; the health care environment and health care providers; geographical factors; other interventions; the delivery mechanism for the drug, vaccine or other intervention; the disease stage and specific aetiology; economic, social and cultural characteritics of the population and individuals within it…and other unknown factors. This can be even more complex in understanding systematic reviews of randomised trials (where heterogeneity is often incompletely reported), and is one reason why there is a need for more large-scale implementation trials – not necessarily randomised - that provide insight into local context.

More than one hundred thousand children and their families participated in the randomised trials published this year, and it is to them that the global scientific community should be grateful.

Trevor Duke
July 2011

Acute respiratory infection

(See also Zinc, Pneumococcal vaccine)

Treatment of severe pneumonia

Pediatrics. 2010 Oct;126(4):e807-15. Epub 2010 Sep 20.

Randomized controlled trial of day care versus hospital care of severe pneumonia in Bangladesh.

Ashraf H, Mahmud R, Alam NH, Jahan SA, Kamal SM, Haque F, Salam MA, Gyr N.

Source

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Abstract

OBJECTIVE: A randomized controlled trial compared day care versus hospital care management of pneumonia. METHODS: Children 2 to 59 months of age with severe pneumonia received either day care, with antibiotic treatment, feeding, and supportive care from 8:00 am to 5:00 pm, or hospital care, with similar 24-hour treatment. RESULTS: In 2006-2008, 360 children were assigned randomly to receive either day care or hospital care; 189 (53%) had hypoxemia, with a mean±SD oxygen saturation of 93±4%, which increased to 99±1% after oxygen therapy. The mean±SD durations of day care and hospital care were 7.1±2.3 and 6.5±2.8 days, respectively. Successful management was possible for 156 (87.7% [95% confidence interval [CI]: 80.9%-90.9%]) of 180 children in the day care group and 173 (96.1% [95% CI: 92.2%-98.1%]) of 180 children in the hospital care group (P=.001). Twenty-three children in the day care group (12.8% [95% CI: 8.7%-18.4%] and 4 children in the hospital care group (2.2% [95% CI: 0.9%-5.6%] required referral to hospitals (P<.001). During the follow-up period, 22 children in the day care group (14.1% [95% CI: 9.5%-20.4%]) and 11 children in the hospital care group (6.4% [95% CI: 3.6%-11%]) required readmission to hospitals (P=.01). The estimated costs per child treated successfully at the clinic and the hospital were US$114 and US$178, respectively. CONCLUSION: Severe childhood pneumonia without severe malnutrition can be successfully managed at day care clinics, except for children with hypoxemia who require prolonged oxygen therapy.

Trop Med Int Health. 2011 May 4. doi: 10.1111/j.1365-3156.2011.02787.x.

Outpatient treatment of children with severe pneumonia with oral amoxicillin in four countries: the MASS study.

Addo-Yobo E, Anh DD, El-Sayed HF, Fox LM, Fox MP, Macleod W, Saha S, Tuan TA, Thea DM, Qazi S; for the Multicenter Amoxicillin Severe pneumonia Study (MASS) Group.

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Objective
A recent randomized clinical trial demonstrated home-based treatment of WHO-defined severe pneumonia with oral amoxicillin was equivalent to hospital-based therapy and parenteral antibiotics. We aimed to determine whether this finding is generalizable across four countries.
Methods
Multicentre observational study in Bangladesh, Egypt, Ghana and Vietnam between November 2005 and May 2008. Children aged 3–59 months with WHO-defined severe pneumonia were enrolled at participating health centres and managed at home with oral amoxicillin (80–90 mg⁄kg per day) for 5 days. Children were followed up at home on days 1, 2, 3 and 6 and at a facility on day 14 to look for cumulative treatment failure through day 6 and relapse between days 6 and 14.
Results
Of 6582 children screened, 873 were included, of whom 823 had an outcome ascertained. There was substantial variation in presenting characteristics by site. Bangladesh and Ghana had fever (97%) as a more common symptom than Egypt (74%) and Vietnam (66%), while in Vietnam, audible wheeze was more common (49%) than at other sites (range 2–16%). Treatment failure by day 6 was 9.2% (95% CI: 7.3–11.2%) across all sites, varying from 6.4% (95% CI: 3.1–9.8%) in Ghana to 13.2% (95% CI: 8.4–18.0%) in Vietnam; 2.7% (95% CI: 1.5–3.9%) of the 733 children well on day 6 relapsed by day 14. The most common causes of treatment failure were persistence of lower chest wall indrawing (LCI) at day 6 (3.8%; 95% CI: 2.6–5.2%), abnormally sleepy or difficult to wake (1.3%; 95% CI: 0.7–2.3%) and central cyanosis (1.3%; 95% CI: 0.7–2.3%). All children survived and only one adverse drug reaction occurred. Treatment failure was more frequent in young infants and those presenting with rapid respiratory rates.
Conclusions
Clinical treatment failure and adverse event rates among children with severe pneumonia treated at home with oral amoxicillin did not substantially differ across geographic areas. Thus, home-based therapy of severe pneumonia can be applied to a wide variety of settings.

Comment

The above two studies contribute to the body of evidence on the treatment of WHO-defined severe pneumonia outside hospital in-patient wards. Following an RCT of severe pneumonia in Pakistan (Lancet 2008; 371:49-56) that showed WHO-defined severe pneumonia among urban children could be safely managed with amoxicillin at home. The above 4-country study adds to this, showing similar efficacy in other settings.

There are several important issues that will be vital for the implementation of these studies: the potential ambiguity of WHO's current pneumonia severity classification system, and the need to identify high-risk pneumonia cases.

In the 4-country severe pneumonia study no children died. This is good news, but suggests the current WHO classification of severe pneumonia into "non-severe", "severe" and "very severe" does not well reflect disease severity. One problem is that while in a properly conducted study exclusion criteria can be carefully applied, health workers in clinical settings rarely diagnose "very severe pneumonia"; rather they call it "severe pneumonia". Thus they are likely to be confused when they are told that children with severe pneumonia can be managed at home. It might make more sense to use the classification of mild (replacing non-severe), moderate (replacing severe) and severe (replacing very severe) or simply pneumonia (for current non-severe and severe) and severe (for very severe). This might enable health

workers and parents to have the confidence to manage what we now call "severe" pneumonia at home.

The study in Bangladesh on day-case management of severe pneumonia also adds a lot to knowledge in this area. Investigators in Dhaka found that although day-case management was safe and effective for 87% of children with WHO-defined severe pneumonia, it was not so for children with hypoxaemia, who were likely to fail day-case treatment and require inpatient admission. This underlines the importance of having a method of identifying high risk children. Most danger signs, such as cyanosis, sleepiness and inability to feed, are associated with an increased probability of hypoxaemia, but these can be hard to detect. Hypoxaemia is the most precise indicator of mortality risk in pneumonia. In the application of research on day-case or outpatient management of severe pneumonia pulse oximetry is needed to help identify children who need hospitalization from those who can be safely treated outside.

Treatment of non-severe pneumonia

Clin Infect Dis. 2011 Feb 1;52(3):293-300. Epub 2010 Dec 28.

Comparison of oral amoxicillin with placebo for the treatment of world health organization-defined nonsevere pneumonia in children aged 2-59 months: a multicenter, double-blind, randomized, placebo-controlled trial in pakistan.

Hazir T, Nisar YB, Abbasi S, Ashraf YP, Khurshid J, Tariq P, Asghar R, Murtaza A, Masood T, Maqbool S.

Source

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Abstract

BACKGROUND: World Health Organization (WHO) acute respiratory illness case management guidelines classify children with fast breathing as having pneumonia and recommend treatment with an antibiotic. There is concern that many of these children may not have pneumonia and are receiving antibiotics unnecessarily. This could increase antibiotic resistance in the community. The aim was to compare the clinical outcome at 72 h in children with WHO-defined nonsevere pneumonia when treated with amoxicillin, compared with placebo. METHODS: we performed a double-blind, randomized, equivalence trial in 4 tertiary hospitals in Pakistan. Nine hundred children aged 2-59 months with WHO defined nonsevere pneumonia were randomized to receive either 3 days of oral amoxicillin (45mg/kg/day) or placebo; 873 children completed the study. All children were followed up on days 3, 5, and 14. The primary outcome was therapy failure defined a priori at 72 h. RESULTS: in per-protocol analysis at day 3, 31 (7.2%) of the 431 children in the amoxicillin arm and 37 (8.3%) of the 442 in placebo group had therapy failure. This difference was not statistically significant (odds ratio [OR], .85; 95%CI, .50-1.43; P = .60). The multivariate analysis identified history of difficult breathing (OR, 2.86; 95% CI, 1.29-7.23; P = .027) and temperature >37.5°C 100°F at presentation (OR, 1.99; 95% CI, 1.37-2.90; P = .0001) as risk factors for treatment failure by day 5. CONCLUSION: clinical outcome in children aged 2-59 months with WHO-defined nonsevere pneumonia is not different when treated with an antibiotic or placebo. Similar trials are needed in countries with a high burden of pneumonia to rationalize the use of antibiotics in these communities.

Micronutrients and pneumonia

Trop Med Int Health. 2010 Oct;15(10):1148-55. doi: 10.1111/j.1365-3156.2010.02578.x. Epub 2010 Aug 17.

Effects of vitamin D supplementation to children diagnosed with pneumonia in Kabul: a randomised controlled trial.

Manaseki-Holland S, Qader G, Isaq Masher M, Bruce J, Zulf Mughal M, Chandramohan D, Walraven G.

Source

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Abstract

OBJECTIVES: To determine whether (i) supplementation of oral 100,000 iu of vitamin D(3) (cholecalciferol) along with antibiotics will reduce the duration of illness in children with pneumonia; (ii) supplementation will reduce the risk of repeat episodes. METHODS: Double-blind individually randomised placebo-controlled trial in an inner-city hospital in Kabul, of 453 children aged 1-36 months, diagnosed with non-severe or severe pneumonia at the outpatient clinic. Children with rickets, other concurrent severe diseases, very severe pneumonia or wheeze, were excluded. Children were given vitamin D(3) or placebo drops additional to routine pneumonia treatment. RESULTS: Two hundred and twenty-four children received vitamin D(3;) and 229 received placebo. There was no significant difference in the mean number of days to recovery between the vitamin D(3) (4.74 days; SD 2.22) and placebo arms (4.98 days; SD 2.89; P = 0.17). **The risk of a repeat episode of pneumonia within 90 days of supplementation was lower in the intervention (92/204; 45%) than the placebo group [122/211; (58%; relative risk 0.78; 95% CI 0.64, 0.94; P = 0.01].** Children in the vitamin D(3) group survived longer without experiencing a repeat episode (72 days vs. 59 days; HR 0.71; 95% CI 0.53-0.95; P = 0.02). CONCLUSION: A single high-dose oral vitamin D(3) supplementation to young children along with antibiotic treatment for pneumonia could reduce the occurrence of repeat episodes of pneumonia.

Indian J Pediatr. 2011 Jan;78(1):33-7. Epub 2010 Sep 30.

Zinc supplementation in severe acute lower respiratory tract infection in children: a triple-blind randomized placebo controlled trial.

Bansal A, Parmar VR, Basu S, Kaur J, Jain S, Saha A, Chawla D.

Source

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Abstract

OBJECTIVE: To evaluate the efficacy of zinc supplementation on duration of illness in children with severe acute lower respiratory tract infection (ALRTI). METHODS: This randomized triple-blind placebo-controlled trial was conducted in pediatric emergency of a teaching referral hospital. Children in the age group of 2-24 months presenting to pediatric emergency with severe ALRTI were included. Eligible children were randomly allocated to zinc (n=53) or control (n=53) groups. Zinc group received 20 mg of elemental zinc per day (5 ml syrup per day) as a single daily dose for 5 days. Control group received an equal amount of placebo which was appropriately modified to give the taste, smell, color and consistency similar to zinc mixture. Primary outcome was 'time to be asymptomatic', a composite outcome defined

as resolution of all four of the following: danger signs, respiratory distress, tachypnea and hypoxia in room air. RESULTS: Age, gender, nutritional status, pretreatment zinc levels and other demographic and clinical variables were similar in the two groups. 'Time to be asymptomatic' was comparable in the two groups (h; median (IQR): 60 (24-78) vs. 54 (30-72), P=0.98]. At any time point a similar proportion of children were symptomatic in both the groups. Time to resolution of respiratory distress, tachypnea, dangers signs and hypoxia were also similar in two groups. Duration of hospital stay was shorter by 9 h in the zinc group but the difference was statistically insignificant. CONCLUSION: Zinc supplementation did not reduce recovery time and duration of hospital stay in children with ALRTI. Larger randomized controlled trials are needed to evaluate role of zinc in ALRTI.

Indian J Pediatr. 2011 Jun 10. [Epub ahead of print]

A Randomized Controlled Trial of Oral Zinc in Acute Pneumonia in Children Aged between 2 Months to 5 Years.

Ganguly A, Chakraborty S, Datta K, Hazra A, Datta S, Chakraborty J.

Source

Department of Pharmacology, Institute of Post Graduate Medical Education & Research, Kolkata, India.

Abstract

OBJECTIVE: To evaluate the effectiveness and safety of zinc supplementation as adjuvant in treatment of pneumonia. METHODS: Ninety-eight children with acute bacterial pneumonia, aged between 2 months to 5 years, were studied in a randomized controlled single blind design. They received either zinc supplementation, as zinc acetate syrup, or placebo, as vitamin B-complex syrup, for 14 days, concomitantly with antimicrobial treatment (49 per group). Chest radiograph and blood tests were done for confirmation of diagnosis and severity of pneumonia was assessed by breathing rate, chest in-drawing and body temperature. Potentially immunosuppressed children or those with serious comorbidity were excluded. Follow-up was done daily while subjects were admitted (generally 7 days) and the final assessment made on the 14th day on out-patient basis. RESULTS: Children enrolled in zinc and placebo groups were of comparable age [17 ± 10 and 10 ± 30 months (median ± interquartile range) respectively] and sex distribution [34 (69.4%) vs 31 (63.3%) males respectively]. Duration of illness at diagnosis was also comparable. Patients supplemented with zinc showed no difference in clinical cure rate at 14 days when compared with placebo. Fast breathing was present after 1 wk of treatment in 49% subjects in zinc supplemented vs 43% on placebo (p = 0.685). There was also no difference in breathing rate at study end. Regarding fever, the mean temperature was <99°F in both groups at study end. Hemoglobin, total leukocyte count, standard liver function tests and creatinine showed no difference between groups either at baseline or at study end. There were no treatment emergent adverse events attributable to zinc. CONCLUSIONS: Though well tolerated; the addition of zinc does not improve symptom duration or cure rate in acute bacterial pneumonia in under-five children.

Comment

Two studies this year from India of the effect of zinc treatment for pneumonia failed to find a clinical benefit.

The value of vitamin D in the treatment of pneumonia is interesting. In some populations, such as in Iran (Pediatr Pulmonol. 2009; 44:1207–1215) vitamin D deficiency is common in children with very severe pneumonia. Although the seasonality of pneumonia - clustering in winter months - was traditionally attributed to household crowding, vitamin D deficiency, due to reduced ultraviolet irradiation in winter, may also contribute to the seasonality of pneumonia, and is worth exploring further in populations likely to be at risk.

Pediatr Infect Dis J. 2010 Dec;29(12):1099-04.

Role of Streptococcus pneumoniae in hospitalization for acute community-acquired pneumonia associated with culture-confirmed Mycobacterium tuberculosis in children: a pneumococcal conjugate vaccine probe study.

Moore DP, Klugman KP, Madhi SA.

Source

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Abstract

INTRODUCTION: African children hospitalized with symptoms of severe acute pneumonia, which resolves following empiric antibiotic therapy, are sometimes identified to have underlying culture-confirmed pulmonary tuberculosis (PTB). Experimental studies suggest Mycobacterium tuberculosis infection predisposes to Streptococcus pneumoniae infection; however, diagnostic limitations make it difficult to quantify this association in children. We aimed to probe the extent of pneumococcal coinfection in children with PTB, using a vaccine-probe design study. MATERIALS AND METHODS: A post hoc analysis of PTB cases occurring among 39,836 participants in a phase III randomized, double-blind placebo-controlled 9-valent pneumococcal polysaccharide-protein conjugate vaccine (PCV9) trial in South Africa was undertaken. Hospitalization for PTB occurring during the 5.3 years of follow-up were identified and categorized as culture-confirmed PTB or probable/possible-PTB. The incidence rates of hospitalized PTB were compared between PCV9 vaccinees and placebo recipients. RESULTS: Hospitalization for culture-confirmed PTB was 43.4% (95% CI, 9.7%–65.1%) less likely among vaccinees (n = 30) compared with placebo recipients (n = 53), incidence, 20 versus 35 per 100,000 child-years of follow-up (P = 0.0117). In HIV-infected children, culture-confirmed PTB was 47.3% (95% CI, 8.6%–69.6%) less likely among vaccinees (n = 19) compared with placebo recipients (n = 36), P = 0.0203. The incidence of possible/probable PTB did not differ by vaccination status. CONCLUSIONS: This vaccine-probe design study suggests that in a setting with high HIV and TB prevalence, culture-confirmed PTB in African children, which frequently presents with symptoms of acute pneumonia, is probably associated with superimposed pneumococcal pneumonia. Children admitted with pneumonia in these settings should be investigated for underlying PTB.

Clin Infect Dis. 2010 Nov 1;51(9):1053-61.

Influenza virus contamination of common household surfaces during the 2009 influenza A (H1N1) pandemic in Bangkok, Thailand: implications for contact transmission.

Simmerman JM, Suntarattiwong P, Levy J, Gibbons RV, Cruz C, Shaman J, Jarman RG, Chotpitayasunondh T.

Source
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Abstract
BACKGROUND: Rational infection control guidance requires an improved understanding of influenza transmission. We studied households with an influenza-infected child to measure the prevalence of influenza contamination, the effect of hand washing, and associations with humidity and temperature. METHODOLOGY: We identified children with influenza and randomly assigned their households to hand washing and control arms. Six common household surfaces and the fingertips of the index patient and symptomatic family members were swabbed. Specimens were tested by real-time reverse-transcription polymerase chain reaction (rRT-PCR), and specimens with positive results were placed on cell culture. A handheld psychrometer measured meteorological data. RESULTS: Sixteen (17.8%) of 90 households had influenza A-positive surfaces by rRT-PCR, but no viruses could be cultured. The fingertips of 15 (16.6%) of the index patients had results positive for influenza A, and 1 virus was cultured. Index patients with seasonal influenza infections shed more virus than did patients with pandemic influenza infection. Control households had a higher prevalence of surface contamination (11 [24.4%] of 45) than did hand washing households (5 [11.1%] of 45); prevalence risk difference (PRD), 13.3%; [95% confidence interval {CI}, −2.2% to 28.9%]; P = .09). Households in which the age of the index patient was ≤8 years had a significantly higher prevalence of contamination (PRD ,19.1%; 95% CI, 5.3% -32.9%; P = .02). Within the strata of households with secondary infections, an effect of lower absolute humidity is suggested (P = .07). CONCLUSIONS: We documented influenza virus RNA contamination on household surfaces and on the fingertips of ill children. Homes with younger children were more likely than homes of older children to have contaminated surfaces. Lower absolute humidity favors surface contamination in households with multiple infections. Increased hand washing can reduce influenza contamination in the home.

Indian Pediatr. 2010 Dec;47(12):1047-50.

Steam inhalation in respiratory illnesses--full steam ahead or full stop? A systematic review of randomized controlled trial.

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There is not enough evidence supporting benefit of steam inhalation in acute (upper and lower) respiratory illnesses in children

Adolescent health

Child Abuse Negl. 2010 Nov;34(11):833-41. Epub 2010 Oct 12.

Associations between childhood adversity and depression, substance abuse and HIV and HSV2 incident infections in rural South African youth.

Jewkes RK, Dunkle K, Nduna M, Jama PN, Puren A.

Source
Gender and Health Research Unit, Medical Research Council, South Africa.
Abstract
OBJECTIVES: To describe prevalence of childhood experiences of adversity in rural South African youth and their associations with health outcomes. METHODS: We analyzed questionnaires and blood specimens collected during a baseline survey for a cluster randomized controlled trial of a behavioral intervention, and also tested blood HIV and herpes simplex type 2 virus at 12- and 24-month follow up; 1,367 male and 1,415 female volunteers were recruited from 70 rural villages. RESULTS: **Both women and men before 18 had experienced physical punishment (89.3% and 94.4%), physical hardship (65.8% and 46.8%), emotional abuse (54.7% and 56.4%), emotional neglect (41.6% and 39.6%), and sexual abuse (39.1% and 16.7%).** Incident HIV infections were more common in women who experienced emotional abuse (IRR 1.96, 95% CI 1.25, 3.06, p=.003), sexual abuse (IRR 1.66 95% CI 1.04, 2.63, p=.03), and physical punishment (IRR 2.13 95% CI 1.04, 4.37, p=.04). Emotional neglect in women was associated with depression (aOR 1.82, 95% CI 1.15, 2.88, p=.01), suicidality (aOR 5.07, 95% CI 2.07, 12.45, p<.0001), alcohol abuse (aOR 2.17, 95% CI .99, 4.72, p=.05), and incident HSV2 infections (IRR 1.62, 95% CI 1.01, 2.59, p=.04). In men emotional neglect was associated with depression (aOR 3.41, 95% CI 1.87, 6.20, p<.0001) and drug use (aOR 1.98, 95% CI 1.37, 2.88, p<.0001). Sexual abuse was associated with alcohol abuse in men (aOR 3.68, 95% CI 2.00, 6.77, p<.0001) and depression (aOR 2.16, 95% CI 1.34, 3.48, p=.002) and alcohol abuse in women (aOR 3.94, 95% CI 1.90, 8.17, p<.0001). PRACTICE IMPLICATIONS: **Childhood exposure to adversity is very common and influences the health of women and men. All forms of adversity, emotional, physical and sexual, enhance the risk of adverse health outcomes in men and women.** Prevention of child abuse need to be included as part of the HIV prevention agenda in sub-Saharan Africa. Interventions are needed to prevent emotional, sexual, and physical abuse and responses from health and social systems in Africa to psychologically support exposed children must be strengthened.

J Nutr. 2010 Oct;140(10):1879-86. Epub 2010 Aug 11.

Long-term intermittent multiple micronutrient supplementation enhances hemoglobin and micronutrient status more than iron + folic acid supplementation in Bangladeshi rural adolescent girls with nutritional anemia.

Ahmed F, Khan MR, Akhtaruzzaman M, Karim R, Williams G, Torlesse H, Darnton-Hill I, Dalmiya N, Banu CP, Nahar B.
Source
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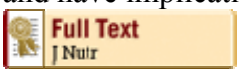
Abstract
Previous short-term supplementation studies showed no additional hematologic benefit of multiple micronutrients (MMN) compared with iron + folic acid (IFA) in adolescent girls. This study examines whether long-term once- or twice-weekly supplementation of MMN can improve hemoglobin (Hb) and micronutrient status more than twice-weekly IFA supplementation in anemic adolescent girls in Bangladesh. Anemic girls (n = 324) aged 11-17 y attending rural schools were given once- or twice-weekly MMN or twice-weekly IFA, containing 60 mg iron/dose in both supplements, for 52 wk in a randomized double-blind trial. Blood samples were collected at baseline and 26 and 52 wk. Intent to treat analysis showed no significant difference in the Hb concentration between treatments at either 26 or 52 wk. However, after excluding girls with hemoglobinopathy and adjustment for baseline Hb, a greater

increase in Hb was observed with twice-weekly MMN at 26 wk (P = 0.045). Although all 3 treatments effectively reduced iron deficiency, once-weekly MMN produced significantly lower serum ferritin concentrations than the other treatments at both 26 and 52 wk. Both once- and twice-weekly MMN significantly improved riboflavin, vitamin A, and vitamin C status compared with IFA. Overall, once-weekly MMN was less efficacious than twice-weekly MMN in improving iron, riboflavin, RBC folic acid, and vitamin A levels. Micronutrient supplementation beyond 26 wk was likely important in sustaining improved micronutrient status. These findings highlight the potential usefulness of MMN intervention in this population and have implications for programming.



Am J Public Health. 2011 Jun;101(6):1082-8. Epub 2011 Apr 14.

Supporting adolescent orphan girls to stay in school as HIV risk prevention: evidence from a randomized controlled trial in Zimbabwe.

Hallfors D, Cho H, Rusakaniko S, Iritani B, Mapfumo J, Halpern C.
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Abstract
OBJECTIVES: Using a randomized controlled trial in rural eastern Zimbabwe, we tested whether comprehensive support to keep orphan adolescent girls in school could reduce HIV risk. METHODS: All orphan girls in grade 6 in 25 primary schools were invited to participate in the study in fall 2007 (n = 329). Primary schools were randomized to condition. **All primary schools received a universal daily feeding program; intervention participants received fees, uniforms, and a school-based helper to monitor attendance and resolve problems.** We conducted annual surveys and collected additional information on school dropout, marriage, and pregnancy rates. We analyzed data using generalized estimating equations over 3 time points, controlling for school and age at baseline. RESULTS**: The intervention reduced school dropout by 82% and marriage by 63% after 2 years. Compared with control participants, the intervention group reported greater school bonding, better future expectations, more equitable gender attitudes, and more concerns about the consequences of sex**.
CONCLUSIONS: We found promising evidence that comprehensive school support may reduce HIV risk for orphan girls. Further study, including assessment of dose response, cost benefit, and HIV and herpes simplex virus 2 biomarker measurement, is warranted.

Comment
This seems like an amazing study of a social intervention that has multiple benefits to the girls involved and to subsequent generations. For other trials of social interventions to relieve poverty, see Esther Duflo http://econ-www.mit.edu/faculty/eduflo/papers

Arch Pediatr Adolesc Med. 2010 Oct;164(10):923-9.

School-based randomized controlled trial of an HIV/STD risk-reduction intervention for South African adolescents.

Jemmott JB 3rd, Jemmott LS, O'Leary A, Ngwane Z, Icard LD, Bellamy SL, Jones SF, Landis JR, Heeren GA, Tyler JC, Makiwane MB.

Source

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Abstract

OBJECTIVE: To test the efficacy of a school-based human immunodeficiency virus/sexually transmitted disease (HIV/STD) risk-reduction intervention for South African adolescents. DESIGN: A cluster-randomized, controlled design with assessments of self-reported sexual behavior collected before intervention and 3, 6, and 12 months after intervention. SETTING: Primary schools in a large, black township and a neighboring rural settlement in Eastern Cape Province, South Africa. PARTICIPANTS: Nine of 17 matched pairs of schools were randomly selected. Sixth-grade students with parent or guardian consent were eligible. INTERVENTIONS: Two 6-session interventions based on behavior-change theories and qualitative research. The HIV/STD risk-reduction intervention targeted sexual risk behaviors; the attention-matched health promotion control intervention targeted health issues unrelated to sexual behavior. OUTCOME MEASURES: The primary outcome was self report of unprotected vaginal intercourse in the previous 3 months averaged over the 3 follow-ups. Secondary outcomes were other sexual behaviors. RESULTS: A total of 1057 (94.5%) of 1118 eligible students (mean age, 12.4 years) participated, with 96.7% retained at the 12-month follow-up. Generalized estimating equation analyses adjusted for clustering from 18 schools revealed that, averaged over the 3 follow-ups, a significantly smaller percentage of HIV/STD risk-reduction intervention participants reported having unprotected vaginal intercourse (odds ratio [OR], 0.51; 95% confidence interval [CI], 0.30-0.85), vaginal intercourse (OR, 0.62; 95% CI, 0.42-0.94), and multiple sexual partners (OR, 0.50; 95% CI, 0.28-0.89), when adjusted for baseline prevalences, compared with health-promotion control participants. CONCLUSION: This is the first large-scale, community-level, randomized intervention trial to show significant effects on the HIV/STD sexual risk behavior of South African adolescents in the earliest stages of entry into sexual activity.

Psychol Health. 2011 Feb;26(2):167-85.

Cognitive-behavioural health-promotion intervention increases fruit and vegetable consumption and physical activity among South African adolescents: a cluster-randomised controlled trial.

Jemmott JB 3rd, Jemmott LS, O'Leary A, Ngwane Z, Icard L, Bellamy S, Jones S, Landis JR, Heeren GA, Tyler JC, Makiwane MB.

Source

Department of Psychiatry, School of Medicine, University of Pennsylvania, Philadelphia, PA, USA. jjemmott@asc.upenn.edu

Abstract

Rates of chronic diseases are high among Black South Africans but few studies have tested **cognitive-behavioural health-promotion** interventions to reduce this problem. We tested the efficacy of such an intervention among adolescents in a cluster-randomised controlled trial. We randomly selected 9 of 17 matched pairs of schools and randomised one school in each pair to the cognitive-behavioural health-promotion intervention designed to encourage health-related behaviours and the other to a human immunodeficiency virus (HIV)/sexually transmitted disease (STD) risk-reduction intervention that served as the control. Interventions were based on social cognitive theory, the theory of planned behaviour and qualitative data from the target population. Data collectors, blind to participants' intervention, administered confidential assessments at baseline and 3, 6 and 12 months post-intervention. **Primary outcomes were fruit and vegetable consumption and physical activity. Participants were 1057 grade 6 learners (mean age = 12.4 years), with 96.7% retained at 12-month follow-up.** Generalised estimating equations revealed that averaged over the follow-ups, a greater percentage of health-

promotion intervention participants than HIV/STD control participants met 5-a-Day fruit and vegetable and physical activity guidelines. **The intervention also increased health-promotion knowledge, attitude and intention, but did not decrease substance use or substance-use attitude and intention.** The findings suggest that theory based and contextually appropriate interventions may increase health behaviours among young adolescents in sub-Saharan Africa.

Int J Adolesc Med Health. 2010 Oct-Dec;22(4):491-502.

Rebuilding psychosocial competence for unmarried adolescent pregnancies using an integrated intervention.

Yu X, Wei W, Gong L.

Source

The Institute of Child and Adolescent Health, School of Public Health, Peking University, Beijing, PR China. yxm@bjmu.edu.cn

Abstract

This study was designed to investigate effects of an integrated intervention on psychosocial competence after abortion in unmarried adolescent pregnancies. STUDY GROUP: Three hundred eighty-five unmarried adolescent pregnancies aged 15 to 24 years (75.1% employed, 24.9% students) were recruited in the study, of which 190 were allocated into the experimental group and the rests as controls. METHODS: The Rosenberg Self-esteem Scale (SES), the shortened version of Tyler's Behavioral Attributes of Psychosocial Competence Scale-Condensed Form (BAPC-C) and the Nowicki-Stricland Internal-External Locus of Control Scale (NSIE- LOC) were applied to measure self-esteem, coping style, and LOC. Questionnaires were simultaneously administered with abortion service and two-months after intervention. The intervention was organized by an interactive and participatory model designed to increase self-awareness and improve ability of coping under stress with a purpose of reducing occurrence of repeat pregnancy and abortion. RESULTS: Our data showed noticeable changes in coping style and LOC in the experimental group, except for self-esteem ability when comparing with the controls. CONCLUSION: The psychosocial competence was significantly improved after receiving the intervention. Our study indicates that appropriate psychological intervention for unmarried adolescent pregnancies is necessary to rebuild their normal life after the strike

Anaemia and iron deficiency

Food Nutr Bull. 2010 Sep;31(3):446-60.

Daily use of Sprinkles micronutrient powder for 2 months reduces anemia among children 6 to 36 months of age in the Kyrgyz Republic: a cluster-randomized trial.

Lundeen E, Schueth T, Toktobaev N, Zlotkin S, Hyder SM, Houser R.

Source

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Abstract

BACKGROUND: Iron-deficiency anemia is widespread among young children in the Kyrgyz Republic, and there is an urgent need to identify an effective intervention to address this significant public health problem. OBJECTIVE: To test the effectiveness of a 2-month

intervention with daily home fortification of complementary food using micronutrient powder (Sprinkles) in reducing anemia among children 6 to 36 months of age in the Kyrgyz Republic. METHODS: In this cluster-randomized, community-based effectiveness trial conducted in three regions of the Kyrgyz Republic**, 24 clusters of children aged 6 to 36 months were randomly assigned to two groups. The intervention group (12 clusters, n = 1,103) received 60 sachets of micronutrient powder (12.5 mg elemental iron), which were taken as one sachet daily for 2 months. The control group (12 clusters, n = 1,090) did not receive micronutrient powder until after the study period.** Blood hemoglobin concentration was assessed at the start and end of the intervention. RESULTS: From baseline to follow-up, **the mean hemoglobin concentration in the intervention group increased by 7 g/L, whereas it decreased by 2 g/L in the control group (p < .001).** The prevalence of anemia (hemoglobin < 110 g/L) in the intervention group decreased from 72% at baseline to 52% at follow-up, whereas it increased from 72% to 75% in the control group (p < .001). Compliance with the intervention was high, with children consuming on average 45 of the 60 sachets given. CONCLUSIONS: **A course of 60 Sprinkles micronutrient powder sachets taken daily for 2 months is effective in improving hemoglobin levels and reducing the prevalence of anemia among young children in the Kyrgyz Republic.**

Anaesthesia and intensive care

Br J Anaesth. 2011 Jan;106(1):96-100. Epub 2010 Oct 14.

Randomized controlled trial comparing morphine or clonidine with bupivacaine for caudal analgesia in children undergoing upper abdominal surgery.

Singh R, Kumar N, Singh P.

Source

Lady Hardinge Medical College and Associated Kalawati Saran Children's Hospital, New Delhi, India.

Abstract

BACKGROUND: Various additives have been used to increase the duration of analgesia provided by bupivacaine administered by single-shot caudal injection in children. METHODS: A prospective, randomized, double-blind controlled study in 50 ASA I-II children (34 boys and 16 girls) aged 1-6 yr undergoing upper abdominal surgery was conducted. Patients were divided into two groups to receive either morphine 30 μg kg $^{-1}$ (MB) or clonidine 2 μg kg $^{-1}$ (CB) in bupivacaine 0.2% (1.25 ml kg $^{-1}$) for caudal analgesia. The duration of analgesia (FLACC scale) and sedation and side-effects such as vomiting, itching, respiratory depression, hypotension, and bradycardia were observed. RESULTS: The mean duration of analgesia was 16.5 (3.6) h in the CB group compared with 10.2 (2.3) h (P<0.01) in the MB group. Subjects who received clonidine (CB) were sedated for longer [7.1 (0.8) h] compared with the MB group [3.8 (0.7) h; P<0.01]. Vomiting was observed in 4% and 12% of subjects in the CB and MB groups, respectively. Sixteen per cent of subjects reported itching in the MB group (P=0.03), and none in the CB group. No hypotension, bradycardia, or respiratory depression was observed in any subjects. CONCLUSIONS: **Caudal clonidine 2 μg kg $^{-1}$ in bupivacaine 0.2% provides a longer duration of analgesia and sedation compared with caudal morphine 30 μg kg $^{-1}$ in bupivacaine 0.2% without significant side-effects in children undergoing upper abdominal surgery**.

Paediatr Anaesth. 2010 Dec;20(12):1111-7. doi: 10.1111/j.1460-9592.2010.03450.x.

Pressure vs. volume control ventilation: effects on gastric insufflation with size-1 LMA.

Sinha A, Sharma B, Sood J.

Source

Department of Anaesthesia, Pain and Perioperative Medicine, Sir Ganga Ram Hospital, New Delhi, India. apsin@hotmail.com

Abstract

BACKGROUND: In this randomized prospective study, peak airway pressure (PAP) and gastric insufflation were compared between volume control ventilation (VCV) and pressure control ventilation (PCV) using size-1 laryngeal mask airway (LMA) in babies weighing 2.5-5 kg. METHODS: Forty ASA I and II children, weighing 2.5-5 kg, undergoing elective infraumbilical surgeries (duration < 60 min) were randomized to two groups of 20 each to receive either PCV or VCV. Patients at risk of aspiration, difficult airway and upper respiratory tract infection, and poor lung compliance were excluded. Anesthesia technique included sevoflurane/O(2)/N(2)O without neuromuscular blockade. PAP in PCV and tidal volume in VCV modes were changed to achieve adequate ventilation (P(E)CO(2) of 5-5.4 kPa). PAP was maintained below 20 cm H(2)O. Chi-squared test, Mann-Whitney U-test and Wilcoxon W-test were applied; $P < 0.05$ was considered significant. RESULTS: Mean PAP (cm H(2)O) was 12.2 ± 1.09 in PCV and 13.60 ± 0.94 in VCV groups ($P = 0.000$). The confidence interval of mean difference of PAP varied from 0.79 to 2.10. Significant increases in abdominal circumference were observed in both groups: PCV: 0.94 ± 1.04 cm and VCV: 2.2 ± 1.3 cm; ($P = 0.000$). The SpO(2) and hemodynamic variables did not differ between the groups. One patient in VCV group (with PAP = 14 cm H(2)O) could not be ventilated to the target P(E)CO(2), and the LMA had to be replaced with tracheal tube. CONCLUSION: In conclusion, **PCV should be the preferred mode to provide positive pressure ventilation (PPV), when using the size-1 cLMA in babies weighing 2.5-5 kg, in view of less gastric insufflation associated with it for surgeries of brief duration.** More studies are required to validate the clinical significance of these two modes of ventilation in longer procedures, in this subpopulation.

Paediatr Anaesth. 2010 Dec;20(12):1092-7. doi: 10.1111/j.1460-9592.2010.03439.x.

Comparison of Bullard laryngoscope and short-handled Macintosh laryngoscope for orotracheal intubation in pediatric patients with simulated restriction of cervical spine movements.

Nileshwar A, Garg V.

Source

Department of Anaesthesiology, Kasturba Medical College, Manipal University, Manipal, Karnataka, India.

Abstract

AIM: To compare time to intubation, time to optimal laryngoscopy, best laryngeal view, and success rate of intubation with pediatric Bullard laryngoscope and short-handled Macintosh laryngoscope in children being intubated with neck stabilization. BACKGROUND: Securing airway of a patient with restricted cervical spine movement has been a challenge faced by anaesthesiologists around the world. Macintosh laryngoscope with manual inline stabilization is most commonly used. Bullard laryngoscope is also useful in this situation as minimal neck movement occurs with its use. METHODS: Forty patients, ASA I or II, aged 2-10 years, were

enrolled in this prospective, controlled, and randomized study. Patients were randomly allocated to one of two groups: Group MB (first laryngoscopy using short-handled Macintosh laryngoscope followed by pediatric Bullard laryngoscope) and Group BM (first laryngoscopy using pediatric Bullard laryngoscope followed by short-handled Macintosh laryngoscope) with manual inline stabilization after induction of anesthesia and paralysis. Trachea was intubated orally using the second equipment. RESULTS: Laryngeal view when obtained was always Grade 1 with Bullard laryngoscope (38/38) when compared to Macintosh laryngoscope [Grade 1 (10/40)]. The mean time to laryngoscopy (and intubation) was shorter with Macintosh laryngoscope [15.53 s (38.15 s)] than Bullard laryngoscope [35.21 s (75.71 s)], respectively. Success rate of intubation was higher with Macintosh laryngoscope (100%) when compared to Bullard laryngoscope (70%). CONCLUSIONS: **Laryngoscopy and intubation is faster using a short-handled Macintosh laryngoscope with a higher success rate compared to pediatric Bullard laryngoscope in pediatric patients when manual inline stabilization is applied.**

Comment

Similar results were shown in earlier trials: (Anesthesiology, December 1997 - Volume 87; 1335–1342)

Paediatr Anaesth. 2010 Dec;20(12):1105-10.

Entropy monitoring decreases isoflurane concentration and recovery time in pediatric day care surgery--a randomized controlled trial.

Talawar P, Chhabra A, Trikha A, Arora MK, Chandralekha.

Source

Department of Anaesthesiology & Intensive Care, All India Institute of Medical Sciences, Ansari Nagar, New Delhi, India.

Abstract

AIM: To assess if titrating anesthesia with entropy would result in faster awakening in children undergoing day care surgery. BACKGROUND: Entropy, an EEG-based anesthesia depth monitor, has been used in children; however, only one other study has evaluated the effectiveness of entropy monitoring in decreasing awakening time and for titrating anesthetic agents in children undergoing short procedures under anesthesia. METHODS: In a randomized prospective single-blind parallel group trial, 50 ASA grade I-II children, aged 2-12 years, scheduled for lower abdominal or urological surgeries were studied after ethics committee approval and parental consent. The children were randomized to the entropy or control group. Following laryngeal mask airway insertion and caudal analgesia, anesthesia was maintained with nitrous oxide, oxygen, isoflurane. In the control group, anesthesia was titrated according to the hemodynamic parameters and the simultaneously monitored entropy values obscured from the anesthesiologist. In the entropy group, the entropy values (between 45 and 65) were used to titrate the anesthesia. RESULTS: Time to awakening from anesthesia was 7 (3-18) min in the entropy group when compared to 10 (5-21) min in the control group. ($P < 0.05$) The difference in the mean time to awakening was 2.72 min 95% CI (0.34, 5.1). The end tidal isoflurane concentrations were lower in the entropy group when compared to the control group 15 s following airway insertion (0.78 ± 0.14 vs 1.24 ± 0.19), 15 s post caudal and skin incision (0.68 ± 0.40 vs 0.84 ± 0.05, 0.68 ± 0.03 vs 0.77 ± 0.32, respectively) as well as 5 min after skin incision 0.67 ± 0.04 vs 0.79 ± 0.02), ($P \leq 0.05$). CONCLUSION: In pediatric day care surgery, entropy monitoring resulted in statistically though not clinically significant faster awakening and significantly lower end – tidal isoflurane concentrations.

Pediatr Crit Care Med. 2011 Jan 28. [Epub ahead of print]

Randomized controlled trial of interrupted versus continuous sedative infusions in ventilated children.

Gupta K, Gupta VK, Jayashree M, Singhi S.

Source

From the Department of Pediatrics, Postgraduate Institute of Medical Education and Research, Chandigarh, India.

Abstract

OBJECTIVE: To compare daily interruption vs. continuous sedative infusions in mechanically ventilated children with respect to lengths of mechanical ventilation and intensive care unit stay. DESIGN: Prospective randomized controlled trial. SETTING: Pediatric intensive care unit of a tertiary care teaching and referral hospital. PATIENTS: One hundred two patients mechanically ventilated for >48 hrs. INTERVENTIONS: **Patients were randomized to receive either continuous (group 1) or interrupted (group 2) sedative infusion (midazolam bolus of 0.1 mg/kg, followed by infusion, to achieve a Ramsay score of 3-4). Each patient in group 2 had daily interruption of infusion at 8:00 am till he/she became fully awake (response to verbal commands) or so agitated/uncomfortable that he/she needed restarting of infusion (whichever was earlier) at a dose 50% less than the previous dose.** Primary outcome variables were the lengths of mechanical ventilation and intensive care unit stay, while the number and percentage of days awake on sedative infusions, frequency of adverse events, and total dose of sedatives required were the secondary outcome variables.MEASUREMENTS AND MAIN RESULTS: Of the 102 patients included in the study, 56 were randomized into the continuous sedation protocol and 46 into the interrupted sedation protocol. Both were statistically similar with respect to demography, primary diagnosis, severity of illness score (Pediatric Risk of Mortality I and III), indication for mechanical ventilation, and initial ventilatory variables except that the patients under the interrupted arm had lower peak inspiratory pressure and positive end-expiratory pressure requirements at the start of ventilation ($p = .002$ and $p = .028$, respectively). **The mean (sd) length of mechanical ventilation in the interrupted sedation protocol was significantly less than that in the continuous sedation protocol (7.0 ± 4.8 days vs. 10.3 ± 8.4 days; p = .021). Similarly, the difference in the median duration of pediatric intensive care unit stay was significantly less in the interrupted sedation as compared to the continuous sedation protocol (10.7 days vs. 14.0 days; p = .048).** The mean total dose of midazolam and the total calculated cost of midazolam in the former were significantly less compared to those of the latter (7.1 ± 4.7 mL vs. 10.9 ± 6.9 mL, $p = .002$; 4827 ± 5445 rupees vs. 13,865 ± 25,338 rupees, $p = .020$). The frequencies of adverse events in both the groups were however similar. CONCLUSION: **The length of mechanical ventilation, duration of intensive care unit stay, total dose of midazolam, and average calculated cost of the therapy were significantly reduced in the interrupted as compared to the continuous group of sedation.**

J Clin Pediatr Dent. 2010 Fall;35(1):105-10.

Midazolam-fentanyl analgo-sedation in pediatric dental patients--a pilot study.

Pandey RK, Padmanabhan MY, Saksena AK, Chandra G.

Source

Department of Pedodontics and Preventive Dentistry, Faculty of Dental Sciences, C.S.M. Medical University, Lucknow, Uttar Pradesh, India.

Abstract

OBJECTIVE: The objective of this study was to comparatively evaluate the effectiveness of submucosal fentanyl when administered in conjunction with oral midazolam during pediatric procedural sedations. STUDY DESIGN: Twenty three uncooperative ASA type I children who met the selection criteria were randomly assigned to receive either **submucosal fentanyl (3 microg/kg) or placebo, along with oral midazolam (0.5 mg/kg).** A triple blind, 2-stage cross-over design was adopted so that each child received both the regimens. RESULTS: Transient oxygen desaturation was observed in 4 children who were sedated with the combination of oral midazolam and submucosalfentanyl. **The overall success was 73.91% with oral midazolam and submucosal fentanyl regimen and 47.83% for oral midazolam and submucosal placebo regimen**. The chances of 'satisfactorily'completing a 45 minute dental procedure in an uncooperative pediatric patient was 2.8 times more, when submucosalfentanyl was used along with oral midazolam. CONCLUSION: **Submucosal fentanyl appears to improve the short working time associated with oral midazolam. But the oxygen desaturation associated with this regimen necessitates further studies to evaluate the efficacy of this combination at relatively lower doses before being used routinely for pediatric procedural sedation and analgesia.**

Community health services

Lancet. 2011 Apr 23;377(9775):1421-8.

Effect on maternal and child health services in Rwanda of payment to primary health-care providers for performance: an impact evaluation.

Basinga P, Gertler PJ, Binagwaho A, Soucat AL, Sturdy J, Vermeersch CM.

Source

National University of Rwanda School of Public Health, Kigali, Rwanda.

Abstract

BACKGROUND: Evidence about the best methods with which to accelerate progress towards achieving the Millennium Development Goals is urgently needed. We assessed the effect of **performance-based payment of health-care providers** (payment for performance; P4P) on **use and quality of child and maternal care services in health-care facilities in Rwanda**. METHODS: 166 facilities were randomly assigned at the district level either to begin P4P funding between June, 2006, and October, 2006 (intervention group; n=80), or to continue with the traditional input-based funding until 23 months after study baseline (control group; n=86). Randomisation was done by coin toss. We surveyed facilities and 2158 households at baseline and after 23 months. **The main outcome measures were prenatal care visits and institutional deliveries, quality of prenatal care, and child preventive care visits and immunisation.** We isolated the incentive effect from the resource effect by increasing comparison facilities' input-based budgets by the average P4P payments made to the treatment facilities. We estimated a multivariate regression specification of the difference-in-difference model in which an individual's outcome is regressed against a dummy variable, indicating whether the facility received P4P that year, a facility-fixed effect, a year indicator, and a series of individual and household characteristics. FINDINGS: Our model estimated that **facilities in the intervention group had a 23% increase in the number of institutional deliveries and increases in the number of preventive care visits by children aged 23 months or younger (56%) and aged between 24 months and 59 months (132%).** No improvements were seen in the number of women completing four prenatal care visits or of children receiving full immunisation schedules. We also estimate an increase of 0·157 standard deviations (95% CI 0·026-0·289) in

prenatal quality as measured by compliance with Rwandan prenatal care clinical practice guidelines. INTERPRETATION: **The P4P scheme in Rwanda had the greatest effect on those services that had the highest payment rates and needed the least effort from the service provider. P4P financial performance incentives can improve both the use and quality of maternal and child health services, and could be a useful intervention to accelerate progress towards Millennium Development Goals for maternal and child health.**

Trials. 2010 Sep 17;11:88.

A cluster randomised controlled trial of the community effectiveness of two interventions in rural Malawi to improve health care and to reduce maternal, newborn and infant mortality.

Lewycka S, Mwansambo C, Kazembe P, Phiri T, Mganga A, Rosato M, Chapota H, Malamba F, Vergnano S, Newell ML, Osrin D, Costello A.

Source

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Abstract

BACKGROUND: The UN Millennium Development Goals call for substantial reductions in maternal and child mortality, to be achieved through reductions in morbidity and mortality during pregnancy, delivery, postpartum and early childhood. The MaiMwana Project aims to test community-based interventions that tackle maternal and child health problems through increasing awareness and local action. METHODS/DESIGN: This study uses a two-by-two factorial cluster-randomised controlled trial design to test the impact of two interventions. The impact of a **community mobilisation intervention run through women's groups, on home care, health care-seeking behaviours and maternal and infant mortality**, will be tested. The impact of a **volunteer-led infant feeding and care support intervention, on rates of exclusive breastfeeding, uptake of HIV-prevention services and infant mortality**, will also be tested. The women's group intervention will employ local female facilitators to guide women's groups through a four-phase cycle of problem identification and prioritisation, strategy identification, implementation and evaluation. Meetings will be held monthly at village level. The infant feeding intervention will select local volunteers to provide advice and support for breastfeeding, birth preparedness, newborn care and immunisation. They will visit pregnant and new mothers in their homes five times during and after pregnancy.The unit of intervention allocation will be clusters of rural villages of 2500-4000 population. 48 clusters have been defined and randomly allocated to either women's groups only, infant feeding support only, both interventions, or no intervention. Study villages are surrounded by 'buffer areas' of non-study villages to reduce contamination between intervention and control areas. Outcome indicators will be measured through a demographic surveillance system. Primary outcomes will be maternal, infant, neonatal and perinatal mortality for the women's group intervention, and exclusive breastfeeding rates and infant mortality for the infant feeding intervention.Structured interviews will be conducted with mothers one-month and six-months after birth to collect detailed quantitative data on care practices and health-care-seeking. Further qualitative, quantitative and economic data will be collected for process and economic evaluations.

Development and mental health

(See also maternal mental health)

Neuropsychology. 2010 Sep;24(5):667-73.

A pilot study of the neuropsychological benefits of computerized cognitive rehabilitation in Ugandan children with HIV.

Boivin MJ, Busman RA, Parikh SM, Bangirana P, Page CF, Opoka RO, Giordani B.
SourceInternational Neurologic and Psychiatric Epidemiology Program, Michigan State University, East Lansing, MI 48824–1315, USA. boivin@msu.edu

Abstract:
OBJECTIVE: Because antiretroviral treatment (ART) fails to improve neurocognitive impairment in children with HIV, we completed a pilot study evaluating the feasibility and cognitive **benefit of computerized cognitive rehabilitation therapy (CCRT) in Ugandan children with HIV.** METHOD: Sixty Ugandan children with HIV (23 on ART) were randomly assigned to 10 sessions of Captain's Log CCRT (Sandford, 2007) training configured for attention and memory skills or no intervention. Kaufman Assessment Battery for Children (2nd ed., KABC-2; Kaufman & Kaufman, 2004) performance at baseline indicated pervasive neurocognitive impairment. Cognitive ability was assessed before and after training using the Cogstate computerized neuropsychological test (Darby, Maruff, Collie, & McStephen, 2002). Viral load along with CD4 and CD8 absolute and activation levels also were measured post-test. RESULTS: CCRT was well received with a 95% adherence rate to scheduled training sessions. CCRT intervention children showed greater improvement on a Cogstate card detection task of simple attention ($p = .02$), and speed of correct moves on a Groton Maze Learning Task ($p < .001$). These analyses were completed using an analysis of covariance model that adjusted Cogstate performance for the child's age, standardized weight for age, gender, socioeconomic status, school grade level, and baseline KABC-2 performance. ART treatment was not related to Cogstate performance or improvement as a result of CCRT. CD4 and CD8 activation levels were correlated with Cogstate improvement specifically for the CCRT group. CONCLUSIONS: CCRT was feasible with our study population and improved maze learning and attention on a detection task. This supports previous findings by our group with cerebral malaria survivors (Bangirana, Giordani, et al., 2009).

J Consult Clin Psychol. 2010 Dec;78(6):818-28.

Mediators and moderators of a psychosocial intervention for children affected by political violence.

Tol WA, Komproe IH, Jordans MJ, Gross AL, Susanty D, Macy RD, de Jong JT.
Source
HealthNet TPO, Amsterdam, the Netherlands and Global Health Initiative, Yale University, USA. wietse.tol@yale.edu

Abstract
OBJECTIVE: The authors examined moderators and mediators of a **school-based psychosocial intervention for children affected by political violence**, according to an ecological resilience theoretical framework. METHOD: The authors examined data from a cluster randomized trial,

involving children aged 8-13 in Central Sulawesi, Indonesia (treatment condition n = 182, waitlist control condition n = 221). Mediators (hope, coping, peer/emotional/play social support) and moderators (gender, age, family connectedness, household size, other forms of social support, exposure to political violence, and displacement) of treatment outcome on posttraumatic stress symptoms and function impairment were examined in parallel process latent growth curve models. RESULTS: Compared with the waitlist group, those receiving treatment showed maintained hope, increased positive coping, maintained peer social support, and increased play social support. Of these putative mediators, only play social support was found to mediate treatment effects, such that increases in play social support were associated with smaller reductions in posttraumatic stress disorder (PTSD) symptoms. Furthermore, the authors identified a number of moderators: Girls showed larger treatment benefits on PTSD symptoms; girls, children in smaller households, and children receiving social support from adults outside the household showed larger treatment benefits on function impairment. CONCLUSIONS: Findings provide limited evidence for an ecological resilience theoretical framework. On the basis of these findings, the authors recommend a stronger separation between universal prevention (e.g., resilience promotion through play) and selective/indicated prevention (e.g., interventions aimed at decreasing posttraumatic stress symptoms). Play-based interventions should be careful to exclude children with psychological distress. In addition, treatment effects may be augmented by selecting girls and socially vulnerable children.

Clin Rehabil. 2011 May;25(5):425-32. Epub 2010 Nov 8.

Effect of strength and balance training in children with Down's syndrome: a randomized controlled trial.

Gupta S, Rao BK, S D K.

Source

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Abstract

OBJECTIVE: The aim of the study was to determine the effect of exercise training on strength and balance in children with Down's syndrome. DESIGN: Randomized controlled trial. SETTING: Rehabilitation school for special children. SUBJECTS AND INTERVENTION: Twenty-three children were randomized to intervention and control group. The intervention group (n = 12) underwent progressive resistive exercises for lower limbs and balance training for six weeks. The control group continued their regular activities followed at school. OUTCOME MEASURE: A handheld dynamometer was used to measure the lower limb muscle strength. Balance was assessed by the balance subscale of Bruininks Oseretsky Test of Motor Proficiency (BOTMP). RESULTS: Following the training, the children in the intervention group showed a statistically significant improvement (P < 0.05) in the lower limb strength of all the muscle groups assessed. The strength of knee extensors was 12.12 lbs in the control group versus 18.4 lbs in the experimental group; in hip flexors it was 12.34 lbs in the control group versus 16.66 lbs in the experimental group post-intervention. The balance of the children also improved significantly with an improvement in scores of the balance subscale of BOTMP (19.50 in the experimental group versus 9.00 in the control group, P = 0.001). CONCLUSION: This study suggests that a specific exercise training programme may improve the strength and balance in children with Down's syndrome.

Diabetes

Diabetes Technol Ther. 2011 Mar;13(3):327-34. Epub 2011 Feb 3.

Comparable efficacy and safety of insulin glulisine and insulin lispro when given as part of a Basal-bolus insulin regimen in a 26-week trial in pediatric patients with type 1 diabetes.

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Abstract

BACKGROUND: We compared the efficacy and safety of insulin glulisine with insulin lispro as part of a basal-bolus regimen in children and adolescents with type 1 diabetes. METHODS: Overall, 572 children and adolescents (4-17 years old) using insulin glargine or neutral protamine Hagedorn insulin as basal insulin were enrolled in a 26-week, multicenter, open, centrally randomized, parallel-group, noninferiority study. Subjects were randomized to receive glulisine (n = 277) or lispro (n= 295) 0-15 min premeal. RESULTS: **Baseline-to-endpoint hemoglobin A1c changes were similar between the two insulins: adjusted mean change (glulisine vs. lispro), 0.10% versus 0.16%; between-treatment difference (glulisine-lispro), &minsu;0.06, 95% confidence interval (-0.24; 0.12)**; and prespecified noninferiority margin, 0.4%. Overall, for all age groups together, the percentage of patients achieving American Diabetes Association age-specific A1c targets at endpoint was significantly higher (P = 0.039) with glulisine (38.4%) versus lispro (32.0%). From Month 4 to endpoint, both "all" and "severe" symptomatic hypoglycemia rates were similar (3.10 vs. 2.91 and 0.06 vs. 0.07 events/patient-month, respectively). Frequency and type of adverse events, serious adverse events, or hypoglycemia reported as serious adverse events were similar between both groups. CONCLUSIONS: Glulisine was as effective as lispro in baseline-to-endpoint A1c change, and both treatments were similarly well tolerated.

Mary Ann Liebert,

Diarrhoea

Trop Med Int Health. 2010 Oct;15(10):1132-9. doi: 10.1111/j.1365-3156.2010.02608.x.

Green banana-supplemented diet in the home management of acute and prolonged diarrhoea in children: a community-based trial in rural Bangladesh.

Rabbani GH, Larson CP, Islam R, Saha UR, Kabir A.

Source

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Abstract

SUMMARY OBJECTIVE: To determine the effectiveness of green banana in the home management of acute (<7 days) or prolonged (≥ 7 days) diarrhoea at the community level. METHODS: A cluster randomized field trial was conducted among 2968 Bangladeshi rural children 6-36 months old. **Wards (villages) were randomly assigned to either a standard care group or a standard care plus green banana group where mothers were instructed to add cooked green banana to the diets of diarrhoeal children.** Through a village-based

surveillance system, diarrhoeal morbidity data (severity, duration, compliance) were collected for 14 days. Treatment effects were determined by analysing cumulative probability of cure by testing Cox proportional hazards models and relative risk (RR). RESULTS: **The cumulative probability of cure was significantly (P < 0.001) different in children receiving GB for both acute [hazard ratio (HR) = 0.63 (95% CI: 0.56-0.67)] and prolonged diarrhoea [HR = 0.38 (95% CI: 0.26-0.59)]. The recovery rates of children with acute diarrhoea receiving GB (vs. control) were significantly more by day 3: 79.9%vs. 53.3% [(RR) = 0.47, 95% CI: 0.41-0.55], (P < 0.001) and day 7: 96.6%vs. 89.1% (RR = 0.32; 0.22-0.46), (P < 0.001). Children with prolonged diarrhoea receiving green banana had significantly higher recovery rates by day 10: 79.8%vs. 51.9% (RR = 0.42; 0.23-0.73), (P < 0.001) and day 14: 93.6%vs. 67.2% (RR = 0.22; 0.08-0.54), (P < 0.001).** CONCLUSION: A green banana-supplemented diet hastened recovery of acute and prolonged childhood diarrhoea managed at home in rural Bangladesh.

Zinc in diarrhoea

Bull World Health Organ. 2010 Oct 1;88(10):754-60. Epub 2010 May 28.

Effectiveness of zinc supplementation plus oral rehydration salts for diarrhoea in infants aged less than 6 months in Haryana state, India.

Mazumder S, Taneja S, Bhandari N, Dube B, Agarwal RC, Mahalanabis D, Fontaine O, Black RE.

Source

Society for Applied Studies, New Delhi, 110016, India.

Abstract

OBJECTIVE: To determine if educating caregivers in providing zinc supplements to infants < 6 months old with acute diarrhoea is effective in treating diarrhoea and preventing acute lower respiratory infections (ALRIs), and whether it leads to a decrease in the use of oral rehydration salts (ORS). METHODS: In this retrospective subgroup analysis of infants aged < 6 months, six clusters were randomly assigned to intervention or control sites. **Care providers were trained to give zinc and ORS to children with acute diarrhoea at intervention sites, and only ORS at control sites.** Surveys were conducted at 3 and 6 months to assess outcomes. Differences between intervention and control sites in episodes of diarrhoea and ALRI in the preceding 24 hours or 14 days and of hospitalizations in the preceding 3 months were analysed by logistic regression. FINDINGS: **Compared with control sites, intervention sites had lower rates of acute diarrhoea in the preceding 14 days at 3 months (odds ratio, OR: 0.60; 95% confidence interval, CI: 0.43-0.84) and 6 months (OR: 0.72; 95% CI: 0.54-0.94); lower rates of acute diarrhoea in the preceding 24 hours at 3 months (0.66; 95% CI: 0.50-0.87) and of ALRI in the preceding 24 hours at 6 months (OR: 0.59; 95% CI: 0.37-0.93); and lower rates of hospitalization at 6 months for all causes (OR: 0.40; 95% CI: 0.34-0.49), diarrhoea (OR: 0.34; 0.18-0.63) and pasli chalna or pneumonia (OR: 0.36; 95% CI: 0.24-0.55).** CONCLUSION: Educating caregivers in zinc supplementation and providing zinc to infants < 6 months old can reduce diarrhoea and ALRI. More studies are needed to confirm these findings as these data are from a subgroup analysis.

J Nutr. 2011 Feb;141(2):312-5. Epub 2010 Dec 8.

Zinc treatment for 5 or 10 days is equally efficacious in preventing diarrhea in the subsequent 3 months among Bangladeshi children.

Alam DS, Yunus M, El Arifeen S, Chowdury HR, Larson CP, Sack DA, Baqui AH, Black RE.

Source

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Abstract

We conducted a randomized, double-blind placebo controlled, community trial in rural Bangladesh in children 4-59 mo of age to compare the efficacy of a 5- and 10-d course of zinc therapy on the incidence and duration of diarrhea over the subsequent 90-d follow-up after initial treatment for an acute childhood diarrheal (ACD) episode. Children (n = 1622) with ACD were randomly allocated to either 5 or 10 d of zinc treatment. Female field workers visited each child daily, supervised the administration of zinc, recorded the duration of current episode, and the occurrence and duration of diarrhea over the subsequent 3 mo. **The incidence of diarrhea over the 90 d of follow-up did not differ between the 5-d (1.08 ± 1.38 episodes) and 10-d (1.02 ± 1.35 episodes) groups (P = 0.35).** Children in both groups experienced a comparable duration of diarrheal episodes (3.1 ± 5.6 d vs. 2.9 ± 5.6 d, 5-d vs. 10-d, respectively; P = 0.64) with a mean difference between groups within the defined range of equivalence. Time to onset of the first episode and the proportion children experiencing diarrhea during the 90-d follow-up also did not differ between groups. These findings suggest that among Bangladeshi children, a 5-d zinc treatment for ACD is as efficacious as 10 d in preventing diarrhea in the subsequent 3 mo.

J Pediatr. 2011 May 16. [Epub ahead of print]

Zinc, Vitamin A, and Micronutrient Supplementation in Children with Diarrhea: A Randomized Controlled Clinical Trial of Combination Therapy versus Monotherapy.

Dutta P, Mitra U, Dutta S, Naik TN, Rajendran K, Chatterjee MK.

Source

National Institute of Cholera and Enteric Diseases, Kolkata, India.

Abstract

OBJECTIVE: To compare the clinical efficacy of supplementation of zinc, zinc plus vitamin A, and zinc plus combination of micronutrients and vitamins (iron, copper, selenium, vitamin B(12), folate, and vitamin A) on acute diarrhea in children. STUDY DESIGN: This was a double-blind, randomized, placebo-controlled trial. **Children aged 6 to 24 months with diarrhea and moderate dehydration were randomized to receive zinc plus placebo vitamin A (group 1), zinc plus other micronutrients plus vitamin A (group 2), zinc plus vitamin A (group 3), or placebo (group 4) as an adjunct to oral rehydration solution.** Duration, volume of diarrhea, and consumption of oral rehydration solution were compared as outcome variables within the supplemented groups and with the placebo group. RESULTS: The 167 study subjects included 41 in group 1, 39 in group 2, 44 in group 3, and 43 in group 4. All 3 supplemented groups demonstrated a significant reduction in outcome variables (P < .0001) compared with the placebo group. Group 3 had the lowest reduction of outcome variables and group 2 had a speedy recovery, but differences among the supplemented groups were not statistically significant. CONCLUSIONS: **Supplementation with a combination of**

micronutrients and vitamins was not superior to zinc alone, confirming the clinical benefit of zinc in children with diarrhea.

J Coll Physicians Surg Pak. 2010 Dec;20(12):837-8.

Effect of zinc in tablet and suspension formulations in the treatment of acute diarrhoea among young children in an emergency setting of earthquake affected region of Pakistan.

Habib MA, Soofi SB, Bhutta ZA.

Source

Department of Paediatrics, The Aga Khan University Hosptial, Karachi.

Abstract

A longitudinal cohort study was conducted at Camp Hospital Batagram in August 2006 to ascertain the effect of Zinc utilization in tablet and suspension formulations on the frequency and recovery rates of diarrhoea among young children in the emergency settings of earthquake affected region of Pakistan. Two hundred patients were recruited and followed up, the patients were allocated either of the 2 groups i.e. A (zinc in tablets form) and B (zinc in suspension form). Both groups also received WHO recommended treatment for diarrhoea. Most of the cases recovered from the illness within 3 days after presentation. Significant p-values were established among Zinc use and reduction in frequency of stools on Day 2 and 3, with better outcome in group B. The study supports the notion that zinc reduces the frequency and improves recovery rates of diarrhoea in any form and has better compliance and outcomes with the use in suspension form.

Probiotics

Epidemiol Infect. 2011 Jun;139(6):919-26. Epub 2010 Jul 30.

Role of probiotic in preventing acute diarrhoea in children: a community-based, randomized, double-blind placebo-controlled field trial in an urban slum.

Sur D, Manna B, Niyogi SK, Ramamurthy T, Palit A, Nomoto K, Takahashi T, Shima T, Tsuji H, Kurakawa T, Takeda Y, Nair GB, Bhattacharya SK.

Source

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Abstract

Acute diarrhoea remains a major public health challenge in developing countries. We examined the role of a probiotic in the prevention of acute diarrhoea to discover if there was an effect directed towards a specific aetiology. A double-blind, randomized, controlled field trial involving 3758 children aged 1-5 years was conducted in an urban slum community in Kolkata, India. **Participants were given either a probiotic drink containing Lactobacillus casei strain Shirota or a nutrient drink daily for 12 weeks.** They were followed up for another 12 weeks. The primary outcome of this study was the occurrence of first episodes of diarrhoea. We assessed this during 12 weeks of intake of study agent and also for 12 weeks of follow-up. **There were 608 subjects with diarrhoea in the probiotic group and 674 subjects in the nutrient group during the study period of 24 weeks. The level of protective efficacy for the probiotic was 14% (95% confidence interval 4-23, P<0·01 in adjusted model).** The reduced

occurrence of acute diarrhoea in the probiotic group compared to nutrient group was not associated with any specific aetiology. No adverse event was observed in children of either probiotic or nutrient groups. The study suggests that daily intake of a probiotic drink can play a role in prevention of acute diarrhoea in young children in a community setting of a developing country.

Trop Med Int Health. 2011 May;16(5):555-61. doi: 10.1111/j.1365-3156.2011.02745.x. Epub 2011 Feb 20.

Randomised controlled clinical trial of Lactobacillus sporogenes (Bacillus coagulans), used as probiotic in clinical practice, on acute watery diarrhoea in children.

Dutta P, Mitra U, Dutta S, Rajendran K, Saha TK, Chatterjee MK.

Source

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Abstract

OBJECTIVE: To assess the clinical efficacy of Lactobacillus sporogenes (Bacillus coagulans), as probiotic preparation, against dehydrating diarrhoea in children. METHODS: Double-blind, randomised, placebo-controlled, hospital-based clinical trial with children aged 6-24 months who had diarrhoea with some dehydration. **Children received tablets of L. sporogenes (B. coagulans) or placebo (control group) and oral rehydration salt solution for correction of initial dehydration as well as maintenance therapy.** Duration, frequency, volume of diarrhoea and intake of ORS of two groups were compared as outcome variables. RESULTS: One hundred and forty-eight children participated, of whom **78 (Study group) received L. sporogenes (B. coagulans) and 70 received placebo (Control group)**. Differences in recovery rate (P=0.2), duration (P=0.5), frequency (P=0.05), volume (P=0.1) of diarrhoea, intake of ORS (P=0.2) and other fluids (P=0.1) were not significant between both groups. Neither did a subgroup analysis of children who had rotavirus as sole enteropathogens show any significant differences in duration (P=0.5), frequency (P=0.6), volume (P=0.8) of diarrhoea, intake of ORS (P=0.8) and other fluids (P=0.8) among both groups. CONCLUSION: **L. sporogenes (B. coagulans), as an adjunct to ORS, had no therapeutic impact on management of acute dehydrating diarrhoea of diverse etiology including rotavirus associated diarrhoea in children**.

Probiotics in the treatment of acute rotavirus diarrhoea. A randomized, double-blind, controlled trial using two different probiotic preparations in Bolivian children.

Grandy G, Medina M, Soria R, Terán CG, Araya M.

Source

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Abstract

BACKGROUND: Evidence suggests that probiotics reduce rotavirus diarrhoea duration. Although there are several probiotic strains potentially useful, daily practice is often limited by

the type and number of products locally available. In general, information about combined products is scarce. In this study we compare the effect of two probiotic products in the treatment of diarrhoea in children less than 2 years of age. METHODS: A Randomized double-blind controlled clinical trial in children hospitalized for acute rotavirus diarrhoea, in the Paediatric Centre Albina Patino, Cochabamba, Bolivia.**Participants were children aged 1 - 23 months, who were randomly assigned to receive one of three treatments: Oral rehydration therapy plus placebo; Oral rehydration solution plus Saccharomyces boulardii; or Oral rehydration solution plus a compound containing Lactobacillus acidophilus, Lactobacillus rhamnosus, Bifidobacterium longum and Saccharomyces boulardii.** Sample size was 20 per group and the outcomes were duration of diarrhoea, of fever, of vomiting and of hospitalization. RESULTS: 64 cases finished the protocol. On admission, patients' characteristics were similar. Median duration of diarrhoea (p = 0.04) in children who received the single species product (58 hours) was shorter than in controls (84.5 hrs). Comparing children that received the single probiotic product and controls showed shorter duration of fever (18 vs 67 hrs) (p = 0.0042) and the mixed probiotic of vomiting (0 vs 42.5 hrs) (p = 0.041). There was no effect on duration of hospitalization (p = 0.31). When experimental groups were merged, statistical significance of changes increased (total duration of diarrhoea, fever and vomiting P = 0.025, P = 0.025 and P = 0.014, respectively). CONCLUSIONS: **Both products decreased the duration of diarrhoea compared to oral rehydration solution alone. This decrease was significant only for the single species product which also decreased the duration of fever.** With the multiple species product there was no vomiting subsequent to the initiation of treatment. The quantity of probiotic bacteria needed for optimum treatment of gastroenteritis remains to be determined, particularly when multiple species are included in the product.Trial registration: ClinicalTrials.gov ID: NCT00981877 Link:

Cochrane Database Syst Rev. 2010 Nov 10;(11):CD003048.

Probiotics for treating acute infectious diarrhoea.

Allen SJ, Martinez EG, Gregorio GV, Dans LF.

Source

School of Medicine, Swansea University, Room 314, The Grove Building, Singleton Park, Swansea, West Glamorgan, UK, SA2 8PP.

Abstract

BACKGROUND: Probiotics may offer a safe intervention in acute infectious diarrhoea to reduce the duration and severity of the illness. OBJECTIVES: To assess the effects of probiotics in proven or presumed acute infectious diarrhoea. SEARCH STRATEGY: We searched the Cochrane Infectious Diseases Group's trials register (July 2010), the Cochrane Controlled Trials Register (The Cochrane Library Issue 2, 2010), MEDLINE (1966 to July 2010), EMBASE (1988 to July 2010), and reference lists from studies and reviews. We also contacted organizations and individuals working in the field, and pharmaceutical companies manufacturing probiotic agents. SELECTION CRITERIA: Randomized and quasi-randomized controlled trials comparing a specified probiotic agent with a placebo or no probiotic in people with acute diarrhoea that is proven or presumed to be caused by an infectious agent. DATA COLLECTION AND ANALYSIS: Two reviewers independently assessed the methodological quality of the trial and extracted data. Primary outcomes were the mean duration of diarrhoea, stool frequency on day 2 after intervention and ongoing diarrhoea on day 4. A random-effects model was used. MAIN RESULTS: Sixty-three studies met the inclusion criteria with a total of 8014 participants. Of these, 56 trials recruited infants and young children. The trials varied in

the definition used for acute diarrhoea and the end of the diarrhoeal illness, as well as in the risk of bias. The trials were undertaken in a wide range of different settings and also varied greatly in organisms tested, dosage, and participants' characteristics. No adverse events were attributed to the probiotic intervention.**Probiotics reduced the duration of diarrhoea, although the size of the effect varied considerably between studies.The average of the effect was significant for mean duration of diarrhoea (mean difference 24.76 hours; 95% confidence interval 15.9 to 33.6 hours; n=4555, trials=35) diarrhoea lasting ≥4 days (risk ratio 0.41; 0.32 to 0.53; n=2853, trials=29) and stool frequency on day 2 (mean difference 0.80; 0.45 to 1.14; n=2751, trials=20).**The differences in effect size between studies was not explained by study quality, probiotic strain, the number of different strains, the viability of the organisms, dosage of organisms, the causes of diarrhoea, or the severity of the diarrhoea, or whether the studies were done in developed or developing countries. AUTHORS' CONCLUSIONS: Used alongside rehydration therapy, probiotics appear to be safe and have clear beneficial effects in shortening the duration and reducing stool frequency in acute infectious diarrhoea. However, more research is needed to guide the use of particular probiotic regimens in specific patient groups.

Gut Pathog. 2010 Aug 29;2(1):10.

Are probiotics a feasible intervention for prevention of diarrhoea in the developing world?

Hajela N, Nair GB, Ganguly NK.

Source

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Abstract

ABSTRACT: With more than 1.4 million of the 9 million child deaths being attributed to diarrhoea in 2008 and 49% of them occurring in five countries namely, India, Nigeria, Democratic Republic of the Congo, Pakistan and China, there is an urgent need for intervention to prevent and control diarrhoeal diseases. Of the various interventions, probiotics offer immense potential. The past decade has witnessed the validation of their utility for the prevention, treatment and management of a variety of infective and non infective disorders. The most investigated field continues to remain infectious diarrhoea and compelling evidence comes from randomized placebo controlled trials. While results from these studies are encouraging most of them reflect the outcomes of the developed world. Developing countries like India continue to struggle with nutritional and health challenges and bear the greatest burden of diarrhoea. A paucity of data from the developing countries limits the definite recommendation of probiotics. In these countries curd, often confused for a probiotic, is practiced as an integral part of the culture. While the nutritional benefits of these products cannot be understated, it is still uncertain whether these products can be classified as a probiotic. The emergence of probiotic foods which are scientifically validated for their efficacy and impart defined health benefits offer an excellent opportunity to improve public health. A recent randomized controlled trial conducted by the National Institute of Cholera and Enteric Diseases in Kolkata, India demonstrated a protective efficacy of 14% in preventing diarrhoea among children who received a probiotic. For the developing world however the vision for probiotics would mean a fundamental change in perception and developing a well planned strategy to allow interventions like probiotics to permeate to impoverished settings, where the assault of micro organisms is on a daily basis. This would mean that probiotics are ingrained into the public health system without being seen as a medicine.

Comment

Several trials this year investigated the effects of probiotics in developing countries. The effect was mixed, with promising effects on prevention in one study from India, but questions remain about feasibility and cost. The above community-based trial from India, where probiotics were given daily for 12 weeks, showed a 14% reduction in the occurrence of diarrhoea. In a hospital-based treatment trial in India probiotics had no effect on the duration of diarrhoea, while in another trial in Bolivia probiotics with ORS reduced the duration of diarrhoea by 30, hours compared to ORS alone. This was consistent with the Cochrane review of 63 trials this year of probiotics for diarrhoea treatment showing an average reduction in diarrhoea duration by about 24 hours, although most of the included trials were in industrialised countries.

J Trop Pediatr. 2011 Apr 27. [Epub ahead of print]

Efficacy of Dioctahedral Smectite in Acute Watery Diarrhea in Indian Children: A Randomized Clinical Trial.

Mujawar QM, Naganoor R, Ali MD, Malagi N, Thobbi AN.

Source

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Abstract

Objective: To determine the effects and safety of dioctahedral smectite (DS) on the duration of acute watery diarrhea in children. Methods: A Randomized, open labeled, clinical controlled trial in a tertiary care hospital outpatient department (OPD) and emergency department. Participants were one hundred and seventeen children without any chronic illness between 2 and 5 years presenting to OPD, having acute watery diarrhea for <48 h with mild to moderate dehydration, not on antibiotics and requiring oral rehydration therapy. Intervention done was DS with a dose of 1.5 g thrice daily. Results: Freshly dissolved DS in a dose of 1.5 g thrice daily for 5 days significantly shortened the duration of acute watery diarrhea in 20 children aged 25 years. There were no adverse effects on the use of DS. DS was acceptable to the children, and its administration was not accompanied with any side effects. Conclusion: DS reduces the duration of diarrhea in Indian children and prevents a prolonged course, and therefore, may consistently reduce the costs in treatment of acute watery diarrhea.

Am J Clin Nutr. 2010 Oct;92(4):928-39. Epub 2010 Aug 18.

Effect of lysine supplementation on health and morbidity in subjects belonging to poor peri-urban households in Accra, Ghana.

Ghosh S, Smriga M, Vuvor F, Suri D, Mohammed H, Armah SM, Scrimshaw NS.

Source

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Abstract

BACKGROUND: Lysine affects diarrhea and anxiety via effects on serotonin receptors, enhanced intestinal repair, and sodium chloride-dependent opioid peptide transport. OBJECTIVE: The objective was to investigate the effects of lysine supplementation on morbidity, growth, and anxiety in children and adults of peri-urban areas of Accra, Ghana. DESIGN: In a double-blind randomized trial, the effect of lysine supplementation (1 g lysine/d)

compared with that of placebo was examined in 2 groups of men, women, and children (n = 271). Primary outcomes included diarrheal and respiratory morbidity, growth, and anxiety and complement C3, C-reactive protein, serum cortisol, transferrin, and ferritin values. Independent-sample t tests, odds ratios, generalized estimating equations, 4-parameter sinusoid regression, and generalized linear models were used. RESULTS: Thirty percent of men, 50% of women, and 15% of children were at risk of lysine inadequacy. **Supplementation in children reduced diarrheal episodes [19 lysine, 35 placebo; odds ratio (OR): 0.52; 95% CI: 0.29, 0.92; P = 0.046] and the total number of days ill (21 lysine, 47 placebo; OR: 0.44; 95% CI: 0.26, 0.74; P = 0.034).** Mean days ill per child per week (0.058 ± 0.039 lysine, 0.132 ± 0.063 placebo; P = 0.017) were negatively associated with weight gain with control for baseline weight and study group (P = 0.04). Men had fewer coryza episodes (23 lysine, 39 placebo; OR: 0.60; 95% CI: 0.36, 1.01; P = 0.05), total number of days ill (lysine: 130; placebo: 266; OR: 0.51; 95% CI: 0.28, 0.93; P = 0.03), and mean days ill per person per week (lysine: 0.21 ± 0.23; placebo: 0.41 ± 0.35; P = 0.04). Serum ferritin (P = 0.045) and C-reactive protein (P = 0.018) decreased in lysine-supplemented women but increased in placebo-supplemented women. CONCLUSION: Lysine supplementation reduced diarrheal morbidity in children and respiratory morbidity in men in Ghana.

Full Text
Am J Clin Nutr

Water purification

PLoS One. 2010 Sep 10;5(9):e12613.

Field assessment of a novel household-based water filtration device: a randomised, placebo-controlled trial in the Democratic Republic of Congo.

Boisson S, Kiyombo M, Sthreshley L, Tumba S, Makambo J, Clasen T.

Source

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Abstract

BACKGROUND: Household water treatment can improve the microbiological quality of drinking water and may prevent diarrheal diseases. However, current methods of treating water at home have certain shortcomings, and there is evidence of bias in the reported health impact of the intervention in open trial designs. METHODS AND FINDINGS: **We undertook a randomised, double-blinded, placebo-controlled trial among 240 households (1,144 persons) in rural Democratic Republic of Congo to assess the field performance, use and effectiveness of a novel filtration device in preventing diarrhea.** Households were followed up monthly for 12 months. Filters and placebos were monitored for longevity and for microbiological performance by comparing thermotolerant coliform (TTC) levels in influent and effluent water samples. Mean longitudinal prevalence of diarrhea was estimated among participants of all ages. Compliance was assessed through self-reported use and presence of water in the top vessel of the device at the time of visit. Over the 12-month follow-up period, data were collected for 11,236 person-weeks of observation (81.8% total possible). After adjusting for clustering within the household, the longitudinal prevalence ratio of diarrhoea was 0.85 (95% confidence interval: 0.61-1.20). The filters achieved a 2.98 log reduction in TTC levels while, for reasons that are unclear, the placebos achieved a 1.05 log reduction ($p<0.0001$). After 8 months, 68% of intervention households met the study's definition of current users, though most (73% of adults and 95% of children) also reported drinking untreated water the

previous day. The filter maintained a constant flow rate over time, though 12.4% of filters were damaged during the course of the study. CONCLUSIONS: **While the filter was effective in improving water quality, our results provide little evidence that it was protective against diarrhea.** The moderate reduction observed nevertheless supports the need for larger studies that measure impact against a neutral placebo.

Environ Sci Technol. 2010 Nov 15;44(22):8744-9.

Solar disinfection of drinking water in the prevention of dysentery in South African children aged under 5 years: the role of participant motivation.

Du Preez M, Mcguigan KG, Conroy RM.

Source

Natural Resources and the Environment, CSIR, Pretoria, South Africa.

Abstract

Solar disinfection (SODIS) effectively improves the microbial quality of drinking water for preventing diarrhea; however, the effect of participant motivation has not been studied. This 1-year randomized controlled trial investigated the effect of SODIS of drinking water and motivation on the incidence of dysentery and nondysentery diarrhea among children of age 6 months to 5 years living in periurban communities in South Africa.We compared 383 children in 297 households using SODIS with 335 children in 267 households with no intervention. At baseline 62.4% of the study households had stored water which met World Health Organization guidelines for zero thermotolerant coliforms per 100 mL. Dysentery was recorded using a pictorial diary. Incidence of dysentery was significantly associated with higher motivation, defined as 75% or better completion of diarrhea data. **Incidence rates were lower in those drinking solar disinfected water (incidence rate ratio 0.64, 95% CI 0.39 - 1.0, P = 0.071) but not statistically significant.** Compared with the control, participants with higher motivation achieved a significant reduction in dysentery (incidence rate ratio 0.36, 95% CI 0.16 - 0.81, P = 0.014). However, there was no significant reduction in risk at lower levels of motivation. **Solar disinfection was not significantly associated with nondysentery diarrhea risk overall (P = 0.419).** A statistically significant reduction in dysentery was achieved only in households with higher motivation, showing that motivation is a significant determinant for measurable health gains. Failure of three-quarters of participants to achieve a significant reduction in dysentery suggests that research into effective implementation is required.

J Water Health. 2010 Dec;8(4):687-702. Epub 2010 Apr 22.

Water and hygiene interventions to reduce diarrhoea in rural Afghanistan: a randomized controlled study.

Opryszko MC, Majeed SW, Hansen PM, Myers JA, Baba D, Thompson RE, Burnham G.

Source

Johns Hopkins Bloomberg School of Public Health, 615 N Wolfe Street E8132, Baltimore, MD 21205, USA.

Abstract

A randomized controlled trial of four interventions was conducted using **tubewells (n=2,486), liquid sodium hypochlorite ('Clorin') distributed with an improved water vessel (n=2,305),**

hygiene promotion (n=1,877), and a combination of the three (n=2,040) to create an evidence-base for water policy in Afghanistan. A fifth group served as a control (n=2,377). Interventions were randomized across 32 villages in Wardak province. Outcomes were measured through two household surveys separated by one year and twice-weekly household surveillance conducted over 16 months. **The households receiving all three interventions showed reduction in diarrhoea compared with the control group, through both longitudinal surveillance data (IRR [95% CI]=0.61 [0.47-0.81]) and cross-sectional survey data (AOR [95% CI]=0.53 [0.30-0.93]).** This reduction was significant when all household members were included, but did not reach significance when only children under five were considered. **These results suggest multi-barrier methods are necessary where there are many opportunities for water contamination**. Surveillance data suggested a greater impact of interventions on reducing diarrhoeal diseases than data from the surveys. Higher economic status as measured through household assets was associated with lower rates of diarrhoea and greater intervention uptake, excepting Clorin. **Use of soap was also associated with lower prevalence of diarrhoea.**

Emergency care

Intravenous fluids

N Engl J Med. 2011 Jun 30;364(26):2483-95. Epub 2011 May 26.

Mortality after fluid bolus in African children with severe infection.

Maitland K, Kiguli S, Opoka RO, Engoru C, Olupot-Olupot P, Akech SO, Nyeko R, Mtove G, Reyburn H, Lang T, Brent B, Evans JA, Tibenderana JK, Crawley J, Russell EC, Levin M, Babiker AG, Gibb DM; FEAST **Trial** Group.

Source

Kilifi Clinical Trials Facility, Kenya Medical Research Institute (KEMRI)-Wellcome Trust Research Programme, Kilifi, Kenya. kathryn.maitland@gmail.com

Abstract

BACKGROUND: The role of fluid resuscitation in the treatment of children with shock and life-threatening infections who live in resource-limited settings is not established. METHODS: We randomly assigned children with severe febrile illness and impaired perfusion to receive boluses of 20 to 40 ml of 5% albumin solution (albumin-bolus group) or 0.9% saline solution (saline-bolus group) per kilogram of body weight or no bolus (control group) at the time of admission to a hospital in Uganda, Kenya, or Tanzania (stratum A); children with severe hypotension were randomly assigned to one of the bolus groups only (stratum B). All children received appropriate antimicrobial treatment, intravenous maintenance fluids, and supportive care, according to guidelines. Children with malnutrition or gastroenteritis were excluded. The primary end point was 48-hour mortality; secondary end points included pulmonary edema, increased intracranial pressure, and mortality or neurologic sequelae at 4 weeks. RESULTS: The data and safety monitoring committee recommended halting recruitment after 3141 of the projected 3600 children in stratum A were enrolled. Malaria status (57% overall) and clinical severity were similar across groups. **The 48-hour mortality was 10.6% (111 of 1050 children), 10.5% (110 of 1047 children), and 7.3% (76 of 1044 children) in the albumin-bolus, saline-bolus, and control groups, respectively (relative risk for saline bolus vs. control, 1.44; 95% confidence interval [CI], 1.09 to 1.90; P=0.01; relative risk for albumin**

bolus vs. saline bolus, 1.01; 95% CI, 0.78 to 1.29; P=0.96; and relative risk for any bolus vs. control, 1.45; 95% CI, 1.13 to 1.86; P=0.003). The 4-week mortality was 12.2%, 12.0%, and 8.7% in the three groups, respectively (P=0.004 for the comparison of bolus with control). Neurologic sequelae occurred in 2.2%, 1.9%, and 2.0% of the children in the respective groups (P=0.92), and pulmonary edema or increased intracranial pressure occurred in 2.6%, 2.2%, and 1.7% (P=0.17), respectively. In stratum B, 69% of the children (9 of 13) in the albumin-bolus group and 56% (9 of 16) in the saline-bolus group died (P=0.45). The results were consistent across centers and across subgroups according to the severity of shock and status with respect to malaria, coma, sepsis, acidosis, and severe anemia. CONCLUSIONS: Fluid boluses significantly increased 48-hour mortality in critically ill children with impaired perfusion in these resource-limited settings in Africa.

Comment

This study is important, complex, and open to misinterpretation. The populations studied included many children with one or more non-specific signs of poor perfusion, many at risk of high antidiuretic hormone levels (such as pneumonia, meningitis, and coma), and many with severe anaemia. The populations excluded included those with diarrhoea and severe dehydration. The study shows that rapid fluid boluses of 20-40ml/kg are dangerous in children with malaria, and in other common febrile illnesses in which ADH secretion is likely to be high. For a commentary: "What the African fluid bolus study means", see: Lancet DOI:10.1016/S0140-6736(11)60881-7

BMC Pediatr. 2010 Oct 6;10:71.

Phase II trial of isotonic fluid resuscitation in Kenyan children with severe malnutrition and hypovolaemia.

Akech SO, Karisa J, Nakamya P, Boga M, Maitland K.

Source

KEMRI-Wellcome Trust Research Programme, Centre for Geographic Medicine Research-Coast, Kilifi, Kenya.

Abstract

BACKGROUND: Children with severe malnutrition who develop shock have a high mortality. Contrary to contemporaneous paediatric practice, current guidelines recommend use of low dose hypotonic fluid resuscitation (half-strength Darrows/5% dextrose (HSD/5D). We evaluated the safety and efficacy of this guideline compared to resuscitation with a standard isotonic solution. METHODS: A Phase II randomised controlled, safety and efficacy trial in Kenyan children aged over 6 months with severe malnutrition and shock including children with severe dehydration/shock and presumptive septic shock (non-diarrhoeal shock). **Eligible children were randomised to HSD/5D or Ringer's Lactate (RL). A maximum of two boluses of 15 ml/kg of HSD/5D were given over two hours (as recommended by guidelines) while those randomised to RL received 10 ml/kg aliquots half hourly (maximum 40 ml/kg).** Primary endpoint was resolution of shock at 8 and 24 hours. Secondary outcomes included resolution of acidosis, adverse events and mortality. RESULTS: 61 children were enrolled: 41 had shock and severe dehydrating diarrhoea, 20 had presumptive septic shock; 69% had decompensated shock. **By 8 hours response to volume resuscitation was poor with shock persisting in most children:-HSD/5D 15/22 (68%) and RL14/25 (52%), p = 0.39.** Oliguria was more prevalent at 8 hours in the HSD/5D group, 9/22 (41%), compared to RL-3/25 (12%), p = 0.02. Mortality was

high, HSD/5D-15/26(58%) and RL 13/29(45%); p = 0.42. Most deaths occurred within 48 hours of admission. Neither pulmonary oedema nor cardiogenic failure was detected.
CONCLUSIONS: **Outcome was universally poor characterised by persistence of shock, oliguria and high case fatality.** Isotonic fluid was associated with modest improvement in shock and survival when compared to HSD/5D but inconclusive due to the limitations of design and effectiveness of either resuscitation strategy. Although isotonic fluid resuscitation did not result in cardiogenic heart failure, as previously feared, we conclude that the modest volumes used and rate of infusion were insufficient to promptly correct shock. The adverse performance of the recommended fluid resuscitation guideline for severe malnutrition should prompt clinical investigation of isotonic fluids for resuscitation of compensated shock, defining rate and volumes required to inform future guidelines.

Pediatr Nephrol. 2010 Nov;25(11):2303-9. Epub 2010 Jul 29.

Intravenous fluid regimen and hyponatraemia among children: a randomized controlled trial.

Kannan L, Lodha R, Vivekanandhan S, Bagga A, Kabra SK, Kabra M.

Source

Department of Pediatrics, All India Institute of Medical Sciences, Ansari Nagar, New Delhi, 110029, India.

Abstract

The aim of this study was to compare the effect of three different intravenous (i.v.) fluid regimes on the incidence of hyponatraemia in hospitalized children ranging in age from 3 months to 12 years. Children who required the administration of i.v. maintenance fluid for at least 24 h following hospitalization were eligible for inclusion. The children were randomized to three i.v. fluid groups: Group A, 0.9% saline in 5% dextrose at the standard maintenance rate; Group B, 0.18% saline in 5% dextrose at the standard maintenance rate; Group C, 0.18% saline in 5% dextrose at two-thirds of the standard maintenance rate. The primary outcome measure was incidence of hyponatraemia (plasma sodium < 130 mEq/L). Of the 167 patients enrolled, 58, 56 and 53 patients were randomized to Group A, B and C, respectively. We observed that 14.3% (8/56) of the children administered 0.18% saline in 5% dextrose at the standard maintenance rate (Group B) developed hyponatraemia compared with 1.72% of the children in Group A and 3.8% of those in Group C. Based on these results, we conclude that the administration of 0.9% saline in 5% dextrose as i.v. maintenance fluid helps in reducing the incidence of hospital-acquired hyponatraemia among children.

Comment

This study adds to several showing the dangers of hypotonic intravenous solutions if the traditional "maintenance fluid" volumes are infused. An alert bulletin issued by the UK National Patient Safety Agency in 2006 recommended the removal of 0.18% NaCl containing solutions from hospital wards. The same practice change - i.e. the removal of 0.18% NaCl from all recommendations and from standard stocks in hospitals, and the recommendation against use of hypotonic solutions for use in resuscitation fluids, has occurred in Australia, New Zealand and Canada.

WHO has recently revised its recommendations on intravenous maintenance fluids:

- *For children who require intravenous fluids for maintenance, options include ringers lactate solution with 5% dextrose, sodium chloride 0.45% with glucose 5%, sodium chloride 0.45% with glucose 2.5%, or 0.9% sodium chloride with glucose 5%.*
- *Low sodium containing solutions, such as sodium chloride 0.18% with glucose 4%, or 5% glucose in water, should* ***not*** *be used as there is an increased risk of hyponatraemia.*
- *There is evidence that there is a greater level of risk of hyponatraemia associated with the use of very low sodium containing solutions in paediatric patients in comparison to fluids where the sodium content is 75-150mmol/L.*
- *Intravenous maintenance fluids should contain glucose to avoid hypoglycaemia and starvation ketosis. Enteral feeding should be used in sick children, as it provides nutrition and avoids complications associated IV fluids, and if oral nutrition is not tolerated, nasogastric tube feeding should be considered.*

Envenomation

S Negl Trop Dis. 2010 Jul 27;4(7):e767.

Randomised controlled double-blind non-inferiority trial of two antivenoms for saw-scaled or carpet viper (Echis ocellatus) envenoming in Nigeria.

Abubakar IS, Abubakar SB, Habib AG, Nasidi A, Durfa N, Yusuf PO, Larnyang S, Garnvwa J, Sokomba E, Salako L, Theakston RD, Juszczak E, Alder N, Warrell DA; Nigeria-UK EchiTab Study Group.

Source

Department of Community Medicine, Bayero University of Kano, Kano, Nigeria.

Abstract

BACKGROUND: In West Africa, envenoming by saw-scaled or carpet vipers (Echis ocellatus) causes great morbidity and mortality, but there is a crisis in supply of effective and affordable antivenom (ISRCTN01257358). METHODS: In a randomised, double-blind, controlled, non-inferiority trial, "EchiTAb Plus-ICP" (ET-Plus) equine antivenom made by Instituto Clodomiro Picado was compared to "EchiTAb G" (ET-G) ovine antivenom made by MicroPharm, which is the standard of care in Nigeria and was developed from the original EchiTAb-Fab introduced in 1998. Both are caprylic acid purified whole IgG antivenoms. ET-G is monospecific for Echis ocellatus antivenom (initial dose 1 vial) and ET-Plus is polyspecific for E. ocellatus, Naja nigricollis and Bitis arietans (initial dose 3 vials). Both had been screened by pre-clinical and preliminary clinical dose-finding and safety studies. **Patients who presented with incoagulable blood, indicative of systemic envenoming by E. ocellatus**, were recruited in Kaltungo, north-eastern Nigeria. **Those eligible and consenting were randomly allocated with equal probability to receive ET-Plus or ET-G. The primary outcome was permanent restoration of blood coagulability 6 hours after the start of treatment, assessed by a simple whole blood clotting test repeated 6, 12, 18, 24 and 48 hr after treatment**. Secondary (safety) outcomes were the incidences of anaphylactic, pyrogenic and late serum sickness-type antivenom reactions. FINDINGS: Initial doses permanently restored blood coagulability at 6 hours in 161/194 (83.0%) of ET-Plus and 156/206 (75.7%) of ET-G treated patients (Relative Risk [RR] 1.10 one-sided 95% CI lower limit 1.01; P = 0.05). ET-Plus caused early reactions on more occasions than did ET-G [50/194 (25.8%) and 39/206 (18.9%) respectively RR (1.36 one-sided 95% CI 1.86 upper limit; P = 0.06). These reactions were classified as severe in 21 (10.8%) and 11 (5.3%) of patients, respectively. CONCLUSION: At these doses, ET-Plus was

slightly more effective but ET-G was slightly safer. Both are recommended for treating E. Ocellatus. *envenoming in Nigeria.*

BMJ. 2011 Jan 5;342:c7136. doi: 10.1136/bmj.c7136.

Efficacy and safety of scorpion antivenom plus prazosin compared with prazosin alone for venomous scorpion (Mesobuthus tamulus) sting: randomised open label clinical trial.

Bawaskar HS, Bawaskar PH.

Source

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Abstract

OBJECTIVE: Envenomation by Mesobuthus tamulus scorpion sting can result in serious cardiovascular effects. Scorpion antivenom is a specific treatment for scorpion sting. Evidence for the benefit of scorpion antivenom and its efficacy compared with that of commonly used vasodilators, such as prazosin, is scarce. **We assessed the efficacy of prazosin combined with scorpion antivenom, compared with prazosin alone, in individuals with autonomic storm caused by scorpion sting.** DESIGN: Prospective, open label randomised controlled trial. SETTING: General hospital inpatients (Bawaskar Hospital and Research Centre Mahad Dist-Raigad Maharashtra, India). PARTICIPANTS: Seventy patients with grade 2 scorpion envenomation, older than six months, with no cardiorespiratory or central nervous system abnormalities. INTERVENTION: Scorpion antivenom plus prazosin (n=35) or prazosin alone (n=35) assigned by block randomisation. Treatment was not masked. Analysis was by intention to treat. MAIN OUTCOME MEASURES: The primary end point was the proportion of patients achieving resolution of the clinical syndrome (sweating, salivation, cool extremities, priapism, hypertension or hypotension, tachycardia) 10 hours after administration of study drugs. Secondary end points were time required for complete resolution of clinical syndrome, prevention of deterioration to higher grade, doses of prazosin required overall and within 10 hours, and adverse events. The study protocol was approved by the independent ethics committee of Mumbai. RESULTS: Mean (SD) recovery times in hours for the prazosin plus scorpion antivenom group compared with the prazosin alone groups were: sweating 3 (1.1) v 6.6 (2.6); salivation 1.9 (0.9) v 3 (1.9); priapism 4.7 (1.5) v 9.4 (1.5). Mean (SD) doses of prazosin in the groups were 2 (2.3) and 4 (3.5), respectively. **32 patients (91.4%, 95% confidence interval 76.9% to 97.8%) in the prazosin plus antivenom group showed complete resolution of the clinical syndrome within 10 hours of administration of treatment compared with eight patients in the prazosin group (22.9%, 11.8% to 39.3%).** Patients from the antivenom plus prazosin group recovered earlier (mean 8 hours, 95% CI 6.5 to 9.5) than those in the control group (17.7 hours, 15.4 to 19.9; mean difference -9.7 hours, -6.9 to -12.4). The number of patients whose condition deteriorated to a higher grade was similar in both groups (antivenom plus prazosin four of 35, prazosin alone five of 35). Hypotension was reported in fewer patients in the antivenom plus prazosin group (12 of 35, 34.3%) than in the prazosin group (19 of 35, 54.3%), but the difference was not statistically significant. No difference was noted in change in blood pressure and pulse rate over time between two groups. CONCLUSION: **Recovery from scorpion sting is hastened by simultaneous administration of scorpion antivenom plus prazosin compared with prazosin alone.**

Epilepsy and acute seizures

Epilepsia. 2011 Apr;52(4):788-93. doi: 10.1111/j.1528-1167.2010.02949.x. Epub 2011 Jan 28.
Intranasal versus intravenous lorazepam for control of acute seizures in children: a randomized open-label study.
Arya R, Gulati S, Kabra M, Sahu JK, Kalra V.

Source

Division of Pediatric Neurology, Department of Pediatrics Department of Pediatrics, All India Institute of Medical Sciences, New Delhi, India.

Abstract

PURPOSE: Intravenous lorazepam is considered the drug of first choice for control of acute convulsive seizures. However, resource or personnel constraints necessitate the study of alternative routes and medications. This study compared the efficacy and adverse effects of intranasal versus intravenous lorazepam in children aged 6-14 years who presented with acute seizures. METHODS: This was a randomized open-label study conducted at an Indian hospital from August 2008 to April 2009. One hundred forty-one consecutive children aged 6-14 years who presented convulsing to the emergency room were included. **After stabilization, the children were randomized to receive either intravenous or intranasal lorazepam (0.1 mg/kg, maximum 4 mg). The primary outcome measure was clinical seizure remission within 10 min of drug administration.** The study was registered with clinicaltrials.gov (NCT00735527). KEY FINDINGS: Seventy patients were randomized to receive intravenous and 71 to receive intranasal lorazepam. The patients in the two groups were comparable at baseline. **Clinical seizure remission within 10 min of drug administration was found in 80% of the intravenous group as compared to 83.1% of intranasal group.** The lower limit of 95% confidence interval for effect size was approximately -9.7%, with an a priori cutoff for noninferiority of -10%. SIGNIFICANCE: Intranasal administration of lorazepam is not found to be inferior to intravenous administration for termination of acute convulsive seizures in children.

Neurology. 2011 Apr 12;76(15):1338-43.
Folic acid supplementation prevents phenytoin-induced gingival overgrowth in children.
Arya R, Gulati S, Kabra M, Sahu JK, Kalra V.

Source

Division of Pediatric Neurology, AIIMS, Ansari Nagar, New Delhi 110 029, India.

Abstract

OBJECTIVE: Gingival overgrowth is an important adverse effect of phenytoin (PHT) therapy, occurring in about half of the patients. **This study aimed to evaluate the effect of oral folic acid supplementation (0.5 mg/day) for the prevention of PHT-induced gingival overgrowth (PIGO) in children with epilepsy aged 6-15 years on PHT monotherapy for 6 months**. METHODS: This was a randomized, double-blind, placebo-controlled trial conducted at a tertiary level hospital from May 2008 to June 2009. Children aged 6-15 years started on PHT monotherapy within last 1 month were eligible for inclusion. Preexisting gingival overgrowth, use of other folic acid antagonists, and macrocytic anemia were exclusion criteria. **Trial subjects were randomized to receive either folic acid or placebo.** The primary outcome

measure was incidence of any degree of gingival overgrowth after 6 months of PHT monotherapy. The trial was registered with clinicaltrials.gov (NCT00781196). RESULTS: A total of 120 children were recruited, 62 and 58, respectively, in folic acid and placebo arms. The 2 arms were comparable at baseline. **Twenty-one percent of patients in the folic acid arm developed PIGO, as compared with 88% receiving placebo ($p < 0.001$).** Absolute risk reduction of PIGO by folic acid was 67% (95% confidence interval 54%-80%), and relative risk reduction was 0.76. CONCLUSIONS: **Oral folic acid was found to decrease the incidence of PIGO in children on PHT monotherapy, in a statistically significant and clinically relevant manner.** Classification of evidence: This study provides Class I evidence that folic acid supplementation, 0.5 mg/day, is associated with prevention of gingival overgrowth in children taking PHT monotherapy.

Hepatitis and liver disease

J Int Med Res. 2010;38(6):2004-10.

Sonographic assessment of ceftriaxone-associated biliary pseudolithiasis in Chinese children.

Meng D, Cao Y, Fu J, Chen R; Lu, Tu Y.

Source

Pharmaceutical Preparation Section, Third Affiliated Hospital, Third Military Medical University, Chongqing, China.

Abstract

In this randomized, single-blind, case-controlled, prospective study, the incidence and outcome of ceftriaxone-associated biliary pseudolithiasis in Chinese children was evaluated via ultrasonography. A total of 108 children diagnosed with hepatobiliary infection or pneumonia were randomized to receive ceftriaxone or ceftazidime. Serial gallbladder sonograms were obtained on days 1, 5 - 7 and 10 - 14 of therapy. **Gallstones were detected in 43.10% of patients in the ceftriaxone-treated group and in 2.00% of the ceftazidime-treated group.** The incidence of pseudolithiasis was significantly higher in the ceftriaxone-treated than the ceftazidime-treated group. Biliary precipitation abnormalities appeared after 2 - 7 days of treatment. After gallstones were found, the drug was stopped and symptoms resolved within 1 - 2 days. This study suggests that the risk of ceftriaxone-associated biliary pseudolithiasis should be considered when treating Chinese children.

Turk J Pediatr. 2010 Sep-Oct;52(5):457-63.

Efficacy of combined interferon alpha and long-term lamivudine therapy in children with chronic hepatitis B.

Kuloğlu Z, Kansu A, Erden E, Girgin N.

Department of Pediatric Gastroenterology, Hepatology and Nutrition, Ankara University Faculty of Medicine, Ankara, Turkey.

Abstract

The aim of this study was to evaluate the efficacy of interferon alpha (IFN-alpha) and long-term lamivudine therapy in children with chronic hepatitis B and to determine the optimal duration of

lamivudine therapy. Thirty-eight HBeAg-positive children simultaneously received IFN-alpha2a 5 MU/m2 to 10 MU/m2 for six months and lamivudine (4 mg/kg/day). Lamivudine was administered until anti-HBe seroconversion and was continued for six months in responders. During the five-year study period, we evaluated the efficacy of treatment, occurrence of YMDD mutants and adverse effects. During the study period, alanine aminotransferase (ALT) normalization, clearance of hepatitis B virus (HBV) DNA, HBeAg/anti-HBeAb, HBsAg/anti-HBsAb seroconversion, and histological response were noted in 27 (71.1%), 14 (36.8%), 13 (34.2%), 2 (5.2%) and 10 (47.9%) patients, respectively. Complete response was determined in 34.2% (13/38), and in 69.2% of these responders, response was achieved within 18 months. Breakthrough and YMDD mutant rates were 65.8% and 55.2%, respectively. Breakthrough time was a median 24 months and was associated with low baseline ALT level ($p < 0.01$). In conclusion, although lamivudine was used for a longer period, the response rate was not higher than in previous reports. We suggest that 18 months' duration of lamivudine treatment is sufficient for combination therapy.

HIV / AIDS

Anti-retroviral treatment

JAMA. 2010 Sep 8;304(10):1082-90.

Reuse of nevirapine in exposed HIV-infected children after protease inhibitor-based viral suppression: a randomized controlled trial.

Coovadia A, Abrams EJ, Stehlau R, Meyers T, Martens L, Sherman G, Hunt G, Hu CC, Tsai WY, Morris L, Kuhn L.

Source

Empilweni Services and Research Unit, Rahima Moosa Mother and Child Hospital, Johannesburg, South Africa.

Abstract

CONTEXT: Protease inhibitor (PI)-based therapy is recommended for infants infected with human immunodeficiency virus (HIV) who were exposed to nevirapine for prevention of mother-to-child HIV transmission. However, there are limitations of continuing PI-based therapy indefinitely and reuse of nevirapine has many advantages. OBJECTIVE: **To test whether nevirapine-exposed infants who initially achieve viral suppression with PI-based therapy can maintain viral suppression when switched to nevirapine-based therapy.** DESIGN, SETTING, AND PATIENTS: Randomized trial conducted between April 2005 and May 2009 at a hospital in Johannesburg, South Africa, among **195 children who achieved viral suppression less than 400 copies/mL for 3 or more months from a cohort of 323 nevirapine-exposed children who initiated PI-based therapy before 24 months of age.** INTERVENTIONS: **Control group children continued to receive ritonavir-boosted lopinavir, stavudine, and lamivudine (n = 99). Switch group children substituted nevirapine for ritonavir-boosted lopinavir (n = 96).** MAIN OUTCOME MEASURES: Children were followed up for 52 weeks after randomization. Plasma HIV-1 RNA of greater than 50 copies/mL was the primary end point. Confirmed viremia greater than 1000 copies/mL was used as a criterion to consider regimen changes for children in either group (safety end point). RESULTS: **Plasma viremia greater than 50 copies/mL occurred less frequently in**

the switch group (Kaplan-Meier probability, 0.438; 95% CI, 0.334-0.537) than in the control group (0.576; 95% CI, 0.470-0.668) (P = .02). Confirmed viremia greater than 1000 copies/mL occurred more frequently in the switch group (0.201; 95% CI, 0.125-0.289) than in the control group (0.022; 95% CI, 0.004-0.069) (P < .001). CD4 cell response was better in the switch group (median CD4 percentage at 52 weeks, 34.7) vs the control group (CD4 percentage, 31.3) (P = .004). Older age (relative hazard [RH], 1.71; 95% CI, 1.08-2.72) was associated with viremia greater than 50 copies/mL in the control group. Inadequate adherence (RH, 4.14; 95% CI, 1.18-14.57) and drug resistance (RH, 4.04; 95% CI, 1.40-11.65) before treatment were associated with confirmed viremia greater than 1000 copies/mL in the switch group. CONCLUSION: **Among HIV-infected children previously exposed to nevirapine, switching to nevirapine-based therapy after achieving viral suppression with a ritonavir-boosted lopinavir regimen resulted in lower rates of viremia greater than 50 copies/mL than maintaining the primary ritonavir-boosted lopinavir regimen.**

Clin Infect Dis. 2010 Nov 1;51(9):1081-9.

Strategies for nevirapine initiation in HIV-infected children taking pediatric fixed-dose combination "baby pills" in Zambia: a randomized controlled trial.

Mulenga V, Cook A, Walker AS, Kabamba D, Chijoka C, Ferrier A, Kalengo C, Kityo C, Kankasa C, Burger D, Thomason M, Chintu C, Gibb DM.

Source

University Teaching Hospital, Lusaka, Zambia.

Abstract

BACKGROUND: **Fixed-dose combination scored dispersible stavudine, lamivudine, and nevirapine minitablets (Triomune Baby and Junior; Cipla Ltd) are simpler and cheaper than liquid formulations and have correct dose ratios for human immunodeficiency virus-infected children. However, they cannot be used for dose escalation (DE) of nevirapine**. METHODS: Children were randomized to initiate antiretroviral therapy with full-dose (FD) nevirapine (Triomune Baby or Junior in the morning and evening) versus DE (half-dose nevirapine for 14 days [Triomune in the morning and stavudine-lamivudine {Lamivir-S} in the evening], then FD), in accordance with World Health Organization weight-band dosing tables. The primary end point was nevirapine-related clinical or laboratory grade 3 or 4 adverse events (AEs). RESULTS: In total, 211 children (median [interquartile range {IQR}] age, 5 [2-9] years; median [IQR] CD4 cell percentage, 13% [8%-18%]) were enrolled and followed up for a median (IQR) of 92 (68-116) weeks. There were 31 grade 3 or 4 AEs that were definitely/probably or uncertainly related to nevirapine in the FD group (18.0 per 100 child-years), compared with 29 in the DE group (16.5 per 100 child-years) (incidence rate ratio, 1.09; 95% confidence interval, 0.63–1.87; P = .74). All were asymptomatic; 11 versus 3 were single grade 3 or 4 elevations in alanine aminotransferase (ALT) or aspartate aminotransferase (AST) levels, all of which resolved without a change in nevirapine dose or interruption. Thirteen (12%) FD versus 2 (2%) DE children had grade 1 (2 in FD) or grade 2 (11 in FD and 2 in DE) rashes. Three (2 in FD and 1 in DE) substituted efavirenz, 3 (FD) continued FD nevirapine, and 9 (8 in FD and 1 in DE) temporarily interrupted nevirapine, followed by successful DE. Predictors of nevirapine rash were older age (P = .003) and higher CD4 cell count for age (P = .03). Twenty-two children died (12 in FD and 10 in DE), 1 FD and 5 DE children at <4 weeks; none were considered to be drug related by independent review. CONCLUSIONS: Rash was more frequent with FD nevirapine, but 88% had no clinical toxicity; elevated AST or ALT levels were transient and resolved spontaneously, suggesting that routine laboratory monitoring

has limited value. Dual pediatric stavudine-lamivudine minitablets are preferred for safe and simple DE; if unavailable, initiating FD Triomune requires timely review for rash, which could be managed by temporary reduction to half-dose Triomune or efavirenz substitution.

J Acquir Immune Defic Syndr. 2010 Oct 1;55(2):245-52.

Comparison of home and clinic-based HIV testing among household members of persons taking antiretroviral therapy in Uganda: results from a randomized trial.

Lugada E, Levin J, Abang B, Mermin J, Mugalanzi E, Namara G, Gupta S, Grosskurth H, Jaffar S, Coutinho A, Bunnell R.

Source

Centers for Disease Control and Prevention-Uganda, Global AIDS Program, National Center for HIV, STD and TB Prevention, Centers for Disease Control and Prevention, Entebbe, Uganda. ericlugada@yahoo.com

Abstract

OBJECTIVE: Due to high rates of undiagnosed and untreated HIV infection in Africa, we compared HIV counseling and testing (VCT) uptake among household members of patients receiving antiretroviral therapy. METHODS: HIV-infected persons attending an AIDS clinic were randomized to a home-based or clinic-based antiretroviral therapy program including VCT for household members. Clinic arm participants were given free VCT vouchers and encouraged to invite their household members to the clinic for VCT. Home arm participants were visited, and their household members offered VCT using a 3-test rapid finger-stick testing algorithm. VCT uptake and HIV prevalence were compared. FINDINGS: Of 7184 household members, 3974 (55.3%) were female and 4798 (66.8%) were in the home arm. Home arm household members were more likely to receive VCT than those from the clinic arm (55.8% vs. 10.9%, odds ratio: 10.41, 95% confidence interval: 7.89 to 13.73; $P < 0.001$), although the proportion of HIV-infected household members was higher in the clinic arm (17.3% vs. 7.1%, odds ratio: 2.76, 95% confidence interval: 1.97 to 3.86, $P < 0.001$). HIV prevalence among all household members tested in the home arm was 56% compared with 27% in the clinic arm. Of 148 spouses of HIV-infected patients, 69 (46.6%) were uninfected. Persons aged 15-24 were less likely to test than other age groups, and in the home arm, women were more likely to test than men. CONCLUSIONS: **Home-based VCT for household members of HIV-infected persons was feasible, associated with lower prevalence, higher uptake, and increased identification of HIV-infected persons than clinic-based provision**.

Management of HIV-related conditions

BMJ. 2011 Mar 31;342:d1617. doi: 10.1136/bmj.d1617.

Protective efficacy of co-trimoxazole prophylaxis against malaria in HIV exposed children in rural Uganda: a randomised clinical trial.

Sandison TG, Homsy J, Arinaitwe E, Wanzira H, Kakuru A, Bigira V, Kalamya J, Vora N, Kublin J, Kamya MR, Dorsey G, Tappero JW.

Source

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Abstract
OBJECTIVE: **To evaluate the protective efficacy of co-trimoxazole prophylaxis against malaria in HIV exposed children** (uninfected children born to HIV infected mothers) in Africa. DESIGN: Non-blinded randomised control trial SETTING: Tororo district, rural Uganda, an area of high malaria transmission intensity PARTICIPANTS: 203 breastfeeding HIV exposed infants enrolled between 6 weeks and 9 months of age. INTERVENTION: **Co-trimoxazole prophylaxis from enrollment until cessation of breast feeding and confirmation of negative HIV status. All children who remained HIV uninfected (n = 185) were then randomised to stop co-trimoxazole prophylaxis immediately or continue co-trimoxazole until 2 years old.** MAIN OUTCOME MEASURE: Incidence of malaria, calculated as the number of antimalarial treatments per person year. RESULTS: The incidence of malaria and prevalence of genotypic mutations associated with antifolate resistance were high throughout the study. Among the 98 infants randomised to continue co-trimoxazole, 299 malaria cases occurred in 92.28 person years (incidence 3.24 cases/person year). Among the 87 infants randomised to stop co-trimoxazole, 400 malaria cases occurred in 71.81 person years (5.57 cases/person year). **Co-trimoxazole prophylaxis yielded a 39% reduction in malaria incidence, after adjustment for age at randomisation (incidence rate ratio 0.61 (95% CI 0.46 to 0.81), P = 0.001). There were no significant differences in the incidence of complicated malaria, diarrhoea, pneumonia, hospitalisations, or deaths between the two treatment arms.** CONCLUSIONS: Co-trimoxazole prophylaxis was moderately protective against malaria in HIV exposed infants when continued beyond the period of HIV exposure despite the high prevalence of Plasmodium genotypes associated with antifolate resistance.

AIDS. 2010 Sep 10;24(14):2225-32.

A randomized controlled trial of intermittent compared with daily cotrimoxazole preventive therapy in HIV-infected children.

Zar HJ, Workman L, le Roux SM, Jennings T, Jele N, Schaaf HS, Barclay-Loggie A, Mulligan C, le Roux DM, Lombard CJ, Cotton MF; INH study team.
Collaborators (8)
Bezuidenhout H, Brink P, Frigati L, Gray D, Hussey G, Rabie H, Streicher R, Walters E.
Source
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Abstract
OBJECTIVE: Cotrimoxazole preventive therapy (CPT) reduces morbidity and mortality in HIV-infected children. The WHO recommends prolonged daily CPT for HIV-infected infants and children. In adults, intermittent CPT has been associated with less adverse events than daily, with increased tolerability and equal efficacy. **We investigated the efficacy and tolerability of intermittent CPT compared with daily CPT in HIV-infected children over a 5-year period.** DESIGN: A prospective randomized controlled study. METHODS: **HIV-infected children aged at least 8 weeks were randomized to thrice weekly or daily CPT. Outcome measures were mortality, bacterial infections, hospitalizations and adverse events.** RESULTS: **Three hundred and twenty-four children (median age 23 months) were followed for 672 child-years**; 165 (51%) were randomized to intermittent CPT. Most children (287, 89%) were Centers for Disease Control and Prevention clinical category B or C; 207 (64%) received HAART

during the study. **Mortality (53 deaths, 16%) was similar in the intermittent CPT compared with the daily CPT group {24 (14%) vs. 29 (18%), hazard ratio 0.75 [95% confidence interval (CI) 0.44-1.29]}.** The predominant causes of death in both groups were sepsis (17, 32%), pneumonia (13, 25%) or diarrhoea (8, 15%). **Intermittent CPT was associated with more bacteraemias [incidence rate ratio 2.36 (95% CI 1.21-4.86)]. Children receiving intermittent CPT also spent more days in hospital [incidence rate ratio 1.15 (95% CI 1.04-1.28)].** The rate of serious adverse events was similar between groups [incidence rate ratio 1.07 (95% CI 0.58-2.02)]. CONCLUSION**: Intermittent CPT was associated with more invasive bacterial disease than daily CPT, but survival was similar.** Both regimens were well tolerated. On balance, daily CPT remains preferable to intermittent therapy for HIV-infected children.

Antimicrob Agents Chemother. 2010 Sep;54(9):3756-62. Epub 2010 Jun 28.

Impact of cotrimoxazole on carriage and antibiotic resistance of Streptococcus pneumoniae and Haemophilus influenzae in HIV-infected children in Zambia.

Mwenya DM, Charalambous BM, Phillips PP, Mwansa JC, Batt SL, Nunn AJ, Walker S, Gibb DM, Gillespie SH.

Source

University Teaching Hospital, Lusaka, Zambia.

Abstract

This is a substudy of a larger randomized controlled trial on HIV-infected Zambian children, which revealed that cotrimoxazole prophylaxis reduced morbidity and mortality despite a background of high cotrimoxazole resistance. The impact of cotrimoxazole on the carriage and antibiotic resistance of Streptococcus pneumoniae and Haemophilus influenzae as major causes of childhood mortality in HIV-infected children was investigated since these are unclear. **Representative nasopharyngeal swabs were taken prior to randomization for 181 of 534 children (92 on cotrimoxazole and 89 on placebo).** Bacterial identification and antibiotic susceptibility were performed by routine methods. Due to reduced mortality, prophylactic cotrimoxazole increased the median time from randomization to the last specimen from 48 to 56 months (P = 0.001). **The carriage of H. influenzae was unaltered by cotrimoxazole. Carriage of S. pneumoniae increased slightly in both arms but was not statistically significant in the placebo arm.** In S. pneumoniae switching between carriage and no carriage in consecutive pairs of samples was unaffected by cotrimoxazole (P = 0.18) with a suggestion that the probability of remaining carriage free was lower (P = 0.10). In H. influenzae cotrimoxazole decreased switching from carriage to no carriage (P = 0.02). Cotrimoxazole resistance levels were higher in postbaseline samples in the cotrimoxazole arm than in the placebo arm (S. pneumoniae, P < 0.0001; H. influenzae, P = 0.005). Cotrimoxazole decreased switching from cotrimoxazole resistance to cotrimoxazole sensitivity in S. pneumoniae (P = 0.002) and reduced the chance of H. influenzae remaining cotrimoxazole sensitive (P = 0.05). No associations were observed between the percentage of CD4 (CD4%), the change in CD4% from baseline, child age at date of specimen, child gender, or sampling month with carriage of either pathogen.

Pediatr Infect Dis J. 2011 May 12. [Epub ahead of print]

Bacteremia in Human Immunodeficiency Virus-infected Children in Cape Town, South Africa.

le Roux DM, Cotton MF, le Roux SM, Whitelaw A, Lombard CJ, Zar HJ.

Source

From the *Department of Paediatrics and Child Health, Red Cross War Memorial Children's Hospital, University of Cape Town, Cape Town, South Africa; †Department of Paediatrics and Child Health, Tygerberg Children's Hospital, Stellenbosch University, Cape Town, South Africa; ‡National Health Laboratory Services, University of Cape Town, Cape Town, South Africa; and §Biostatistics Unit, Medical Research Council, Cape Town, South Africa.

Abstract

Bacteremia contributes to morbidity of HIV-infected children. In a randomized controlled trial evaluating trimethoprim-sulfamethoxazole (TMP-SMX) prophylaxis, 47 bacteremias were detected. The incidence rate of bacteremia increased in the first 3 months after starting combination antiretroviral therapy (cART), but decreased by 74% once children were established on cART for more than 3 months. Children should be prioritized for early cART.

Prevention of parent to child transmission

Am J Clin Nutr. 2010 Oct;92(4):881-6. Epub 2010 Aug 25.

Effect of vitamin supplements on HIV shedding in breast milk.

Villamor E, Koulinska IN, Aboud S, Murrin C, Bosch RJ, Manji KP, Fawzi WW.

Source

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Abstract

BACKGROUND: **Supplementation in lactating HIV-1-infected women with preformed vitamin A and β-carotene (VA/BC) increases the risk of mother-to-child transmission of HIV through breastfeeding.** Identifying a biological mechanism to explain this unexpected finding would lend support to a causal effect. OBJECTIVE: The aim of the study was to evaluate the effect of VA/BC or multivitamin (B complex, vitamin C, and vitamin E) supplementation of HIV-infected women on HIV shedding in breast milk during the first 2 y postpartum. DESIGN: We quantified viral (cell-free) and proviral (cell-associated) HIV loads in breast-milk samples collected ≤15 d after delivery and every 3 mo thereafter from 594 Tanzanian HIV-1-infected women who participated in a randomized trial. Women received 1 of the following 4 daily oral regimens in a 2 × 2 factorial fashion during pregnancy and throughout the first 2 y postpartum: multivitamin, VA/BC, multivitamin including VA/BC, or placebo. RESULTS: **The proportion of breast-milk samples with detectable viral load was significantly higher in women who received VA/BC (51.3%) than in women who were not assigned to VA/BC (44.8%; P = 0.02).** The effect was apparent ≥6 mo postpartum (relative risk: 1.34; 95% CI: 1.04, 1.73). No associations with proviral load were observed. The multivitamin had no effects. In observational analyses, β-carotene but not retinol breast-milk concentrations were significantly associated with an increased viral load in milk. CONCLUSIONS: VA/BC supplementation in lactating women increases the HIV load in breast milk. This finding contributes to explaining the adverse effect of VA/BC on mother-to-child

transmission. β-Carotene appears to have an effect on breast-milk viral load, independent of preformed vitamin A.
http://www.ajcn.org/content/92/4/881.full.pdf+html

J Nutr. 2010 Oct;140(10):1788-92. Epub 2010 Aug 25.

Vitamin supplementation increases risk of subclinical mastitis in HIV-infected women.

Arsenault JE, Aboud S, Manji KP, Fawzi WW, Villamor E.

Source

Department of Nutrition, Harvard School of Public Health, Boston, MA 02115, USA.

Abstract

Subclinical mastitis is common in HIV-infected women and is a risk factor for mother-to-child transmission of HIV. The purpose of this study was to examine the effect of vitamin supplementation [vitamin A + β-carotene, multivitamins (B complex, C, and E), or multivitamins, including vitamin A + β-carotene] on the risk of subclinical mastitis during the first 2 y postpartum among HIV-infected women. The study was a randomized, placebo-controlled, clinical trial including 674 HIV-infected, antiretroviral naïve Tanzanian women who were recruited during pregnancy and followed-up after delivery. Breast milk samples were obtained approximately every 3 mo. Any subclinical mastitis was defined as a ratio of the sodium to potassium (Na:K) breast milk concentrations > 0.6 and further classified as either moderate (Na:K ≥ 0.6 and ≤ 1) or severe (Na:K > 1.0). Fifty-eight percent of women had at least 1 episode of any subclinical mastitis. **Women assigned to multivitamins (B complex, C, and E) had a 33% greater risk of any subclinical mastitis (P = 0.005) and a 75% greater risk of severe subclinical mastitis (P = 0.0006) than women who received the placebo. Vitamin A + β-carotene also increased the risk of severe subclinical mastitis by 45% (P = 0.03).** Among women with CD4+ T-cell counts ≥ 350 cells/μL, multivitamin intake resulted in a 49% increased risk of any subclinical mastitis (P = 0.006); by contrast, there were no treatment effects among women with CD4+ T-cell counts < 350 cells/μL (P- interaction for treatment × CD4+ T-cell count = 0.10). **Supplementation of HIV-infected women with vitamins increased the risk of subclinical mastitis.**

Comment

The above two studies by the same group provide information about the link between multi-vitamins and transmission of HIV through breast milk. The evidence that the effect found above was due to β-carotene is the association with β-carotene levels and viral shedding in breast milk, and the lack of association in the second study between breast milk vitamin A levels and viral shedding. However the mothers who received daily vitamin A/ β-carotene during pregnancy also received 200,000 IU of vitamin A in the post-partum period, and an effect of vitamin A itself cannot be excluded by this study. The authors in the second study also suggested the mechanism may relate to the increased risk of subclinical mastitis, causing viral particles in plasma to leak into the mammary ducts.

A Cochrane review, published in 2010 (http://www.cochranejournalclub.com/art-hiv-pregnant-women-clinical/pdf/CD003648_standard.pdf concluded that trials were inadequate to determine whether there was a beneficial or harmful effect on vitamin A supplementation on mother-to-child transmission of HIV [Risk ratio 1.05 (0.78-1.41)]

*** Lancet Infect Dis. 2011 Mar;11(3):171-80. Epub 2011 Jan 13.

Triple antiretroviral compared with zidovudine and single-dose nevirapine prophylaxis during pregnancy and breastfeeding for prevention of mother-to-child transmission of HIV-1 (Kesho Bora study): a randomised controlled trial.

Kesho Bora Study Group, de Vincenzi I.

BACKGROUND: Breastfeeding is essential for child health and development in low-resource settings but carries a significant risk of transmission of HIV-1, especially in late stages of maternal disease. We aimed to assess the efficacy and safety of triple antiretroviral compared with zidovudine and single-dose nevirapine prophylaxis in pregnant women infected with HIV. METHODS: Pregnant women with WHO stage 1, 2, or 3 HIV-1 infection who had CD4 cell counts of 200-500 cells per μL were enrolled at five study sites in Burkina Faso, Kenya, and South Africa to start study treatment at 28-36 weeks' gestation. Women were randomly assigned (1:1) by a computer generated random sequence to **either triple antiretroviral prophylaxis (a combination of 300 mg zidovudine, 150 mg lamivudine, and 400 mg lopinavir plus 100 mg ritonavir twice daily until cessation of breastfeeding to a maximum of 6·5 months post partum) or zidovudine and single-dose nevirapine (300 mg zidovudine twice daily until delivery and a dose of 600 mg zidovudine plus 200 mg nevirapine at the onset of labour and, after a protocol amendment in December, 2006, 1 week post-partum zidovudine 300 mg twice daily and lamivudine 150 mg twice daily).** All infants received a 0·6 mL dose of nevirapine at birth and, from December, 2006, 4 mg/kg twice daily of zidovudine for 1 week after birth. Patients and investigators were not masked to treatment. The primary endpoints were HIV-free infant survival at 6 weeks and 12 months; HIV-free survival at 12 months in infants who were ever breastfed; AIDS-free survival in mothers at 18 months; and serious adverse events in mothers and babies. Analysis was by intention to treat. This trial is registered with Current Controlled Trials, ISRCTN71468401. FINDINGS: From June, 2005, to August, 2008, 882 women were enrolled, 824 of whom were randomised and gave birth to 805 singleton or first, liveborn infants. The cumulative rate of HIV transmission at 6 weeks was 3·3% (95% CI 1·9-5·6%) in the triple antiretroviral group compared with 5·0% (3·3-7·7%) in the zidovudine and single-dose nevirapine group, and at 12 months was 5·4% (3·6-8·1%) in the triple antiretroviral group compared with 9·5% (7·0-12·9%) in the zidovudine and single-dose nevirapine group (p=0·029). **The cumulative rate of HIV transmission or death at 12 months was 10·2% (95% CI 7·6-13·6%) in the triple antiretroviral group compared with 16·0% (12·7-20·0%) in the zidovudine and single-dose nevirapine group (p=0·017). In infants whose mothers declared they intended to breastfeed, the cumulative rate of HIV transmission at 12 months was 5·6% (95% CI 3·4-8·9%) in the triple antiretroviral group compared with 10·7% (7·6-14·8%) in the zidovudine and single-dose nevirapine group (p=0·02).** AIDS-free survival in mothers at 18 months will be reported in a different publication. The incidence of laboratory and clinical serious adverse events in both mothers and their babies was similar between groups. INTERPRETATION: **Triple antiretroviral prophylaxis during pregnancy and breastfeeding is safe and reduces the risk of HIV transmission to infants.** Revised WHO guidelines now recommend antiretroviral prophylaxis (either to the mother or to the baby) during breastfeeding if the mother is not already receiving antiretroviral treatment for her own health.

THE LANCET Infectious Diseases
FULL-TEXT ARTICLE

Comment

This is a very important study which has changed global recommendations about prophylaxis against parent-to-child transmission of HIV:
http://www.who.int/reproductivehealth/publications/rtis/KeshoBora_study.pdf)

AIDS. 2011 Mar 27;25(6):767-76.

Twelve-month follow-up of Six Week Extended Dose Nevirapine randomized controlled trials: differential impact of extended-dose nevirapine on mother-to-child transmission and infant death by maternal CD4 cell count.

Omer SB; Six Week Extended Dose Nevirapine (SWEN) Study Team.
Bedri A, Gudetta B, Isehak A, Kumbi S, Mengistu Y, Bhore AV, Bhosale R, Gupte N, Sastry J, Suryavanshi N, Tripathy S, Varadhrajan V, Mmiro F, Mubiru M, Musoke P, Nakabiito C, Onyango C, Taylor A, Abashawl A, Adamu R, Antelman G, Bollinger RC, Bright P, Chaudhary MA, Coberly J, Guay L, Fowler MG, Gupta A, Hassen E, Jackson JB, Moulton LH, Nayak U, Omer SB, Propper L, Ram M, Rexroad V, Ruff AJ, Shankar A, Zwerski S.
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Abstract

OBJECTIVES: We previously reported combined analysis of 6-week and 6-month endpoints of three randomized controlled trials [Six Week Extended Dose Nevirapine (SWEN) trials] that compared extended-dose nevirapine through 6 weeks of age to single-dose nevirapine to prevent HIV transmission via breastfeeding and mortality. We now present endpoints through 12 months of age. DESIGN: **Infants in Ethiopia, India, and Uganda born to HIV-infected women who chose to breastfeed were randomized to receive single-dose or extended-dose nevirapine.** MAIN OUTCOMES: HIV transmission, mortality, HIV transmission or death. RESULTS: Primary analysis included 987 and 903 infants in the single-dose and the extended-dose arms, respectively. **HIV transmission was 8.9% in the extended-dose group compared to 10.4% in the single-dose group, but the difference was not significant [risk ratio: 0.87, 95% confidence interval (CI): 0.65-1.15]. Cumulative mortality at 12 months was half in the extended-dose group compared to the single-dose group (risk ratio: 0.53, 95% CI: 0.32-0.85).** The impact of extended-dose nevirapine was highest in infants of mothers with CD4 cell count more than 350 cells/μl. Risk ratios for death (risk ratio: 0.38, 95% CI: 0.17-0.84) and HIV transmission or death (risk ratio: 0.54, 95% CI: 0.35-0.85) were statistically significant for the CD4 cell counts more than 350 cells/μl category, whereas none of the risk ratios were significant for the CD4 cell counts 200 cells/μl or less and CD4 cell counts 201-350 cells/μl categories. CONCLUSION: For populations with limited access to HAART, our results provide evidence for the use of extended-dose regimens to prevent infant deaths and increase HIV-free survival in infants of HIV-infected breastfeeding women, particularly for infants of women with CD4 cell counts more than 350 cells/μl.

J Infect Dis. 2011 Feb 1;203(3):358-63.

Maternal tuberculosis: a risk factor for mother-to-child transmission of human immunodeficiency virus.

Gupta A, Bhosale R, Kinikar A, Gupte N, Bharadwaj R, Kagal A, Joshi S, Khandekar M, Karmarkar A, Kulkarni V, Sastry J, Mave V, Suryavanshi N, Thakar M, Kulkarni S, Tripathy S, Sambarey P, Patil S, Paranjape R, Bollinger RC, Jamkar A; Six Week Extended-Dose Nevirapine (SWEN) India Study Team.

Source

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Abstract

BACKGROUND: Maternal human immunodeficiency virus (HIV) RNA load, CD4 cell count, breast-feeding, antiretroviral use, and malaria are well-established factors associated with

mother-to-child transmission (MTCT) of HIV; the role of maternal tuberculosis (TB), however, has not been well established. METHODS: The study population was 783 HIV-infected Indian mother-infant pair participants in randomized and ancillary HIV-infected cohorts of the Six Week Extended-Dose Nevirapine (SWEN) Study, a study comparing extended nevirapine versus single-dose nevirapine, to reduce MTCT of HIV among breast-fed infants. Using multivariable logistic regression, we assessed the impact of maternal TB occurring during pregnancy and through 12 months after delivery on risk of MTCT. RESULTS: Of 783 mothers, 3 had prevalent TB and 30 had incident TB at 12 months after delivery. **Of 33 mothers with TB, 10 (30%) transmitted HIV to their infants in comparison with 87 of 750 mothers without TB (12%; odds ratio [OR], 3.31; 95% confidence interval [CI], 1.53-7.29; P = .02).** In multivariable analysis, maternal TB was associated with 2.51-fold (95% CI, 1.05-6.02; P = .04) increased odds of HIV transmission adjusting for maternal factors (viral load, CD4 cell count, and antiretroviral therapy) and infant factors (breast-feeding duration, infant nevirapine administration, gestational age, and birth weight) associated with MTCT of HIV. CONCLUSIONS: **Maternal TB is associated with increased MTCT of HIV. Prevention of TB among HIV-infected mothers should be a high priority for communities with significant HIV/TB burden.**

Comment

In TB endemic communities, screening for TB among women at antenatal clinics could reduce parent-to-child transmission of HIV, and reduce maternal mortality. Previous studies in South Africa showed TB and HIV to be strong co-determinants of maternal deaths (AIDS 2001 15:1857-63).

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East Afr J Public Health. 2010 Jun;7(2):160-4.

The use of total lymphocyte count as a surrogate for low CD4+ T lymphocyte cell counts among HIV-1-infected women in Tanzania.

Mgomella GS, Venkatesh PA, Bosch RJ, Mwakagile D, Urassa W, McIntosh K, Hertzmark E, Msamanga G, Fawzi WW.

Source

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Abstract

BACKGROUND: Human Immunodeficiency Virus type 1 (HIV-1) infection leads to a progressive decline in CD4+ T-lymphocyte (CD4) cells. Initiation of prophylaxis against Opportunistic infections in adults (CD4% used for children) and antiretroviral therapy is usually based on CD4 cell counts, but CD4 cell counts measurement is not affordable in most African countries. OBJECTIVE: To examine whether total lymphocyte counts (TLC) may be used as proxies for low CD4 cell counts. DESIGN: Cross-sectional at baseline when women were pregnant and at least six months postpartum. METHODS: 1,078 HIV-1-infected pregnant women from Dar es Salaam, Tanzania were enrolled in a randomized clinical trial. A series of receiver operator characteristic (ROC) curves were created at baseline and at least 6 months postpartum and among women in WHO Stage 3 and above. **The sensitivity and specificity of TLC and hemoglobin in predicting an absolute CD4 count < 200 cells/mm3 were determined for various clinically relevant cut points.** RESULTS: **TLC was not a good predictor of low CD4 cell counts during pregnancy or at least six months postpartum as**

exhibited by low ROC Area Under the Curve (AUCs) of .57 and .62 respectively. No other variable had the ability to predict CD4 < 200 cells/mm3. CONCLUSIONS: The use of TLC as a proxy for the estimation of low CD4 cell counts in a population of HIV-1-infected adults from sub-Saharan Africa was not substantiated. Inexpensive methods to quantify CD4 cell counts in Africa are needed.

Helminth and other gastrointestinal infections

(See also Anaemia, Diarrhoea)

Lancet Infect Dis. 2010 Sep;10(9):603-11. Epub 2010 Aug 10.

Efficacy of artesunate with sulfalene plus pyrimethamine versus praziquantel for treatment of Schistosoma mansoni in Kenyan children: an open-label randomised controlled trial.

Obonyo CO, Muok EM, Mwinzi PN.

Source

Centre for Global Health Research, Kenya Medical Research Institute, Kisumu, Kenya.

Abstract

BACKGROUND: **Schistosomiasis is an important parasitic disease in Kenya. Decreasing susceptibility of schistosomes to praziquantel, the major drug used to reduce disease morbidity, has made assessment of new antischistosomal drugs a priority.** We aimed to assess the safety and efficacy of an artesunate-based combination drug in the treatment of schistosomiasis. METHODS: In this open-label randomised trial in Rarieda district of western Kenya, we enrolled school children (aged 6-15 years) who had Schistosoma mansoni infection according to duplicate Kato-Katz thick smears from a stool sample. Computer-generated block randomisation was used to **assign children (1:1) to receive artesunate (100 mg) with sulfalene (also known as sulfamethoxypyrazine; 250 mg) plus pyrimethamine (12.5 mg) as one dose every 24 h for 3 days or one dose of praziquantel (40 mg/kg per day). The primary efficacy endpoint was the number of participants cured 28 days after treatment.** Analysis was by intention to treat. This trial is registered with ClinicalTrials.gov, number NCT01054651. RESULTS: Between October and December, 2009, **212 children were enrolled and assigned to receive artesunate with sulfalene plus pyrimethamine (n=106) or praziquantel (n=106). 69 patients (65%) were cured in the praziquantel treatment group compared with 15 (14%) in the artesunate with sulfalene plus pyrimethamine treatment group (p<0.0001).** Adverse events were less common in patients taking artesunate with sulfalene plus pyrimethamine than in those taking praziquantel (22% [n=23] vs 49% [n=52], p<0.0001), and no drug-related serious adverse events occurred. INTERPRETATION: **The standard treatment with praziquantel is more effective than artesunate with sulfalene plus pyrimethamine in the treatment of children with S mansoni infection in western Kenya.** Whether artemisinin-based combination therapy has a role in the treatment of schistosomiasis is unclear.

Lancet Infect Dis. 2011 Feb;11(2):110-8. Epub 2010 Nov 24.

Efficacy and safety of mefloquine, artesunate, mefloquine-artesunate, tribendimidine, and praziquantel in patients with Opisthorchis viverrini: a randomised, exploratory, open-label, phase 2 trial.

Soukhathammavong P, Odermatt P, Sayasone S, Vonghachack Y, Vounatsou P, Hatz C, Akkhavong K, Keiser J.

Source

National Institute of Public Health, Ministry of Health, Vientiane, Laos.

Abstract

BACKGROUND: Praziquantel is the only drug available for treatment of Opisthorchis viverrini, although in-vivo studies point to activity of mefloquine, artesunate, and tribendimidine against this liver fluke. We aimed to assess the efficacy and safety of these drugs compared with that of praziquantel in patients with O viverrini infection. METHODS: We did a randomised open-label trial between February and April, 2010, in the Saysetha district, Attapeu Province, Laos. **Eligible patients were school children aged 10-15 years who had O viverrini infections.** Patients were randomly assigned to one of five different treatment groups by use of a computer-generated randomisation code. We assessed efficacy as cure rate and egg reduction rate in intention-to-treat and per-protocol analyses. The trial was registered with Current Controlled Trials, ISRCTN23425032. RESULTS: **125 children were randomly assigned: 25 received mefloquine, 24 artesunate, 24 mefloquine-artesunate, 27 tribendimidine, and 25 praziquantel.** 19 patients were lost to follow-up. In the intention to treat analysis, **14 patients receiving praziquantel were cured compared with none with mefloquine, one with artesunate (odds ratio 0·03, 95% CI 0·004-0·29), one with mefloquine-artesunate (0·03, 0·004-0·29), and 19 with tribendimidine (1·87, 0·60-5·85). Egg reduction rate was 98·4% for praziquantel, 30·2% for mefloquine (egg reduction-rate ratio 1·61, 95% CI 0·21-0·72), 31·5% for artesunate (0·43, 0·23-0·80), 41·3% for mefloquine-artesunate (0·60, 0·31-1·10), and 99·3% for tribendimidine (1·00, 0·44-2·30).** Most adverse events were mild or moderate and affected all treatment groups; serious adverse events--vertigo, nausea, vomiting, and anxiety--were reported only by patients taking mefloquine or mefloquine-artesunate. INTERPRETATION: Tribendimidine seems to be at least as efficacious as the drug of choice, praziquantel, for the treatment of O viverrini infections; both drugs were well tolerated. Mefloquine, artesunate, and mefloquine-artesunate did not show an effect. Tribendimidine should be further investigated with large clinical trials.

Clin Infect Dis. 2010 Dec 15;51(12):1420-8. Epub 2010 Nov 9.

Albendazole and mebendazole administered alone or in combination with ivermectin against Trichuris trichiura: a randomized controlled trial.

Knopp S, Mohammed KA, Speich B, Hattendorf J, Khamis IS, Khamis AN, Stothard JR, Rollinson D, Marti H, Utzinger J.

Source

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Abstract

BACKGROUND: Single-dose albendazole and mebendazole show limited efficacy in the treatment of trichuriasis. The combination of albendazole with ivermectin improves efficacy, but

a mebendazole-ivermectin combination has not been previously investigated. METHODS: We performed a randomized controlled trial in 2 schools in Zanzibar, Tanzania, to assess the **efficacy and safety of albendazole (400 mg) plus placebo, albendazole plus ivermectin (200 µg/kg), mebendazole (500 mg) plus placebo, and mebendazole plus ivermectin in children with a parasitologically confirmed Trichuris trichiura infection.** Cure rate (CR) and egg reduction rate were assessed by intent-to-treat analysis. Adverse events were monitored within 48 h after treatment. RESULTS: Complete data records were available for 548 children. **The highest CR against T. trichiura was achieved with a mebendazole-ivermectin combination (55%). Low CRs were observed with albendazole-ivermectin (38%), mebendazole (19%), and albendazole (10%).** Compared with placebo, the use of ivermectin statistically significantly increased the CRs from 14% to 47% (odds ratio, 0.19; 95% confidence interval [CI], 0.12-0.28). The highest egg reduction rate (97%; 95% CI, 95%-98%) was observed using the mebendazole-ivermectin combination, followed by albendazole-ivermectin (91%; 95% CI, 87%-94%), mebendazole (67%; 95% CI, 52%-77%), and albendazole (40%; 95% CI, 22%-56%). The adverse events, reported by 136 children, were generally mild, with no significant difference between the treatment arms. CONCLUSIONS: **Addition of ivermectin improves the therapeutic outcomes of both albendazole and mebendazole against T. trichiura and may be considered for use in soil-transmitted helminth control programs and individual patient management.**

Hygiene

Trop Med Int Health. 2010 Dec;15(12):1508-16. doi: 10.1111/j.1365-3156.2010.02648.x. Epub 2010 Oct 19.

A community-randomised controlled trial promoting waterless hand sanitizer and handwashing with soap, Dhaka, Bangladesh.

Luby SP, Kadir MA, Yushuf Sharker MA, Yeasmin F, Unicomb L, Sirajul Islam M.

Source

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Abstract

OBJECTIVES: To pilot two intensive hand hygiene promotion interventions, one using soap and one using a waterless hand sanitizer, in low-income housing compounds in Dhaka, Bangladesh and assess subsequent changes in handwashing behaviour and hand microbiology. METHODS: **Fieldworkers randomized 30 housing compounds: 10 received handwashing promotion with free soap, 10 received handwashing promotion with free waterless hand sanitizer and 10 were non-intervention controls.** Fieldworkers assessed handwashing behaviour by structured observation and collected hand rinse specimens. RESULTS: At baseline, compound residents washed their hands with soap 26% of the time after defecation and 30% after cleaning a child's anus but <1% at other times. **Compared with baseline, residents of soap intervention compounds were much more likely to wash their hands with soap after faecal contact (85-91%), before preparing food (26%) and before eating (26%).** Compounds that received waterless hand sanitizer cleansed their hands more commonly than control compounds that used soap (10.4%vs. 2.3%), but less commonly than soap intervention compounds used soap (25%). Post-intervention hand rinse samples from soap and sanitizer compounds had lower concentrations of faecal indicator bacteria compared with baseline and

control compounds. CONCLUSIONS: **Waterless hand sanitizer was readily adopted by this low-income community and reduced hand contamination but did not improve the frequency of handwashing compared with soap.** Future deployments of waterless hand sanitizers may improve hand hygiene more effectively by targeting settings where soap and water is unavailable.

Integrated management of childhood illness

PLoS Med. 2010 Sep 21;7(9):e1000340.

Community case management of fever due to malaria and pneumonia in children under five in Zambia: a cluster randomized controlled trial.

Yeboah-Antwi K, Pilingana P, Macleod WB, Semrau K, Siazeele K, Kalesha P, Hamainza B, Seidenberg P, Mazimba A, Sabin L, Kamholz K, Thea DM, Hamer DH.

Source

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Abstract

BACKGROUND: Pneumonia and malaria, two of the leading causes of morbidity and mortality among children under five in Zambia, often have overlapping clinical manifestations. Zambia is piloting the use of artemether-lumefantrine (AL) by community health workers (CHWs) to treat uncomplicated malaria. Valid concerns about potential overuse of AL could be addressed by the use of malaria rapid diagnostics employed at the community level. Currently, CHWs in Zambia evaluate and treat children with suspected malaria in rural areas, but they refer children with suspected pneumonia to the nearest health facility. This study was designed to assess the effectiveness and feasibility of using CHWs to manage nonsevere pneumonia and uncomplicated malaria with the aid of rapid diagnostic tests (RDTs). METHODS AND FINDINGS: Community health posts staffed by CHWs were matched and randomly allocated to intervention and control arms. Children between the ages of 6 months and 5 years were managed according to the study protocol, as follows. **Intervention CHWs performed RDTs, treated test-positive children with AL, and treated those with nonsevere pneumonia (increased respiratory rate) with amoxicillin. Control CHWs did not perform RDTs, treated all febrile children with AL, and referred those with signs of pneumonia to the health facility, as per Ministry of Health policy.** The primary outcomes were the use of AL in children with fever and early and appropriate treatment with antibiotics for nonsevere pneumonia. A total of 3,125 children with fever and/or difficult/fast breathing were managed over a 12-month period. **In the intervention arm, 27.5% (265/963) of children with fever received AL compared to 99.1% (2066/2084) of control children (risk ratio 0.23, 95% confidence interval 0.14-0.38). For children classified with nonsevere pneumonia, 68.2% (247/362) in the intervention arm and 13.3% (22/203) in the control arm received early and appropriate treatment (risk ratio 5.32, 95% confidence interval 2.19-8.94). There were two deaths in the intervention and one in the control arm.** CONCLUSIONS: The potential for CHWs to use RDTs, AL, and amoxicillin to manage both malaria and pneumonia at the community level is promising and might reduce overuse of AL, as well as provide early and appropriate treatment to children with nonsevere pneumonia.

Comment
This is an important study showing that the use of RDTs for malaria by community health workers can result in more rational prescribing of artemether-lumefantrine, with significant decreases in inappropriate prescribing, and a significant increase in the prescribing of amoxicillin for pneumonia. CHWs adhered closely to the guidelines based on RDTs (in contrast to some earlier studies where health workers treated regardless of the result). Although not strictly a study of IMCI, this RCT explores the integration of management for two common diseases, and how to incorporate RDTs into IMCI algorithms is a current issue for many developing countries.

Leishmaniasis

Visceral leishmaniasis

PLoS Negl Trop Dis. 2010 Oct 26;4(10):e709.

Geographical variation in the response of visceral leishmaniasis to paromomycin in East Africa: a multicentre, open-label, randomized trial.

Hailu A, Musa A, Wasunna M, Balasegaram M, Yifru S, Mengistu G, Hurissa Z, Hailu W, Weldegebreal T, Tesfaye S, Makonnen E, Khalil E, Ahmed O, Fadlalla A, El-Hassan A, Raheem M, Mueller M, Koummuki Y, Rashid J, Mbui J, Mucee G, Njoroge S, Manduku V, Musibi A, Mutuma G, Kirui F, Lodenyo H, Mutea D, Kirigi G, Edwards T, Smith P, Muthami L, Royce C, Ellis S, Alobo M, Omollo R, Kesusu J, Owiti R, Kinuthia J; Leishmaniasis East **Africa** Platform (LEAP) group.

Source
Addis Ababa University, Addis Ababa, Ethiopia.

AbstractBACKGROUND: Visceral leishmaniasis (VL) is a major health problem in developing countries. The untreated disease is fatal, available treatment is expensive and often toxic, and drug resistance is increasing. Improved treatment options are needed. Paromomycin was shown to be an efficacious first-line treatment with low toxicity in India. METHODS: This was a 3-arm multicentre, open-label, randomized, controlled clinical trial **to compare three treatment regimens for VL in East Africa: paromomycin sulphate (PM) at 15 mg/kg/day for 21 days versus sodium stibogluconate (SSG) at 20 mg/kg/day for 30 days; and the combination of both dose regimens for 17 days.** The primary efficacy endpoint was cure based on parasite-free tissue aspirates taken 6 months after treatment. FINDINGS: Overall, 135 patients per arm were enrolled at five centres in Sudan (2 sites), Kenya (1) and Ethiopia (2), when the PM arm had to be discontinued due to poor efficacy. The trial has continued with the higher dose of PM as well as the combination of PM and SSG arms. These results will be reported later. Baseline patient characteristics were similar among treatment arms. **The overall cure with PM was significantly inferior to that with SSG (63.8% versus 92.2%; difference 28.5%, 95%CI 18.8% to 38.8%, p<0.001).** The efficacy of PM varied among centres and was significantly lower in Sudan (14.3% and 46.7%) than in Kenya (80.0%) and Ethiopia (75.0% and 96.6%). No major safety issues with PM were identified. CONCLUSION: **The efficacy of PM at 15 mg/kg/day for 21 days was inadequate, particularly in Sudan.** The efficacy of higher doses and the combination treatment warrant further studies.

PLoS Negl Trop Dis. 2010 Oct 26;4(10):e855.

Paromomycin for the treatment of visceral leishmaniasis in Sudan: a randomized, open-label, dose-finding study.

Musa AM, Younis B, Fadlalla A, Royce C, Balasegaram M, Wasunna M, Hailu A, Edwards T, Omollo R, Mudawi M, Kokwaro G, El-Hassan A, Khalil E.

Source

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Abstract

BACKGROUND: A recent study has shown that treatment of visceral leishmaniasis (VL) with the standard dose of 15 mg/kg/day of paromomycin sulphate (PM) for 21 days was not efficacious in patients in Sudan. We therefore decided **to test the efficacy of paramomycin for a longer treatment duration (15 mg/kg/day for 28 days) and at the higher dose of 20 mg/kg/day for 21 days.** METHODS: This randomized, open-label, dose-finding, phase II study assessed the two above high-dose PM treatment regimens. Patients with clinical features and positive bone-marrow aspirates for VL were enrolled. All patients received their assigned courses of PM intramuscularly and adverse events were monitored. Parasite clearance in bone-marrow aspirates was tested by microscopy at end of treatment (EOT, primary efficacy endpoint), 3 months (in patients who were not clinically well) and 6 months after EOT (secondary efficacy endpoint). Pharmacokinetic data were obtained from a subset of patients weighing over 30 kg. FINDINGS: **42 patients (21 per group) aged between 4 and 60 years were enrolled.** At EOT, 85% of patients (95% confidence interval [CI]: 63.7% to 97.0%) in the 20 mg/kg/day group and 90% of patients (95% CI: 69.6% to 98.8%) in the 15 mg/kg/day group had parasite clearance. **Six months after treatment, efficacy was 80.0% (95% CI: 56.3% to 94.3%) and 81.0% (95% CI: 58.1% to 94.6%) in the 20 mg/kg/day and 15 mg/kg/day groups, respectively.** There were no serious adverse events. Pharmacokinetic profiles suggested a difference between the two doses, although numbers of patients recruited were too few to make it significant (n = 3 and n = 6 in the 20 mg/kg/day and 15 mg/kg/day groups, respectively). CONCLUSION: **Data suggest that both high dose regimens were more efficacious than the standard 15 mg/kg/day PM for 21 days and could be further evaluated in phase III studies in East Africa.**

Comment

The above two studies follow-on from each other. After finding that standard dose paramycin for 21 days was inadequate, investigators in Sudan conducted a study with high doses or for longer duation, finding higher cure rates than in the previous trial. Other investigators in India (below) evaluated combination drug treatment for visceral leishmaniasis with amphetericin B alone, or amphetericin B and miltefosine, or paramycin and miltefisine, finding even more complete cure rates.

Lancet. 2011 Feb 5;377(9764):477-86. Epub 2011 Jan 20.

Comparison of short-course multidrug treatment with standard therapy for visceral leishmaniasis in India: an open-label, non-inferiority, randomised controlled trial.

Sundar S, Sinha PK, Rai M, Verma DK, Nawin K, Alam S, Chakravarty J, Vaillant M, Verma N, Pandey K, Kumari P, Lal CS, Arora R, Sharma B, Ellis S, Strub-Wourgaft N, Balasegaram M, Olliaro P, Das P, Modabber F.

Source

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Abstract

BACKGROUND: Improved treatment approaches are needed for visceral leishmaniasis. We assessed the efficacy and safety of three potential short-course combination treatments compared with the standard monotherapy in India. METHODS: **Standard treatment (1 mg/kg amphotericin B infusion on alternate days for 30 days, total dose 15 mg/kg) was compared with three drug combinations (single injection of 5 mg/kg liposomal amphotericin B and 7-day 50 mg oral miltefosine or single 10-day 11 mg/kg intramuscular paromomycin; or 10 days each of miltefosine and paromomycin) in an open-label, parallel-group, non-inferiority, randomised controlled trial in two hospital sites in Bihar, India.** Patients aged 5-60 years with parasitologically confirmed visceral leishmaniasis were randomly assigned one of the four treatments by the trial statistician by use of a computer-generated list. Clinical assessments were done at the end of treatment (15 days on combination treatment; 31 days for standard treatment) and after 45 days and 6 months. The primary endpoint was definitive cure (defined as no sign or symptom of visceral leishmaniasis and parasitologically cured to the last follow-up). Analyses were done both by intention to treat and per protocol. This trial is registered with ClinicalTrials.gov, number NCT00696969. FINDINGS: Between June, 2008, and July, 2009, **634 patients were assigned amphotericin B (n=157), liposomal amphotericin B with miltefosine (n=160) or paromomycin (n=158), or miltefosine and paromomycin (n=159). 618 patients were in the per-protocol population.** There were two relapses in each group. **The numbers with definitive cure at 6 months for the intention-to-treat population were 146 (cure rate 93·0%; CI 87·5-96·3) for amphotericin B, 156 (97·5%; 93·3-99·2) for liposomal amphotericin B and miltefosine, 154 (97·5%; 93·24-99·2) for liposomal amphotericin B and paromomycin, and 157 (98·7%; 95·1-99·8) for miltefosine and paromomycin.** All combinations were non-inferior to the standard treatment, in both the intention-to-treat and per-protocol populations. Patients in the combination groups had fewer adverse events than did those assigned standard treatment. INTERPRETATION: **Combination treatments for visceral leishmaniasis are efficacious and safe, and decrease the duration of therapy, thereby encouraging adherence and reducing emergence of drug-resistant parasites**.

THE LANCET
FULL-TEXT ARTICLE

Cutaneous leismaniasis

PLoS Negl Trop Dis. 2010 Dec 21;4(12):e912.

Miltefosine in the treatment of cutaneous leishmaniasis caused by Leishmania braziliensis in Brazil: a randomized and controlled trial.

Machado PR, Ampuero J, Guimarães LH, Villasboas L, Rocha AT, Schriefer A, Sousa RS, Talhari A, Penna G, Carvalho EM.

Source

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Abstract

BACKGROUND: Cutaneous leishmaniasis (CL) is treated with parenteral drugs for decades with decreasing rate cures. Miltefosine is an oral medication with anti-leishmania activity and may increase the cure rates and improve compliance. METHODOLOGY/PRINCIPAL FINDINGS: This study is a randomized, open-label, controlled clinical trial aimed **to evaluate the efficacy and safety of miltefosine versus pentavalent antimony (Sb(v)) in the treatment of patients with CL caused by Leishmania braziliensis in Bahia, Brazil.** A total of 90 patients were enrolled in the trial; 60 were assigned to receive miltefosine and 30 to receive Sb(v). **Six months after treatment, in the intention-to-treat analyses, the definitive cure rate was 53.3% in the Sb(v) group and 75% in the miltefosine group (difference of 21.7%, 95% CI 0.08% to 42.7%, p=0.04).** Miltefosine was more effective than Sb(v) in the age group of 13-65 years-old compared to 2-12 years-old group (78.9% versus 45% p = 0.02; 68.2% versus 70% p = 1.0, respectively). The incidence of adverse events was similar in the Sb(v) and miltefosine groups (76.7% vs. 78.3%). Vomiting (41.7%), nausea (40%), and abdominal pain (23.3%) were significantly more frequent in the miltefosine group while arthralgias (20.7%), mialgias (20.7%) and fever (23.3%) were significantly more frequent in the Sb(v) group. CONCLUSIONS: **This study demonstrates that miltefosine therapy is more effective than standard Sb(v)** and safe for the treatment of CL caused by Leishmania braziliensis in Bahia, Brazil.

Am J Trop Med Hyg. 2011 Feb;84(2):255-60.

Randomized controlled clinical trial to access efficacy and safety of miltefosine in the treatment of cutaneous leishmaniasis Caused by Leishmania (Viannia) guyanensis in Manaus, Brazil.

Chrusciak-Talhari A, Dietze R, Chrusciak Talhari C, da Silva RM, Gadelha Yamashita EP, de Oliveira Penna G, Lima Machado PR, Talhari S.

Source

Fundação de Medicina Tropical do Amazonas and Universidade Estadual do Amazonas, Manaus, AM, Brasil. anettetalhari@terra.com.br

Abstract

Miltefosine has been used in the treatment of several new world cutaneous leishmaniasis (CL) species with variable efficacy. Our study is the first evidence on its clinical efficacy in

Leishmania (Viannia) guyanensis. In this phase II/III randomized clinical trial, **90 CL patients were randomly allocated (2:1) to oral miltefosine (2.5 mg/kg/day/28 days) (N = 60) or parenteral antimony (15-20 mg/Sb/kg/day/20 days) (N = 30) according to age groups: 2-12 y/o and 13-65 y/o.** Patients were human immunodeficiency virus (HIV) noninfected parasitological proven CL without previous treatment. Definitive cure was accessed at 6 months follow-up visit. No severe adverse events occurred. Vomiting was the most frequent adverse event (48.3%) followed by nausea (8.6%) and diarrhea (6.7%). **Cure rates were 71.4% (95% confidence interval [CI] = 57.8-82.7) and 53.6% (95% CI = 33.9-72.5) (P = 0.05) for miltefosine and antimonial, respectively.** There were no differences in cure rates between age groups within the same treatment arms. Miltefosine was safe and relatively well tolerated and cure rate was higher than antimony.

Malaria

Malar J. 2011 Mar 15;10:61.

Randomized controlled trials of malaria intervention trials in Africa, 1948 to 2007: a descriptive analysis.

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Abstract

BACKGROUND: Nine out of ten deaths from malaria occur in sub-Saharan Africa. Various control measures have achieved some progress in the control of the disease, but malaria is still a major public health problem in Africa. Randomized controlled trials (RCTs) are universally considered the best study type to rigorously assess whether an intervention is effective. The study reported here provides a descriptive analysis of RCTs reporting interventions for the prevention and treatment of malaria conducted in Africa, with the aim of providing detailed information on their main clinical and methodological characteristics, that could be used by researchers and policy makers to help plan future research. METHODS: Systematic searches for malaria RCTs were conducted using electronic databases (Medline, Embase, the Cochrane Library), and an African geographic search filter to identify RCTs conducted in Africa was applied. Results were exported to the statistical package STATA 8 to obtain a random sample from the overall data set. Final analysis of trial characteristics was done in a double blinded fashion by two authors using a standardized data extraction form. RESULTS: A random sample of 92 confirmed RCTs (from a total of 943 reports obtained between 1948 and 2007) was prepared. **Most trials investigated drug treatment in children with uncomplicated malaria. Few trials reported on treatment of severe malaria or on interventions in pregnant women.** Most trials were of medium size (100-500 participants), individually randomized and based in a single centre. Reporting of trial quality was variable. Although three-quarter of trials provided information on participants' informed consent and ethics approval, more details are needed. CONCLUSIONS: The majority of malaria RCT conducted in Africa report on drug treatment and prevention in children; there is need for more research done in pregnant women. Sources of funding, informed consent and trial quality were often poorly reported. Overall, clearer reporting of trials is needed.

Malaria vaccines

J Infect Dis. 2010 Oct 1;202(7):1076-87.

Evaluation of the safety and immunogenicity of the RTS,S/AS01E malaria candidate vaccine when integrated in the expanded program of immunization.

Agnandji ST, Asante KP, Lyimo J, Vekemans J, Soulanoudjingar SS, Owusu R, Shomari M, Leach A, Fernandes J, Dosoo D, Chikawe M, Issifou S, Osei-Kwakye K, Lievens M, Paricek M, Apanga S, Mwangoka G, Okissi B, Kwara E, Minja R, Lange J, Boahen O, Kayan K, Adjei G, Chandramohan D, Jongert E, Demoitié MA, Dubois MC, Carter T, Vansadia P, Villafana T, Sillman M, Savarese B, Lapierre D, Ballou WR, Greenwood B, Tanner M, Cohen J, Kremsner PG, Lell B, Owusu-Agyei S, Abdulla S.

Source

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Abstract

BACKGROUND: The RTS,S/AS01(E) malaria candidate vaccine is being developed for immunization of African infants through the Expanded Program of Immunization (EPI). METHODS: This phase 2, randomized, open, controlled trial conducted in Ghana, Tanzania, and Gabon evaluated the safety and immunogenicity of RTS,S/AS01(E) when coadministered with EPI vaccines. **Five hundred eleven infants were randomized to receive RTS,S/AS01(E) at 0, 1, and 2 months** (in 3 doses with diphtheria, tetanus, and whole-cell pertussis conjugate [DTPw]; hepatitis B [HepB]; Haemophilus influenzae type b [Hib]; and oral polio vaccine [OPV]), RTS,S/AS01(E) at 0, 1, and 7 months (2 doses with DTPwHepB/Hib+OPV and 1 dose with measles and yellow fever), **or EPI vaccines only**. RESULTS: The occurrences of serious adverse events were balanced across groups; none were vaccine-related. One child from the control group died. Mild to moderate fever and diaper dermatitis occurred more frequently in the RTS,S/AS01(E) coadministration groups. RTS,S/AS01(E) generated high anti-circumsporozoite protein and anti-hepatitis B surface antigen antibody levels. Regarding EPI vaccine responses upon coadministration when considering both immunization schedules, despite a tendency toward lower geometric mean titers to some EPI antigens, predefined noninferiority criteria were met for all EPI antigens except for polio 3 when EPI vaccines were given with RTS,S/AS01(E) at 0, 1, and 2 months. However, when antibody levels at screening were taken into account, the rates of response to polio 3 antigens were comparable between groups. CONCLUSION: **RTS,S/AS01(E) integrated in the EPI showed a favorable safety and immunogenicity evaluation.** Trial registration. ClinicalTrials.gov identifier: NCT00436007 . GlaxoSmithKline study ID number: 106369 (Malaria-050).

PLoS One. 2010 Nov 4;5(11):e13838.

Safety, immunogenicity and duration of protection of the RTS,S/AS02(D) malaria vaccine: one year follow-up of a randomized controlled phase I/IIb trial.

Aide P, Aponte JJ, Renom M, Nhampossa T, Sacarlal J, Mandomando I, Bassat Q, Manaca MN, Leach A, Lievens M, Vekemans J, Dubois MC, Loucq C, Ballou WR, Cohen J, Alonso PL.

Source

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Abstract
BACKGROUND: The RTS,S/AS02(D) vaccine has been shown to have a promising safety profile, to be immunogenic and to confer protection against malaria in children and infants. METHODS AND FINDINGS: **We did a randomized, controlled, phase I/IIb trial of RTS,S/AS02(D) given at 10, 14 and 18 weeks of age staggered with routine immunization vaccines in 214 Mozambican infants.** The study was double-blind until the young child completed 6 months of follow-up over which period vaccine efficacy against new Plasmodium falciparum infections was estimated at 65.9% (95% CI 42.6-79.8, p<0.0001). We now report safety, immunogenicity and estimated efficacy against clinical malaria up to 14 months after study start. Vaccine efficacy was assessed using Cox regression models. The frequency of serious adverse events was 32.7% in the RTS,S/AS02(D) and 31.8% in the control group. The geometric mean titers of anti-circumsporozoite antibodies declined from 199.9 to 7.3 EU/mL from one to 12 months post dose three of RTS,S/AS02(D), remaining 15-fold higher than in the control group. **Vaccine efficacy against clinical malaria was 33% (95% CI: -4.3-56.9, p = 0.076) over 14 months of follow-up.** The hazard rate of disease per 2-fold increase in anti-CS titers was reduced by 84% (95% CI 35.1-88.2, p = 0.003). CONCLUSION: **The RTS,S/AS02(D) malaria vaccine administered to young infants has a good safety profile and remains efficacious over 14 months.** A strong association between anti-CS antibodies and risk of clinical malaria has been described for the first time. The results also suggest a decrease of both anti-CS antibodies and vaccine efficacy over time.

PLoS One. 2010 Nov 29;5(11):e14090.
Safety of the malaria vaccine candidate, RTS,S/AS01E in 5 to 17 month old Kenyan and Tanzanian Children.
Lusingu J, Olotu A, Leach A, Lievens M, Vekemans J, Olivier A, Benns S, Olomi R, Msham S, Lang T, Gould J, Hallez K, Guerra Y, Njuguna P, Awuondo KO, Malabeja A, Abdul O, Gesase S, Dekker D, Malle L, Ismael S, Mturi N, Drakeley CJ, Savarese B, Villafana T, Ballou WR, Cohen J, Riley EM, Lemnge MM, Marsh K, Bejon P, von Seidlein L.
Source
National Institute for Medical Research, Tanga, Tanzania.
Abstract
The malaria vaccine candidate, RTS,S/AS01(E), showed promising protective efficacy in a trial of Kenyan and Tanzanian children aged 5 to 17 months. Here we report on the vaccine's safety and tolerability. The experimental design was a Phase 2b, two-centre, double-blind (observer- and participant-blind), randomised (1 1 ratio) controlled trial. Three doses of study or control (rabies) vaccines were administered intramuscularly at 1 month intervals. Solicited adverse events (AEs) were collected for 7 days after each vaccination. There was surveillance and reporting for unsolicited adverse events for 30 days after each vaccination. Serious adverse events (SAEs) were recorded throughout the study period which lasted for 14 months after dose 1 in Korogwe, Tanzania and an average of 18 months post-dose 1 in Kilifi, Kenya. Blood samples for safety monitoring of haematological, renal and hepatic functions were taken at baseline, 3, 10 and 14 months after dose 1. A total of 894 children received RTS,S/AS01(E) or rabies vaccine between March and August 2007. Overall, children vaccinated with RTS,S/AS01(E) had fewer SAEs (51/447) than children in the control group (88/447). One SAE episode in a RTS,S/AS01(E) recipient and nine episodes among eight rabies vaccine recipients met the criteria for severe malaria. Unsolicited AEs were reported in 78% of subjects in the RTS,S/AS01(E) group and 74% of subjects in the rabies vaccine group. In both vaccine groups, gastroenteritis and pneumonia were the most frequently reported unsolicited AE. Fever was the

most frequently observed solicited AE and was recorded after 11% of RTS,S/AS01(E) doses compared to 31% of doses of rabies vaccine. **The candidate vaccine RTS,S/AS01(E) showed an acceptable safety profile in children living in a malaria-endemic area in East Africa.** More data on the safety of RTS,S/AS01(E) will become available from the Phase 3 programme.

Lancet Infect Dis. 2011 Feb;11(2):102-9. Epub 2011 Jan 13.

Efficacy of RTS,S/AS01E malaria vaccine and exploratory analysis on anti-circumsporozoite antibody titres and protection in children aged 5-17 months in Kenya and Tanzania: a randomised controlled trial.

Olotu A, Lusingu J, Leach A, Lievens M, Vekemans J, Msham S, Lang T, Gould J, Dubois MC, Jongert E, Vansadia P, Carter T, Njuguna P, Awuondo KO, Malabeja A, Abdul O, Gesase S, Mturi N, Drakeley CJ, Savarese B, Villafana T, Lapierre D, Ballou WR, Cohen J, Lemnge MM, Peshu N, Marsh K, Riley EM, von Seidlein L, Bejon P.

Source

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Abstract

BACKGROUND: RTS,S/AS01E is the lead candidate malaria vaccine. We recently showed efficacy against clinical falciparum malaria in 5-17 month old children, during an average of 8 months follow-up. We aimed to assess the efficacy of RTS,S/AS01E during 15 months of follow-up. METHODS: Between March, 2007, and October, 2008, we enrolled healthy children aged 5-17 months in Kilifi, Kenya, and Korogwe, Tanzania. Computer-generated block randomisation was used to randomly assign participants (1:1) to receive three doses (at month 0, 1, and 2) of either RTS,S/AS01E or human diploid-cell rabies vaccine. **The primary endpoint was time to first clinical malaria episode, defined as the presence of fever (temperature ≥37·5°C) and a Plasmodium falciparum density of 2500/μL or more**. Follow-up was 12 months for children from Korogwe and 15 months for children from Kilifi. Primary analysis was per protocol. In a post-hoc modelling analysis we characterised the associations between anti-circumsporozoite antibodies and protection against clinical malaria episodes. This study is registered with ClinicalTrials.gov, number NCT00380393. FINDINGS: **894 children were assigned, 447 in each treatment group. In the per-protocol analysis, 82 of 415 children in the RTS,S/AS01E group and 125 of 420 in the rabies vaccine group had first or only clinical malaria episode by 12 months, vaccine efficacy 39·2% (95% CI 19·5-54·1, p=0·0005). At 15 months follow-up, 58 of 209 children in the RTS,S/AS01E group and 85 of 206 in the rabies vaccine group had first or only clinical malaria episode, vaccine efficacy 45·8% (24·1-61·3, p=0·0004).** At 12 months after the third dose, anti-circumsporozoite antibody titre data were available for 390 children in the RTS,S/AS01E group and 391 in the rabies group. A mean of 15 months (range 12-18 months) data were available for 172 children in the RTS,S/AS01E group and 155 in the rabies group. These titres at 1 month after the third dose were not associated with protection, but titres at 6·5 months were. The level of protection increased abruptly over a narrow range of antibody concentrations. The most common adverse events were pneumonia, febrile convulsion, gastroenteritis, and P falciparum malaria. INTERPRETATION: **RTS,S/AS01E confers sustained efficacy for at least 15 months and shows promise as a potential public health intervention against childhood malaria in malaria endemic countries**.

Malar J. 2011 Jan 19;10:13.

Anaemia in a phase 2 study of a blood stage falciparum malaria vaccine.

Ellis RD, Fay MP, Sagara I, Dicko A, Miura K, Guindo MA, Guindo A, Sissoko MS, Doumbo OK, Diallo D.

Source

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Abstract

BACKGROUND: A Phase 1-2b study of the blood stage malaria vaccine AMA1-C1/Alhydrogel was conducted in 336 children in Donéguébougou and Bancoumana, Mali. In the Phase 2 portion of the study (n = 300), no impact on parasite density or clinical malaria was seen; however, children who received the study vaccine had a higher frequency of anaemia (defined as haemoglobin < 8.5 g/dL) compared to those who received the comparator vaccine (Hiberix). This effect was one of many tested and was not significant after adjusting for multiple comparisons. METHODS: To further investigate the possible impact of vaccination on anaemia, additional analyses were conducted including patients from the Phase 1 portion of the study and controlling for baseline haemoglobin, haemoglobin types S or C, alpha-thalassaemia, G6PD deficiency, and age. A multiplicative intensity model was used, which generalizes Cox regression to allow for multiple events. Frailty effects for each subject were used to account for correlation of multiple anaemia events within the same subject. Intensity rates were calculated with reference to calendar time instead of time after randomization in order to account for staggered enrollment and seasonal effects of malaria incidence. Associations of anaemia with anti-AMA1 antibody were further explored using a similar analysis. RESULTS: **A strong effect of vaccine on the incidence of anaemia (risk ratio [AMA1-C1 to comparator (Hiberix)]= 2.01, 95% confidence interval [1.26,3.20]) was demonstrated even after adjusting for baseline haemoglobin, haemoglobinopathies, and age, and using more sophisticated statistical models.** Anti-AMA1 antibody levels were not associated with this effect. CONCLUSIONS: While these additional analyses show a robust effect of vaccination on anaemia, this is an intensive exploration of secondary results and should, therefore, be interpreted with caution. Possible mechanisms of the apparent adverse effect on haemoglobin of vaccination with AMA1-C1/Alhydrogel and implications for blood stage vaccine development are discussed. The potential impact on malaria-associated anaemia should be closely evaluated in clinical trials of AMA1 and other blood stage vaccines in malaria-exposed populations.

Intermittent preventative treatment

Malar J. 2010 Aug 26;9:244.

Multiplicity of Plasmodium falciparum infection following intermittent preventive treatment in infants.

Buchholz U, Kobbe R, Danquah I, Zanger P, Reither K, Abruquah HH, Grobusch MP, Ziniel P, May J, Mockenhaupt FP.

Source

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Abstract

BACKGROUND: Intermittent preventive treatment in infants with sulphadoxine-pyrimethamine (IPTi-SP) reduces malaria morbidity by 20% to 33%. Potentially, however, this intervention may compromise the acquisition of immunity, including the tolerance towards multiple infections with Plasmodium falciparum. METHODS: Plasmodium falciparum isolates were obtained from children participating in two Ghanaian IPTi-SP trials (Tamale, Afigya Sekyere) at 15 months of age, i.e., six months after they had received the second dose of IPTi-SP or placebo. By typing the polymorphic merozoite surface protein 1 (msp1) and msp2 genes, multiplicity of infection (MOI) was assessed in 389 isolates. A total of additional 133 samples were collected in Tamale at 3, 6, 9, and 12 months of age. Comparisons of MOI between groups were done by non-parametric statistical tests. RESULTS: The number of distinguishable P. falciparum clones (MOI) ranged between one and six. Mean MOI in Tamale was stable at 2.13 - 2.17 during the first year of life, and increased to 2.57 at age 15 months ($P = 0.01$). At no age did MOI differ between the IPTi-SP and placebo groups (each, $P \geq 0.5$). At 15 months of age, i.e., six months after the second dose, MOI was very similar for children who had received IPTi or placebo (means, 2.25 vs. 2.33; $P = 0.55$) as was the proportion of polyclonal infections (69.6% vs. 69.7%; $P = 0.99$). Adjusting for study site, current and prior malaria, parasite density, and season did not change this finding. CONCLUSIONS: **IPTi-SP appears to have no impact on the multiplicity of infection during infancy and thereafter.** This suggests that tolerance of multiple infections, a component of protective immunity in highly endemic areas, is not affected by this intervention.

PLoS One. 2010 Aug 17;5(8):e12223.

Cost effectiveness of seasonal intermittent preventive treatment using amodiaquine & artesunate or sulphadoxine-pyrimethamine in Ghanaian children.

Conteh L, Patouillard E, Kweku M, Legood R, Greenwood B, Chandramohan D.

Source

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Abstract

BACKGROUND: Intermittent preventive treatment for malaria in children (IPTc) involves the administration of a full course of an anti-malarial treatment to children under 5 years old at specified time points regardless of whether or not they are known to be infected, in areas where malaria transmission is seasonal. It is important to determine the costs associated with IPTc delivery via community based volunteers and also the potential savings to health care providers and caretakers due to malaria episodes averted as a consequence of IPTc. METHODS: **Two thousand four hundred and fifty-one children aged 3-59 months were randomly allocated to four groups to receive: three days of artesunate plus amodiaquine (AS+AQ) monthly, three days of AS+AQ bimonthly, one dose of sulphadoxine-pyrimethamine (SP) bi-monthly or placebo.** This paper focuses on incremental cost effectiveness ratios (ICERs) of the three IPTc drug regimens as delivered by community based volunteers (CBV) in Hohoe, Ghana compared to current practice, i.e. case management in the absence of IPTc. Financial and economic costs from the publicly funded health system perspective are presented. Treatment costs borne by patients and their caretakers are also estimated to present societal costs. The costs

and effects of IPTc during the intervention period were considered with and without a one year follow up. Probabilistic sensitivity analysis was undertaken to account for uncertainty. RESULTS: **Economic costs per child receiving at least the first dose of each course of IPTc show SP bimonthly, at US$8.19, is the cheapest to deliver, followed by AS+AQ bimonthly at US$10.67 and then by AS+AQ monthly at US$14.79. Training, drug delivery and supervision accounted for approximately 20-30% each of total unit costs.** During the intervention period AS & AQ monthly was the most cost effective IPTc drug regimen at US$67.77 (61.71-74.75, CI 95%) per malaria case averted based on intervention costs only, US$64.93 (58.92-71.92, CI 95%) per malaria case averted once the provider cost savings are included and US$61.00 (54.98, 67.99, CI 95%) when direct household cost savings are also taken into account. SP bimonthly was US$105.35 (75.01-157.31, CI 95%) and AS & AQ bimonthly US$211.80 (127.05-399.14, CI 95%) per malaria case averted based on intervention costs only. The incidence of malaria in the post intervention period was higher in children who were <1 year old when they received AS+AQ monthly compared to the placebo group leading to higher cost effectiveness ratios when one year follow up is included. The cost per child enrolled fell considerably when modelled to district level as compared to those encountered under trial conditions. CONCLUSIONS: We demonstrate how cost-effective IPTc is using three different drug regimens and the possibilities for reducing costs further if the intervention was to be scaled up to the district level. The need for effective training, drug delivery channels and supervision to support a strong network of community based volunteers is emphasised.

PLoS One. 2010 Oct 19;5(10):e13438.

Efficacy, safety, and tolerability of three regimens for prevention of malaria: a randomized, placebo-controlled trial in Ugandan schoolchildren.

Nankabirwa J, Cundill B, Clarke S, Kabatereine N, Rosenthal PJ, Dorsey G, Brooker S, Staedke SG.

Source

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Abstract

BACKGROUND: Intermittent preventive treatment (IPT) is a promising malaria control strategy; however, the optimal regimen remains unclear. We conducted a randomized, single-blinded, placebo-controlled trial to evaluate the efficacy, safety, and tolerability of a single course of sulfadoxine-pyrimethamine (SP), amodiaquine + SP (AQ+SP) or dihydroartemisinin-piperaquine (DP) among schoolchildren to inform IPT. METHODS: **Asymptomatic girls aged 8 to 12 years and boys aged 8 to 14 years enrolled in two primary schools in Tororo, Uganda were randomized to receive one of the study regimens or placebo, regardless of presence of parasitemia at enrollment, and followed for 42 days.** The primary outcome was risk of parasitemia at 42 days. Survival analysis was used to assess differences between regimens. RESULTS: Of 780 enrolled participants, 769 (98.6%) completed follow-up and were assigned a treatment outcome. **The risk of parasitemia at 42 days varied significantly between DP (11.7% [95% confidence interval (CI): 7.9, 17.1]), AQ+SP (44.3% [37.6, 51.5]), and SP (79.7% [95% CI: 73.6, 85.2], p<0.001). The risk of parasitemia in SP-treated children was no different than in those receiving placebo (84.6% [95% CI: 79.1, 89.3], p = 0.22).** No serious adverse events occurred, but AQ+SP was associated with increased risk of vomiting compared to placebo (13.0% [95% CI: 9.1, 18.5] vs. 4.7% [95% CI: 2.5, 8.8], respectively, p = 0.003). CONCLUSIONS: **DP was the most efficacious and well-tolerated regimen tested, although AQ+SP appears to be a suitable alternative for IPT in**

schoolchildren. Use of SP for IPT may not be appropriate in areas with high-level SP resistance in Africa.

PLoS One. 2010 Oct 27;5(10):e13649.

Influences of intermittent preventive treatment and persistent multiclonal Plasmodium falciparum infections on clinical malaria risk.

Liljander A, Chandramohan D, Kweku M, Olsson D, Montgomery SM, Greenwood B, Färnert A.

Source

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Abstract

BACKGROUND: Intermittent preventive treatment (IPT) of malaria involves administration of curative doses of antimalarials at specified time points to vulnerable populations in endemic areas, regardless whether a subject is known to be infected. The effect of this new intervention on the development and maintenance of protective immunity needs further understanding. We have investigated how seasonal IPT affects the genetic diversity of Plasmodium falciparum infections and the risk of subsequent clinical malaria. MATERIAL AND METHODS: **The study included 2227 Ghanaian children (3-59 months) who were given sulphadoxine-pyrimethamine (SP) bimonthly, artesunate plus amodiaquine (AS+AQ) monthly or bimonthly, or placebo monthly for six months spanning the malaria transmission season.** Blood samples collected at three post-interventional surveys were analysed by genotyping of the polymorphic merozoite surface protein 2 gene. Malaria morbidity and anaemia was monitored during 12 months follow-up. RESULTS: Monthly IPT with AS+AQ resulted in a marked reduction in number of concurrent clones and only children parasite negative just after the intervention period developed clinical malaria during follow-up. In the placebo group, children without parasites as well as those infected with ≥2 clones had a reduced risk of subsequent malaria. The bimonthly SP or AS+AQ groups had similar number of clones as placebo after intervention; however, diversity and parasite negativity did not predict the risk of malaria. An interaction effect showed that multiclonal infections were only associated with protection in children without intermittent treatment. CONCLUSION: Molecular typing revealed effects of the intervention not detected by ordinary microscopy. **Effective seasonal IPT temporarily reduced the prevalence and genetic diversity of P. falciparum infections.** The reduced risk of malaria in children with multiclonal infections only seen in untreated children suggests that persistence of antigenically diverse P. falciparum infections is important for the maintenance of protective malaria immunity in high transmission settings.

Trop Med Int Health. 2011 Mar;16(3):280-9. doi: 10.1111/j.1365-3156.2010.02699.x. Epub 2010 Dec 16.

The clinical impact of combining intermittent preventive treatment with home management of malaria in children aged below 5 years: cluster randomised trial.

Tagbor H, Cairns M, Nakwa E, Browne E, Sarkodie B, Counihan H, Meek S, Chandramohan D.

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Abstract

OBJECTIVE: To investigate the impact of seasonal intermittent preventive treatment (IPTc) on malaria-related morbidity in children <5 years of age who already had access to home-based management of malaria (HMM) for presumptive treatment of fevers. METHOD: Thirty community-based drug distributors (CDDs) from all 13 communities of a rural subdistrict in Ghana were trained to provide prompt treatment for presumptive malaria using artesunate-amodiaquine (AS+AQ) to all children under 5 years of age. **Six communities were randomised to also receive bimonthly courses of seasonal IPTc with AS+AQ in May, July and September of 2007.** The primary outcome was the incidence rate of febrile episodes diagnosed presumptively as malaria by the CDDs in the communities in each intervention group. Cross-sectional surveys were conducted to determine the prevalence of parasitaemia and anaemia among the study children. RESULTS: **During the 6 months in which IPTc was delivered, incidence of fevers in communities given HMM+IPTc was lower than in communities given HMM alone, but this difference was not statistically significant (protective efficacy: 37.0%(95% CI: -9.7 to 63.8; P = 0.14).** However, incidence of presumptive malaria was significantly lower in IPTc communities when only children who received all three courses of IPTc were included in the analysis: protective 0.018). Protection with IPTc was not = efficacy 61.5% (95% CI:31.2-78.5; P followed by rebound morbidity in the following year. **At the end of the intervention period, prevalence of asymptomatic parasitaemia was lower in communities that had received IPTc, but there were no differences in anaemia or haemoglobin concentration.** CONCLUSION: In this study area, incidence of fevers was lower in communities given three courses of IPTc during the time of peak transmission than in communities that received only HMM. However, high levels of coverage for IPTc will be necessary for maximum impact.

Malar J. 2011 Jan 7;10:2.

A trial of intermittent preventive treatment and home-based management of malaria in a rural area of The Gambia.

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Medical Research Council Laboratories, Banjul, The Gambia.

Abstract

BACKGROUND: Individual malaria interventions provide only partial protection in most epidemiological situations. Thus, there is a need to investigate whether combining interventions provides added benefit in reducing mortality and morbidity from malaria. The potential benefits of combining IPT in children (IPTc) with home management of malaria (HMM) was investigated. METHODS: During the 2008 malaria transmission season, 1,277 children under five years of age resident in villages within the rural Farafenni demographic surveillance system (DSS) in North Bank Region, The Gambia were randomized to receive monthly IPTc with a single dose of sulphadoxine/pyrimethamine (SP) plus three doses of amodiaquine (AQ) or SP and AQ placebos given by village health workers (VHWs) on three occasions during the months of September, October and November, in a double-blind trial. Children in all study villages who developed an acute febrile illness suggestive of malaria were treated by VHWs who had been taught how to manage malaria with artemether-lumefantrine (Coartem™). **The primary aims of the project were to determine whether IPTc added significant benefit to HMM and**

whether VHWs could effectively combine the delivery of both interventions. RESULTS: The incidence of clinical attacks of malaria was very low in both study groups. **The incidence rate of malaria in children who received IPTc was 0.44 clinical attacks per 1,000 child months at risk while that for control children was 1.32 per 1,000 child months at risk, a protective efficacy of 66% (95% CI -23% to 96%; p = 0.35).** The mean (standard deviation) haemoglobin concentration at the end of the malaria transmission season was similar in the two treatment groups: 10.2 (1.6) g/dL in the IPTc group compared to 10.3 (1.5) g/dL in the placebo group. Coverage with IPTc was high, with 94% of children receiving all three treatments during the study period. CONCLUSION: Due to the very low incidence of malaria, no firm conclusion can be drawn on the added benefit of IPTc in preventing clinical episodes of malaria among children who had access to HMM in The Gambia. However, the study showed that VHWs can successfully combine provision of HMM with provision of IPTc.

PLoS Med. 2011 Feb 1;8(2):e1000408.

Intermittent preventive treatment of malaria provides substantial protection against malaria in children already protected by an insecticide-treated bednet in Burkina Faso: a randomised, double-blind, placebo-controlled trial.

Konaté AT, Yaro JB, Ouédraogo AZ, Diarra A, Gansané A, Soulama I, Kangoyé DT, Kaboré Y, Ouédraogo E, Ouédraogo A, Tiono AB, Ouédraogo IN, Chandramohan D, Cousens S, Milligan PJ, Sirima SB, Greenwood B, Diallo DA.

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Abstract

BACKGROUND: Intermittent preventive treatment of malaria in children (IPTc) is a promising new approach to the control of malaria in areas of seasonal malaria transmission but it is not known if IPTc adds to the protection provided by an insecticide-treated net (ITN). METHODS AND FINDINGS: An individually randomised, double-blind, placebo-controlled trial of seasonal IPTc was conducted in Burkina Faso in children aged 3 to 59 months who were provided with a long-lasting insecticide-treated bednet (LLIN). **Three rounds of treatment with sulphadoxine pyrimethamine plus amodiaquine or placebos were given at monthly intervals during the malaria transmission season.** Passive surveillance for malaria episodes was established, a cross-sectional survey was conducted at the end of the malaria transmission season, and use of ITNs was monitored during the intervention period. Incidence rates of malaria were compared using a Cox regression model and generalized linear models were fitted to examine the effect of IPTc on the prevalence of malaria infection, anaemia, and on anthropometric indicators. 3,052 children were screened and 3,014 were enrolled in the trial; 1,505 in the control arm and 1,509 in the intervention arm. Similar proportions of children in the two treatment arms were reported to sleep under an LLIN during the intervention period (93%). The incidence of malaria, defined as fever or history of fever with parasitaemia ≥ 5,000/µl, was 2.88 (95% confidence interval [CI] 2.70-3.06) per child during the intervention period in the control arm versus 0.87 (95% CI 0.78-0.97) in the intervention arm, a protective efficacy (PE) of 70% (95% CI 66%-74%) (p<0.001). **There was a 69% (95% CI 6%-90%) reduction in incidence of severe malaria (p = 0.04) and a 46% (95% CI 7%-69%) (p = 0.03) reduction in the incidence of all-cause hospital admissions.** IPTc reduced the prevalence of malaria infection at the end of the malaria transmission season by 73% (95% CI 68%-77%) (p<0.001) and that of moderately severe anaemia by 56% (95% CI 36%-70%) (p<0.001). IPTc reduced the risks of wasting (risk ratio [RR] = 0.79; 95% CI 0.65-1.00) (p = 0.05) and of being underweight (RR = 0.84; 95% CI 0.72-0.99) (p = 0.03). Children who received IPTc were 2.8

(95% CI 2.3-3.5) (p<0.001) times more likely to vomit than children who received placebo but no drug-related serious adverse event was recorded. CONCLUSIONS: IPT of malaria provides substantial protection against malaria in children who sleep under an ITN. There is now strong evidence to support the integration of IPTc into malaria control strategies in areas of seasonal malaria transmission.

PLoS Med. 2011 Feb 1;8(2):e1000407.

Intermittent preventive treatment of malaria provides substantial protection against malaria in children already protected by an insecticide-treated bednet in Mali: a randomised, double-blind, placebo-controlled trial.

Dicko A, Diallo AI, Tembine I, Dicko Y, Dara N, Sidibe Y, Santara G, Diawara H, Conaré T, Djimde A, Chandramohan D, Cousens S, Milligan PJ, Diallo DA, Doumbo OK, Greenwood B.

Source

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Abstract

BACKGROUND: Previous studies have shown that in areas of seasonal malaria transmission, intermittent preventive treatment of malaria in children (IPTc), targeting the transmission season, reduces the incidence of clinical malaria. However, these studies were conducted in communities with low coverage with insecticide-treated nets (ITNs). Whether IPTc provides additional protection to children sleeping under an ITN has not been established. METHODS AND FINDINGS: **To assess whether IPTc provides additional protection to children sleeping under an ITN, we conducted a randomised, double-blind, placebo-controlled trial of IPTc with sulphadoxine pyrimethamine (SP) plus amodiaquine (AQ) in three localities in Kati, Mali.** After screening, eligible children aged 3-59 mo were given a long-lasting insecticide-treated net (LLIN) and randomised to receive three rounds of active drugs or placebos. Treatments were administered under observation at monthly intervals during the high malaria transmission season in August, September, and October 2008. Adverse events were monitored immediately after the administration of each course of IPTc and throughout the follow-up period. The primary endpoint was clinical episodes of malaria recorded through passive surveillance by study clinicians available at all times during the follow-up. Cross-sectional surveys were conducted in 150 randomly selected children weekly and in all children at the end of the malaria transmission season to assess usage of ITNs and the impact of IPTc on the prevalence of malaria, anaemia, and malnutrition. Cox regression was used to compare incidence rates between intervention and control arms. The effects of IPTc on the prevalence of malaria infection and anaemia were estimated using logistic regression. 3,065 children were screened and 3,017 (1,508 in the control and 1,509 in the intervention arm) were enrolled in the study. 1,485 children (98.5%) in the control arm and 1,481 (98.1%) in the intervention arm completed follow-up. During the intervention period, the proportion of children reported to have slept under an ITN was 99.7% in the control and 99.3% in intervention arm (p = 0.45). A total of 672 episodes of clinical malaria defined as fever or a history of fever and the presence of at least 5,000 asexual forms of Plasmodium falciparum per microlitre (incidence rate of 1.90; 95% confidence interval [CI] 1.76-2.05 episodes per person year) were observed in the control arm versus 126 (incidence rate of 0.34; 95% CI 0.29-0.41 episodes per person year) in the intervention arm, indicating a protective effect (PE) of 82% (95% CI 78%-85%) (p<0.001) on the primary endpoint. **There were 15 episodes of severe malaria in children in the control**

arm compared to two in children in the intervention group giving a PE of 87% (95% CI 42%-99%) (p = 0.001). IPTc reduced the prevalence of malaria infection by 85% (95% CI 73%-92%) (p<0.001) during the intervention period and by 46% (95% CI 31%-68%) (p<0.001) at the end of the intervention period. **The prevalence of moderate anaemia (haemoglobin [Hb] <8 g/dl) was reduced by 47% (95% CI 15%-67%) (p<0.007) at the end of intervention period.** The frequencies of adverse events were similar between the two arms. There was no drug-related serious adverse event. CONCLUSIONS: IPTc given during the malaria transmission season provided substantial protection against clinical episodes of malaria, malaria infection, and anaemia in children using an LLIN. SP+AQ was safe and well tolerated. These findings indicate that IPTc could make a valuable contribution to malaria control in areas of seasonal malaria transmission alongside other interventions.

Malar J. 2011 Feb 14;10(1):41.

Evaluating the effectiveness of IPTi on malaria using routine health information from sentinel health centres in southern Tanzania.

Willey BA, Armstrong Schellenberg JR, Maokola W, Shirima K, Chemba M, Mshinda H, Alonso P, Tanner M, Schellenberg D.

Source

Faculty of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, UK.

Abstract

BACKGROUND: Intermittent preventive treatment of malaria in infants (IPTi) consists of the administration of a treatment dose of sulphadoxine-pyrimethamine (SP) at the time of routine vaccinations. The use of routine Health Management and Information Services (HMIS) data to investigate the effect of IPTi on malaria, anaemia, and all-cause attendance in children aged 2-11 months presenting to 11 health centres in southern Tanzania is described. METHODS: Clinical diagnosis of malaria was confirmed with a positive blood slide reading from a quality assurance laboratory. Anaemia was defined using two thresholds (mild [Hb<11 g/dL], severe [Hb<8 g/dL]). Incidence rates between IPTi and non-implementing health centres were calculated using Poisson regression, and all statistical testing was based on the t test due to the clustered nature of the data. RESULTS: Seventy two per cent of infants presenting in intervention areas received at least one dose of IPTi--22% received all three. During March 2006-April 2007, the incidence of all cause attendance was two attendances per person, per year (pppy), including 0.2 episodes pppy of malaria, 0.7 episodes of mild and 0.13 episodes of severe anaemia. Point estimates for the effect of IPTi on malaria varied between 18% and 52%, depending on the scope of the analysis, although adjustment for clustering rendered these not statistically significant. CONCLUSIONS: The point estimate of the effect of IPTi on malaria is consistent with that from a large pooled analysis of randomized control trials. As such, it is plausible that the difference seen in health centre data is due to IPTi, even thought the effect did not reach statistical significance. Findings draw attention to the challenges of robust inference of effects of interventions based on routine health centre data. Analysis of routine health information can reassure that interventions are being made available and having desired effects, but unanticipated effects should trigger data collection from representative samples of the target population.

Clin Infect Dis. 2011 Jan 1;52(1):41-8.

HIV and placental infection modulate the appearance of drug-resistant Plasmodium falciparum in pregnant women who receive intermittent preventive treatment.

Menéndez C, Serra-Casas E, Scahill MD, Sanz S, Nhabomba A, Bardají A, Sigauque B, Cisteró P, Mandomando I, Dobaño C, Alonso PL, Mayor A.

Source

Barcelona Centre for International Health Research, Hospital Clínic, Universitat de Barcelona, Barcelona, Spain.

Abstract

BACKGROUND: Factors involved in the development of resistance to sulphadoxine-pyrimethamine (SP) by Plasmodium falciparum, particularly in the context of intermittent preventive treatment during pregnancy (IPTp), are not well known. We aimed to determine the impact of IPTp and human immunodeficiency virus (HIV) infection on molecular markers of SP resistance and the clinical relevance of resistant infections. METHODS: SP resistance alleles were determined in peripheral (n = 125) and placental (n = 145) P. falciparum isolates obtained from pregnant women enrolled in a randomized, placebo-controlled trial of IPTp in Manhiça, Mozambique. RESULTS: Prevalence of quintuple mutant infections was 12% (23 of 185 isolates) in pregnant women who received placebo and 24% (20 of 85 isolates) in those who received SP (P = .031). When the last IPTp dose was administered at late pregnancy, mutant infections at delivery were more prevalent in placental samples (7 [23%] of 30, samples) than in peripheral blood samples (2 [7%] of 30 samples; P = .025), more prevalent in women who received IPTp-SP than in those who received placebo (odds ratio [OR], 8.13; 95% confidence interval [CI], 1.69-39.08), and more prevalent in HIV-positive women than in HIV-negative women (OR, 5.17; 95% CI, 1.23-21.66). No association was found between mutant infections and increased parasite density or malaria-related morbidity in mothers and children. CONCLUSIONS: IPTp with SP increases the prevalence of resistance markers in the placenta and in HIV-infected women at delivery, which suggests that host immunity is key for the clearance of drug-resistant infections. However, this effect of IPTp is limited to the period when blood levels of SP are likely to be significant and does not translate into more-severe infections or adverse clinical outcomes.

Other preventative strategies

Am J Trop Med Hyg. 2010 Nov;83(5):965-72.

Social acceptability and durability of two different house screening interventions against exposure to malaria vectors, Plasmodium falciparum infection, and anemia in children in the Gambia, West Africa.

Kirby MJ, Bah P, Jones CO, Kelly AH, Jasseh M, Lindsay SW.

Source

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Abstract
The social acceptability and durability of two house screening interventions were addressed using focus group discussions, questionnaires, indoor climate measurements, and durability surveys. Participants recognized that screening stopped mosquitoes (79-96%) and other insects (86-98%) entering their houses. These and other benefits were appreciated by significantly more recipients of full screening than users of screened ceilings. Full screened houses were 0.26°C hotter at night (P = 0.05) than houses with screened ceilings and 0.51°C (P < 0.001) hotter than houses with no screening (28.43°C), though only 9% of full screened house users and 17% of screened ceiling users complained about the heat. Although 71% of screened doors and 85% of ceilings had suffered some damage after 12 months, the average number of holes of any size was < 5 for doors and < 7 for ceilings. In conclusion, house screening is a well-appreciated and durable vector control tool.

Treatment of uncomplicated malaria

*** PLoS One. 2010 Jul 30;5(7):e11759.

Incidence of malaria and efficacy of combination antimalarial therapies over 4 years in an urban cohort of Ugandan children.

Clark TD, Njama-Meya D, Nzarubara B, Maiteki-Sebuguzi C, Greenhouse B, Staedke SG, Kamya MR, Dorsey G, Rosenthal PJ.

Source
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Abstract
BACKGROUND: Combination therapies are now recommended to treat uncomplicated malaria. We used a longitudinal design to assess the incidence of malaria and compare the efficacies of 3 combination regimens in Kampala, Uganda. METHODOLOGY/PRINCIPAL FINDINGS: Children aged 1-10 years were enrolled from randomly selected households in 2004-05 and 2007, and were followed at least monthly through 2008. Insecticide-treated bednets (ITNs) were provided in 2006. Children were randomized upon their first episode, and then treated for all episodes of uncomplicated malaria with amodiaquine/sulfadoxine-pyrimethamine (AQ/SP), artesunate/amodiaquine (AS/AQ), or artemether/lumefantrine (AL). Risks of parasitological failure were determined for each episode of uncomplicated malaria and clinical parameters were followed. A total of 690 children experienced 1464 episodes of malaria. 96% of these episodes were uncomplicated malaria and treated with study drugs; 94% were due to Plasmodium falciparum. The rank order of treatment efficacy was AL > AS/AQ > AQ/SP. Failure rates increased over time for AQ/SP, but not the artemisinin-based regimens. Over the 4-year course of the study the prevalence of asymptomatic parasitemia decreased from 11.8% to 1.4%, the incidence of malaria decreased from 1.55 to 0.32 per person year, and the prevalence of anemia (hemoglobin <10 gm/dL) decreased from 5.9% to 1.0%. No episodes of severe malaria (based on WHO criteria) and no deaths were seen. CONCLUSIONS / SIGNIFICANCE: **With ready access to combination therapies and distribution of ITNs, responses were excellent for artemisinin-containing regimens, severe malaria was not seen, and the incidence of malaria and prevalence of parasitemia and anemia decreased steadily over time.**

Comment

This study shows the benefit of a multifaceted approach to malaria control; with use of ITNs, artemisinin-based combination therapy, and in other studies IPTi, the elimination of serious morbidity and deaths due to malaria is possible.

Afr Health Sci. 2010 Dec;10(4):332-40.

Effectiveness of a community intervention on malaria in rural Tanzania - a randomised controlled trial.

Eriksen J, Mujinja P, Warsame M, Nsimba S, Kouyaté B, Gustafsson LL, Jahn A, Müller O, Sauerborn R, Tomson G.

Source

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Abstract

BACKGROUND: Malaria infections are a major public health problem in Africa and prompt treatment is one way of controlling the disease and saving lives. METHODS: This cluster-randomised controlled community intervention conducted in 2003-2005 aimed at improving early malaria case management in under five children. Health workers were trained to train community-based women groups in recognizing malaria symptoms, providing first-line treatment for uncomplicated malaria and referring severe cases. Evaluation was through a pre-(2004) and a post-intervention survey (2005). Anaemia prevalence was the primary outcome. RESULTS: **1715 children aged 6-59 months were included in the pre-intervention survey and 2169 in the post-intervention survey. The prevalence of anaemia decreased significantly from 37% [95% CI 34.7-39.3] to 0.5% [95% CI 0.2-0.7] after the intervention (p<0.001); slightly more in the intervention (from 43.9% to 0.8%) than in the control (30.8% to 0.17%) group (p=0.038). Fever and reported fever decreased significantly and the mean body weight of the children increased significantly over the study period in both control and intervention groups.** CONCLUSION: The decrease in anaemia was significantly associated with the intervention, whereas the fever and body weight trends might be explained by other malaria control activities or seasonal/climate effects in the area. The community intervention was shown to be feasible in the study context.

Malar J. 2010 Sep 3;9:253.

Early clinical development of artemether-lumefantrine dispersible tablet: palatability of three flavours and bioavailability in healthy subjects.

Abdulla S, Amuri B, Kabanywanyi AM, Ubben D, Reynolds C, Pascoe S, Fitoussi S, Yeh CM, Nuortti M, Séchaud R, Kaiser G, Lefèvre G.

Source

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Abstract

BACKGROUND: Efforts to ease administration and enhance acceptability of the oral anti-malarial artemether-lumefantrine (A-L) crushed tablet to infants and children triggered the

development of a novel dispersible tablet of A-L. During early development of this new formulation, two studies were performed in healthy subjects, one to evaluate the palatability of three flavours of A-L, and a second one to compare the bioavailability of active principles between the dispersible tablet and the tablet (administered crushed and intact). METHODS: Study 1 was performed in 48 healthy schoolchildren in Tanzania. Within 1 day, all subjects tasted a strawberry-, orange- and cherry-flavoured oral A-L suspension for 10 seconds (without swallowing) in a randomized, single-blind, crossover fashion. The palatability of each formulation was rated using a visual analogue scale (VAS). Study 2 was an open, randomized crossover trial in 48 healthy adults given single doses of A-L (80 mg artemether + 480 mg lumefantrine) with food. The objectives were to compare the bioavailability of artemether, dihydroartemisinin (DHA) and lumefantrine between the dispersible tablet and the tablet administered crushed (primary objective) and intact (secondary objective). RESULTS: Study 1 showed no statistically significant difference in VAS scores between the three flavours but cherry had the highest score in several ratings (particularly for overall liking). Study 2 demonstrated that the dispersible and crushed tablets delivered bioequivalent artemether, DHA and lumefantrine systemic exposure (area under the curve [AUC]); mean ± SD AUC0-tlast were 208 ± 113 vs 195 ± 93 h.ng/ml for artemether, 206 ± 81 vs 199 ± 84 h.ng/ml for DHA and 262 ± 107 vs 291 ± 106 h x µg/ml for lumefantrine. Bioequivalence was also shown for peak plasma concentrations (Cmax) of DHA and lumefantrine. Compared with the intact tablet, the dispersible tablet resulted in bioequivalent lumefantrine exposure, but AUC and Cmax values of artemether and DHA were 20-35% lower. CONCLUSIONS: Considering that cherry was the preferred flavour, and that the novel A-L dispersible tablet demonstrated similar pharmacokinetic performances to the tablet administered crushed, a cherry-flavoured A-L dispersible tablet formulation was selected for further development and testing in a large efficacy and safety study in African children with malaria.

Lancet Infect Dis. 2010 Oct;10(10):673-81. Epub 2010 Sep 9

Effectiveness of five artemisinin combination regimens with or without primaquine in uncomplicated falciparum malaria: an open-label randomised trial.

Smithuis F, Kyaw MK, Phe O, Win T, Aung PP, Oo AP, Naing AL, Nyo MY, Myint NZ, Imwong M, Ashley E, Lee SJ, White NJ.

Source

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Abstract

BACKGROUND: Artemisinin-combination therapy (ACT) is recommended as first-line treatment of falciparum malaria throughout the world, and fixed-dose combinations are preferred by WHO; whether a single gametocytocidal dose of primaquine should be added is unknown. We aimed to compare effectiveness of four fixed-dose ACTs and a loose tablet combination of artesunate and mefloquine, and assess the addition of a single gametocytocidal dose of primaquine. METHODS: **In an open-label randomised trial in clinics in Rakhine state, Kachin state, and Shan state in Myanmar (Burma) between Dec 30, 2008, and March 20, 2009, we compared the effectiveness of all four WHO-recommended fixed-dose ACTs (artesunate-mefloquine, artesunate-amodiaquine, dihydroartemisinin-piperaquine, artemether-lumefantrine) and loose artesunate-mefloquine in Burmese adults and children.** Eligible patients were those who presented to the clinics with acute uncomplicated Plasmodium falciparum malaria or mixed infection, who were older than 6 months, and who weighed more than 5 kg. Treatments were randomised in equal numbers within blocks of 50 and allocation was in sealed envelopes. All patients were also randomly assigned to receive either a

single dose of primaquine 0·75 mg base/kg or not. Patients were followed up for 63 days. Treatment groups were compared by analysis of variance and multiple logistic regression. The primary outcome was the 63 day recrudescence rate. This study is registered with clinicaltrials.gov, number NCT00902811. FINDINGS: 155 patients received artesunate-amodiaquine, 162 artemether-lumefantrine, 169 artesunate-mefloquine, 161 loose artesunate-mefloquine, and 161 dihydroartemisinin-piperaquine. **By day 63 of follow-up, 14 patients (9·4%; 95% CI 5·7-15·3%) on artesunate-amodiaquine had recrudescent P falciparum infections, a rate significantly higher than for artemether-lumefantrine (two patients; 1·4%; 0·3-5·3; p=0·0013), fixed-dose artesunate-mefloquine (0 patients; 0-2·3; p<0·0001), loose artesunate-mefloquine (two patients; 1·3%; 0·3-5·3; p=0·0018), and dihydroartemisinin-piperaquine (two patients 1·3%; 0·3-5·2%; p=0·0012).** Hazard ratios for re-infection (95% CI) after artesunate-amodiaquine were 3·2 (1·3-8·0) compared with the two artesunate-mefloquine groups (p=0·01), 2·6 (1·0-6-0) compared with artemether-lumefantrine (p=0·04), and 2·3 (0·9-6·0) compared with dihydroartemisinin-piperaquine (p=0·08). Mixed falciparum and vivax infections were common: 129 (16%) had a mixed infection at presentation and 330 (41%) patients had one or more episodes of Plasmodium vivax infection during follow-up. The addition of a single dose of primaquine (0·75 mg/kg) reduced P falciparum gametocyte carriage substantially: rate ratio 11·9 (95% CI 7·4-20·5). All regimens were well tolerated. Adverse events were reported by 599 patients, most commonly vomiting and dizziness. Other side-effects were less common and were not related to a specific treatment. INTERPRETATION: **Artesunate-amodiaquine should not be used in Myanmar, because the other ACTs are substantially more effective. Artesunate-mefloquine provided the greatest post-treatment suppression of malaria.** Adding a single dose of primaquine would substantially reduce transmission potential. Vivax malaria, not recurrent falciparum malaria, is the main complication after treatment of P falciparum infections in this region.

PLoS One. 2010 Jul 30;5(7):e11880.

An open-label, randomised study of dihydroartemisinin-piperaquine versus artesunate-mefloquine for falciparum malaria in Asia.

Valecha N, Phyo AP, Mayxay M, Newton PN, Krudsood S, Keomany S, Khanthavong M, Pongvongsa T, Ruangveerayuth R, Uthaisil C, Ubben D, Duparc S, Bacchieri A, Corsi M, Rao BH, Bhattacharya PC, Dubhashi N, Ghosh SK, Dev V, Kumar A, Pukrittayakamee S.

Source

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Abstract

BACKGROUND: The artemisinin-based combination treatment (ACT) of dihydroartemisinin (DHA) and piperaquine (PQP) is a promising novel anti-malarial drug effective against multi-drug resistant falciparum malaria. The aim of this study was to show non-inferiority of DHA/PQP vs. artesunate-mefloquine (AS+MQ) in Asia. METHODS AND FINDINGS: This was an **open-label, randomised, non-inferiority, 63-day follow-up study conducted in Thailand, Laos and India.** Patients aged 3 months to 65 years with Plasmodium falciparum mono-infection or mixed infection were randomised with an allocation ratio of 2:1 to a fixed-dose DHA/PQP combination tablet (adults: 40 mg/320 mg; children: 20 mg/160 mg; n = 769) or loose combination of AS+MQ (AS: 50 mg, MQ: 250 mg; n = 381). The cumulative doses of study treatment over the 3 days were of about 6.75 mg/kg of DHA and 54 mg/kg of PQP and about 12 mg/kg of AS and 25 mg/kg of MQ. Doses were rounded up to the nearest half tablet. The primary endpoint was day-63 polymerase chain reaction (PCR) genotype-corrected cure

rate. **Results were 87.9% for DHA/PQP and 86.6% for AS+MQ in the intention-to-treat (ITT; 97.5% one-sided confidence interval, CI: >-2.87%), and 98.7% and 97.0%, respectively, in the per protocol population (97.5% CI: >-0.39%).** No country effect was observed. Kaplan-Meier estimates of proportions of patients with new infections on day 63 (secondary endpoint) were significantly lower for DHA/PQP than AS+MQ: 22.7% versus 30.3% (p = 0.0042; ITT). Overall gametocyte prevalence (days 7 to 63; secondary endpoint), measured as person-gametocyte-weeks, was significantly higher for DHA/PQP than AS+MQ (10.15% versus 4.88%; p = 0.003; ITT). Fifteen serious adverse events were reported, 12 (1.6%) in DHA/PQP and three (0.8%) in AS+MQ, among which six (0.8%) were considered related to DHA/PQP and three (0.8%) to AS+MQ. CONCLUSIONS: **DHA/PQP was a highly efficacious drug for P. falciparum malaria in areas where multidrug parasites are prevalent.** The DHA/PQP combination can play an important role in the first-line treatment of uncomplicated falciparum malaria.

J Vector Borne Dis. 2010 Sep;47(3):145-50.

Comparative study of efficacy of artesunate plus cotrimoxazole and artesunate plus chloroquine in the treatment of malaria in Nigerian children: a preliminary report.

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Source

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Abstract

BACKGROUND & OBJECTIVES: The study was undertaken to evaluate the efficacy of cotrimoxazole plus artesunate and to compare the efficacy of this combination with that of artesunate plus chloroquine in the treatment of acute uncomplicated falciparum malaria in children. METHODS: Children aged between 0.5 and 12 yr with clinical and parasitological evidence of Plasmodium falciparum malaria were randomized to receive either artesunate plus cotrimoxazole or artesunate plus chloroquine. They were followed-up with clinical and parasitological assessment for a period of 14 days. RESULTS: In all, **57 out of 81 (31 in the artesunate plus cotrimoxazole group and 26 in artesunate plus chloroquine group) completed the study as per protocol and were evaluated. Pre-treatment clinical and parasitological parameters were similar in the two treatment groups. The time to clear fever and other symptoms were similar in the two groups 1.0 +/- 0 vs 1.14 +/- 0.38 (p > 0.05).** Parasite clearance times were also similar; 1.65 +/- 0.49 days vs 1.58 +/- 0.67 days respectively for artesunate plus cotrimoxazole and artesunate plus chloroquine (p > 0.05). The cure rates on Day 14 were 100% for both artesunate plus cotrimoxazole and artesunate plus chloroquine groups. Both drug combinations were well-tolerated in the small population of children. CONCLUSION: These results indicate that **artesunate plus cotrimoxazole has similar efficacy to artesunate plus chloroquine** in the treatment of acute uncomplicated P. falciparum malaria in children resident in an endemic area of south-west Nigeria.

Am J Trop Med Hyg. 2010 Oct;83(4):873-5.

Increased risk of early vomiting among infants and young children treated with dihydroartemisinin-piperaquine compared with artemether-lumefantrine for uncomplicated malaria.

Creek D, Bigira V, Arinaitwe E, Wanzira H, Kakuru A, Tappero J, Kamya MR, Dorsey G, Sandison TG.

Source

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Abstract

Artemether-lumefantrine (AL) and dihydroartemisinin-piperaquine (DP) are highly efficacious antimalarial therapies in Africa. However, there are limited data regarding the tolerability of these drugs in young children. We used data from a randomized control trial in rural Uganda to compare the risk of early vomiting (within one hour of dosing) for children 6-24 months of age randomized to receive DP (n = 240) or AL (n = 228) for treatment of uncomplicated malaria. Overall, **DP was associated with a higher risk of early vomiting than AL (15.1% versus 7.1%; P = 0.007). The increased risk of early vomiting with DP was only present among breastfeeding children (relative risk [RR] = 3.35, P = 0.001)** compared with children who were not breastfeeding (RR = 1.03, P = 0.94). Age less than 18 months was a risk factor for early vomiting independent of treatment (RR = 3.27, P = 0.02). Our findings indicate that AL may be better tolerated than DP among young breastfeeding children treated for uncomplicated malaria.

Trans R Soc Trop Med Hyg. 2011 Jan;105(1):23-31. Epub 2010 Nov 5.

Is parasite clearance clinically important after malaria treatment in a high transmission area? A 3-month follow-up of home-based management with herbal medicine or ACT.

Willcox ML, Graz B, Diakite C, Falquet J, Dackouo F, Sidibe O, Giani S, Diallo D.

Source

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Abstract

Argemone mexicana (AM), a validated herbal medicine for uncomplicated malaria, seems to prevent severe malaria without completely clearing parasites in most patients. This study, in a high transmission area of South Mali, explores whether residual parasitaemia at day 28 was associated with subsequent malaria episodes and/or anaemia. Three hundred and one patients were randomly assigned to AM or artesunate/amodiaquine as first line treatment, of whom 294 were followed up beyond the standard 28 days, to 84 days. From day 29 to day 84, there were no significant differences between treatment groups in new clinical episodes of uncomplicated malaria (0.33 vs 0.31 episodes/patient), severe malaria (< 6% per month of patients aged ≤ 5 years) or moderate anaemia (hematocrit < 24%: 1.1% in both groups at day 84). Total parasite clearance at day 28 was not correlated with incidence of uncomplicated or severe malaria or of moderate anaemia over the subsequent two months. Total parasite clearance at day 28 was not clinically important in the context of high transmission. If this finding can be confirmed, some antimalarials which are clinically effective but do not completely clear parasites could

nevertheless be appropriate in high transmission areas. Such a policy could be tested as a way to delay resistance to artemisinin combination therapies.

Antimicrob Agents Chemother. 2010 Nov;54(11):4780-8. Epub 2010 Aug 16.

Population pharmacokinetics and pharmacodynamics of artemether and lumefantrine during combination treatment in children with uncomplicated falciparum malaria in Tanzania.

Hietala SF, Mårtensson A, Ngasala B, Dahlström S, Lindegårdh N, Annerberg A, Premji Z, Färnert A, Gil P, Björkman A, Ashton M.

Source

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Abstract

The combination of artemether (ARM) and lumefantrine is currently the first-line treatment of uncomplicated falciparum malaria in mainland Tanzania. While the exposure to lumefantrine has been associated with the probability of adequate clinical and parasitological cure, increasing exposure to artemether and the active metabolite dihydroartemisinin (DHA) has been shown to decrease the parasite clearance time. The aim of this analysis was to describe the pharmacokinetics and pharmacodynamics of artemether, dihydroartemisinin, and lumefantrine in African children with uncomplicated malaria. In addition to drug concentrations and parasitemias from 50 Tanzanian children with falciparum malaria, peripheral parasite densities from 11 asymptomatic children were included in the model of the parasite dynamics. The population pharmacokinetics and pharmacodynamics of artemether, dihydroartemisinin, and lumefantrine were modeled in NONMEM. The distribution of artemether was described by a two-compartment model with a rapid absorption and elimination through metabolism to dihydroartemisinin. Dihydroartemisinin concentrations were adequately illustrated by a one-compartment model. The pharmacokinetics of artemether was time dependent, with typical oral clearance increasing from 2.6 liters/h/kg on day 1 to 10 liters/h/kg on day 3. The pharmacokinetics of lumefantrine was sufficiently described by a one-compartment model with an absorption lag time. The typical value of oral clearance was estimated to 77 ml/h/kg. The proposed semimechanistic model of parasite dynamics, while a rough approximation of the complex interplay between malaria parasite and the human host, adequately described the early effect of ARM and DHA concentrations on the parasite density in malaria patients. However, the poor precision in some parameters illustrates the need for further data to support and refine this model.

Malar J. 2010 Nov 21;9:332.

Plasmodium falciparum clearance with artemisinin-based combination therapy (ACT) in patients with glucose-6-phosphate dehydrogenase deficiency in Mali.

Kone AK, Sagara I, Thera MA, Dicko A, Guindo A, Diakite S, Kurantsin-Mills J, Djimde A, Walcourt A, Doumbo O.

Source

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Abstract
BACKGROUND: Artemisinin-based combination therapy (ACT) is currently the most effective medicine for the treatment of uncomplicated malaria. Artemisinin has previously been shown to increase the clearance of Plasmodium falciparum in malaria patients with haemoglobin E trait, but it did not increase parasite inhibition in an in vitro study using haemoglobin AS erythrocytes. The current study describes the efficacy of artemisinin derivatives on P. falciparum clearance in patients with glucose-6-phosphate dehydrogenase deficiency (G6PD), a haemoglobin enzyme deficiency, not yet studied in the same context, but nonetheless is a common in malaria endemic areas, associated with host protection against uncomplicated and severe malaria. The impact of G6PD deficiency on parasite clearance with ACT treatment was compared between G6PD-deficient patients and G6PD-normal group. METHODS: Blood samples from children and adults participants (1 to 70 years old) with uncomplicated P. falciparum malaria residing in Kambila, Mali were analysed. **Study participants were randomly assigned to receive either artemether-lumefantrine (Coartem®) or artesunate plus mefloquine (Artequin™).** A restriction-fragment length polymorphism analysis of PCR-amplified DNA samples was used to identify the (A-) allele of the gene mutation responsible for G6PD deficiency (G6PD*A-). 470 blood samples were thus analysed and of these, DNA was extracted from 315 samples using the QIAamp kit for PCR to identify the G6PD*A- gene. RESULTS: The DNA amplified from 315 samples using PCR showed that G6PD*A- deficiency was present in 56 participants (17.8%). The distribution of the specific deficiency was 1%, 7% and, 9.8% respectively for homozygous, hemizygous, and heterozygous genotypes. Before treatment, the median parasitaemia and other baseline characteristics (mean haemoglobin, sex and age groups) between G6PD deficiency (hemizygous, heterozygous, and homozygous) and G6PD-normal participants were comparable ($p > 0.05$). **After treatment, parasite clearance did not change significantly whether the participants were G6PD deficient or G6PD normal on day 1 (OR = 1.3; CI = 0.70-2.47; p > 0.05) and on day 2 (OR = 0.859; CI = 0.097-7.61; p > 0.05)**. CONCLUSIONS: **The presence of G6PD deficiency does not appear to significantly influence the clearance of P. falciparum in the treatment of uncomplicated malaria using ACT.**

Malar J. 2010 Nov 22;9:335.

Early variations in plasmodium falciparum dynamics in Nigerian children after treatment with two artemisinin-based combinations: implications on delayed parasite clearance.

Michael OS, Gbotosho GO, Folarin OA, Okuboyejo T, Sowunmi A, Oduola AM, Happi CT.
Source
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Abstract
BACKGROUND: Combination treatments, preferably containing an artemisinin derivative, are recommended to improve efficacy and prevent Plasmodium falciparum drug resistance. Artemether-lumefantrine (AL) and artesunate-amodiaquine (AA) are efficacious regimens that have been widely adopted in sub-Saharan Africa. However, most study designs ignore the effects of these regimens on peripheral parasitaemia in the first 24 hours of therapy. The study protocol was designed to evaluate more closely the early effects and the standard measures of efficacies of these two regimens. METHODS: In an open label, randomized controlled clinical

trial, **children aged 12 months to 132 months were randomized to receive AL (5-14 kg, one tablet; 15-24 kg, two tablets and 25-34 kg, three tablets twice daily) or artesunate (4 mg/kg daily) plus amodiaquine (10 mg/kg daily) for three days.** Peripheral blood smears were made hourly in the first 4 hours, 8 h, 16 h, 24 h, and daily on days 2-7, and on days 7, 14, 21, 28, 35, and 42 for microscopic identification and quantification of Plasmodium falciparum. RESULTS: A total of 193 children were randomized to receive either AL (97) or AA (96). **In children that received both medications, early response of peripheral parasitaemia showed that 42% of children who received AL and 36.7% of those who received AA had an immediate rise in peripheral parasitaemia (0-4 h after treatment) followed by a rapid fall. The rise in parasitaemia was significant and seems to suggest a mobilization of asexual parasites from the deep tissues to the periphery.** Days 3, 7, 14, 28, and 42 cure rates in the per protocol (PP) population were > 90% in both groups of children. Both drug combinations were well tolerated with minimal side effects. CONCLUSION: The study showed the high efficacy of AL and AA in Nigerian children. In addition the study demonstrated the **mobilisation of asexual parasites from the deep to the periphery in the early hours of commencing ACT treatment in a subset of patients in both study groups**. It is unclear whether the early parasite dynamics discovered in this study play any role in the development of drug resistance and thus it is important to further evaluate this discovery. It may be useful for studies investigating delay in parasite clearance of artemisinin derivatives as a way of monitoring the development of resistance to artemisinin to assess the early effects of the drugs on the parasites.

Am J Trop Med Hyg. 2010 Dec;83(6):1221-9.

A phase III, randomized, non-inferiority trial to assess the efficacy and safety of dihydroartemisinin-piperaquine in comparison with artesunate-mefloquine in patients with uncomplicated Plasmodium falciparum malaria in southern Laos.

Mayxay M, Keomany S, Khanthavong M, Souvannasing P, Stepniewska K, Khomthilath T, Keola S, Pongvongsa T, Phompida S, Ubben D, Valecha N, White NJ, Newton PN.

Source

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Abstract

We conducted an open, randomized clinical trial of oral dihydroartemisinin-piperaquine (DP) versus artesunate-mefloquine (AM) in 300 patients in Laos with uncomplicated Plasmodium falciparum malaria as part of a multicentre study in Asia. Survival analysis and adjustment for re-infection showed that the 63-day cure rates (95% confidence interval [CI]) were 100% for AM and 99.5% (96.4-99.8%) for DP. The 63-day cure rates per protocol were 99% (97 of 98) for AM and 99.5% (196 of 197) for DP (P = 0.55). The difference (AM minus DP) in cure rates (95% CI) was -0.5% (-5.1 to 2.0%), which is within the 5% non-inferiority margin. The median fever and parasite clearance times were also similar for AM and DP. The proportion of patients with at least one recorded potential adverse event was significantly higher in the AM group (38 of 87, 44%) than in the DP group (57 of 182, 31%) (relative risk = 0.6, 95% CI = 0.4-0.9; P = 0.04). **Dihydroartemisinin-piperaquine is not inferior to AM in the treatment of uncomplicated P. falciparum malaria in Laos and is associated with fewer adverse effects.** The results of this study were similar to those of the larger multicentre study.

J Infect Dis. 2011 Jan 1;203(1):109-16.

Similar efficacy and tolerability of double-dose chloroquine and artemether-lumefantrine for treatment of Plasmodium falciparum infection in Guinea-Bissau: a randomized trial.

Ursing J, Kofoed PE, Rodrigues A, Blessborn D, Thoft-Nielsen R, Björkman A, Rombo L.

Source

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Abstract

BACKGROUND: In 2008, Guinea-Bissau introduced artemether-lumefantrine for treatment of uncomplicated malaria. Previously, 3 times the standard dose of chloroquine, that was probably efficacious against Plasmodium falciparum with the resistance-associated chloroquine-resistance transporter (pfcrt) 76T allele, was routinely used. The present study compared the efficacy and tolerability of a double standard dose of chloroquine with the efficacy and tolerability of artemether-lumefantrine. METHODS: In a randomized open-label clinical trial, artemether-lumefantrine or chloroquine (50 mg/kg) were given as 6 divided doses over 3 days to children aged 6 months--15 years who had uncomplicated P. falciparum monoinfection. Drug concentrations were measured on day 7. P. falciparum multidrug resistance gene N86Y and pfcrt K76T alleles were identified. RESULTS: The polymerase chain reaction-adjusted day 28 and 42 treatment efficacies were 162 (97%) of 168 and 155 (97%) of 161, respectively, for artemether-lumefantrine and 150 (95%) of 158 and 138 (94%) of 148, respectively, for chloroquine. When parasites with resistance-associated pfcrt 76T were treated, the day 28 efficacy of chloroquine was 87%. No severe drug-related adverse events were detected. Symptom resolution was similar with both treatments. CONCLUSIONS: Both treatments achieved the World Health Organization-recommended efficacy for antimalarials that will be adopted as policy. High-dose chloroquine treatment regimes should be further evaluated with the aim of assessing chloroquine as a potential partner drug to artemisinin derivatives.

Malar J. 2010 Dec 31;9:378.

An open randomized clinical trial in comparing two artesunate-based combination treatments on Plasmodium falciparum malaria in Nigerian children: artesunate/sulphamethoxypyrazine/pyrimethamine (fixed dose over 24 hours) versus artesunate/amodiaquine (fixed dose over 48 hours).

Ayede IA, Falade AG, Sowunmi A, Jansen FH.

Source

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Abstract

BACKGROUND: Several studies have demonstrated the efficacy of artemisinin-combination therapy (ACT) across malaria zones of the world. Fixed dose ACT with shorter courses and fewer tablets may be key determinants to ease of administration and compliance. METHODS: Children aged one year to 13 years presenting with uncomplicated Plasmodium falciparum malaria were recruited in Ibadan, south-western Nigeria. A total of 250 children each were randomly assigned to receive three doses of **artesunate / sulphamethoxypyrazine / pyrimethamine (AS + SMP) (12 hourly doses over 24 hours) or three doses of artesunate/amodiaquine (AS + AQ) (daily doses over 48 hours)**. Efficacy and safety of the

two drugs were assessed using a 28-day follow-up and the primary outcome was PCR- corrected parasitological cure rate and clinical response. RESULTS: **There were two (0.4%) early treatment failures, one in each treatment arm.** The PCR corrected cure rates for day 28 was 97.9% in the AS + AQ arm and 95.6% in the AS + SMP arm (p = 0.15). **The re-infection rate was 1.7% in the AS + AQ arm and 5.7% in the AS + SMP arm (p = 0.021).** The fever clearance time was similar in the two treatment groups: 1 - 2 days for both AS + SMP and AS + AQ (p = 0.271). The parasite clearance time was also similar in the two treatment groups with 1 - 7 days for AS + SMP and 1 - 4 days for AS + AQ (p = 0.941). The proportion of children with gametocytes over the follow-up period was similar in both treatment groups. Serious Adverse Events were not reported in any of the patients and in all children, laboratory values (packed cell volume, liver enzymes, bilirubin) remained within normal levels during the follow-up period but the packed cell volume was significantly lower in the AS + SMP group. CONCLUSIONS: This study demonstrates that AS + SMP FDC given as three doses over 24 hours (12-hour intervals) has similar efficacy as AS + AQ FDC given as three doses over 48 hours (24-hour interval) for the treatment of uncomplicated Plasmodium falciparum malaria in children in Nigeria. Both drugs also proved to be safe. Therefore, AS + SMP could be an alternative to currently recommended first-line ACT with continuous resistance surveillance.

Cochrane Database Syst Rev. 2011 Feb 16;(2):CD006688.

Azithromycin for treating uncomplicated malaria.

van Eijk AM, Terlouw DJ.
Child & Reproductive Health Group, Liverpool School of Tropical Medicine, Pembroke Place, Liverpool, UK, L3 5QA.

Abstract

BACKGROUND: To prevent the development of drug resistance, the World Health Organization (WHO) recommends treating malaria with combination therapy. Azithromycin, an antibiotic with antimalarial properties, may be a useful additional option for antimalarial therapy. OBJECTIVES: To compare the use of azithromycin alone or in combination with other antimalarial drugs with the use of alternative antimalarial drugs for treating uncomplicated malaria caused by Plasmodium falciparum or Plasmodium vivax. SEARCH STRATEGY: We searched the Cochrane Infectious Diseases Group Specialized Register (August 2010); CENTRAL (The Cochrane Library Issue 3, 2010); MEDLINE (1966 to August 2010); EMBASE (1974 to August 2010); LILACS (August 2010); the metaRegister of Controlled Trials (mRCT, August 2010); conference proceedings; and reference lists. We also contacted researchers and a pharmaceutical company. SELECTION CRITERIA: Randomized controlled trials comparing azithromycin, either alone or combined with another antimalarial drug, with another antimalarial drug used alone or combined with another antimalarial drug, or with azithromycin combined with another antimalarial drug if different combinations or doses of azithromycin were used. The primary outcome was treatment failure by day 28, defined as parasitological or clinical evidence of treatment failure between the start of treatment and day 28. Secondary outcomes included treatment failure by day 28 corrected for new infections confirmed by polymerase chain reaction (PCR), fever and parasite clearance time, and adverse events. DATA COLLECTION AND ANALYSIS: Two people independently applied the inclusion criteria, extracted data and assessed methodological quality. We used risk ratio (RR) and 95% confidence intervals (CI). MAIN RESULTS: **Fifteen trials met the inclusion criteria (2284 participants, 69% males, 16% children).** They were conducted in disparate malaria endemic areas, with the earlier studies conducted in Thailand (five) and India (two), and

the more recent studies (eight) spread across three continents (South America, Africa, Asia). The 15 studies involved 41 treatment arms, 12 different drugs, and 28 different treatment regimens. Two studies examined P. vivax.**Three-day azithromycin (AZ) monotherapy did not perform well for P. vivax or P. falciparum** (Thailand: P. vivax failure rate 0.5 g daily, 56%, 95% CI 31 to 78. India: P. vivax failure rate 1 g daily,12%, 95% CI 7 to 21; P. falciparum failure rate 1 g daily, 64%, 95% CI 36 to 86.) A 1 g azithromycin and 0.6 g chloroquine combination daily for three days for uncomplicated P. falciparum infections was associated with increased treatment failure in India and Indonesia compared with the combination of sulphadoxine-pyrimethamine and chloroquine (pooled RR 2.66, 95% CI 1.25 to 5.67), and compared with the combination atovaquone-proguanil in a multicentre trial in Columbia and Surinam (RR 24.72, 95% CI 6.16 to 99.20). No increased risk of treatment failure was seen in two studies in Africa with mefloquine as the comparator drug (pooled RR 2.02, 95% CI 0.51 to 7.96, P = 0.3); the pooled RR for PCR-corrected data for the combination versus mefloquine was 1.01, 95% CI 0.18 to 5.84 (P = 1.0). **An increased treatment failure risk was seen when comparing azithromycin in a dose of 1.2 to 1.5 mg in combination with artesunate (200 mg per day for three days) with artemether-lumefantrine (pooled RR 3.08, 95% CI 2.09 to 4.55; PCR-corrected pooled RR 3.63, 95% CI 2.02 to 6.52).**Serious adverse events and treatment discontinuation were similar across treatment arms. More adverse events were reported when comparing the 1 g azithromycin/ 0.6 g chloroquine combination with mefloquine (pooled RR 1.20, 95% CI 1.06 to 1.36) or atovaquone-proguanil (RR 1.41, 95% CI 1.09 to1.83). AUTHORS' CONCLUSIONS: **Currently, there is no evidence for the superiority or equivalence of azithromycin monotherapy or combination therapy for the treatment of P. falciparum or P. vivax compared with other antimalarials or with the current first-line antimalarial combinations. The available evidence suggests that azithromycin is a weak antimalarial with some appealing safety characteristics.** Unless the ongoing dose, formulation and product optimisation process results in a universally efficacious product, or a specific niche application is identified that is complementary to the current scala of more efficacious antimalarial combinations, azithromycin's future for the treatment of malaria does not look promising.

Malar J. 2011 Feb 28;10:50.

Safety and efficacy of dihydroartemisinin-piperaquine versus artemether-lumefantrine in the treatment of uncomplicated Plasmodium falciparum malaria in Zambian children.

Nambozi M, Van Geertruyden JP, Hachizovu S, Chaponda M, Mukwamataba D, Mulenga M, Ubben D, D'Alessandro U.

Source

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Abstract

BACKGROUND: Malaria in Zambia remains a public health and developmental challenge, affecting mostly children under five and pregnant women. In 2002, the first-line treatment for uncomplicated malaria was changed to artemether-lumefantrine (AL) that has proved to be highly efficacious against multidrug resistant Plasmodium falciparum. OBJECTIVE: The study objective was to determine whether dihydroartemisinin-piperaquine (DHA/PQP) had similar efficacy, safety and tolerability as AL for the treatment of children with uncomplicated P. falciparum malaria in Ndola, Zambia. METHODS: Between 2005 and 2006, 304 children (6-

59 months old) with uncomplicated P. falciparum were enrolled, randomized to AL (101) or DHA/PQP (203) and followed up for 42 days. Outcome of treatment was defined according to the standard WHO classification, i.e. early treatment failure (ETF), late clinical failure (LCF, late parasitological failure (LPF) and adequate clinical and parasitological response (ACPR). Recurrent infections were genotyped to distinguish between recrudescence and new infection. RESULTS: No ETF was observed. At day 28, PCR-uncorrected ACPR was 92% in the DHA/PQP and 74% in the AL arm (OR: 4.05; 95%CI: 1.89-8.74; p < 0.001). Most failure were new infections and PCR-corrected ACPR was similar in the two study arms (OR: 0.69; 95%CI: 0.22-2.26; p = 0.33). Similar results were observed for day 42, i.e. higher PCR-uncorrected ACPR for DHA/PQP, mainly due to the difference observed up to day 28, while the PCR-corrected ACPR was similar: DHA/PQP: 93% (179/192), AL: 93% (84/90), (OR: 0.92; 95%CI: 0.30-2.64; p = 0.85). Except for cough, more frequent in the DHA/PQP arm (p = 0.04), there were no differences between treatment arms in the occurrence of adverse events. Two serious adverse events were probably associated to AL treatment. CONCLUSION: **DHA/PQP was as efficacious, safe and well tolerated in treatment of uncomplicated malaria as AL**, though in the latter group more new infections during the follow up were observed. DHA/PQP seems a potential candidate to be used as an alternative first-line or rescue treatment in Zambia.

Am J Trop Med Hyg. 2011 May;84(5):813-9.

Therapeutic efficacy and effects of artemether-lumefantrine and artesunate-amodiaquine coformulated or copackaged on malaria-associated anemia in children with uncomplicated Plasmodium falciparum malaria in Southwest Nigeria.

Gbotosho GO, Sowunmi A, Okuboyejo TM, Happi CT, Folarin OA, Michael OS, Adewoye EO.

Source

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Abstract

The therapeutic efficacy and effects of artemether-lumefantrine (AL) and artesunate-amodiaquine co-formulated (AAcf) or co-packaged (AAcp) on malaria-associated anemia (MAA) were evaluated in 285 children < 12 years of age with uncomplicated Plasmodium falciparum malaria randomized to receive one of the three drug combinations. Fever and parasite clearance times were similar in all treatment groups. Mean drug-attributable fall in hematocrit (DAFH), defined as difference between hematocrit values pre- and 3 d post-initiation of treatment, was low (< 4.5%) and rates of recovery from MAA were similar with all treatments. Mean areas under curve (AUCs) of the plot of deficit in hematocrit levels from 30% versus time in anemic children were similar in all groups. All regimens were well tolerated. AL, AAcf and AAcp cleared fever and parasitemia rapidly and had similar rates of resolution of MAA after treatment in malarious Nigerian children.

Am J Trop Med Hyg. 2010 Oct;83(4):843-7.

A comparison of iron and folate with folate alone in hematologic recovery of children treated for acute malaria.

Gara SN, Madaki AJ, Thacher TD.

Source
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Abstract
Concern has been raised that iron supplementation for treatment of acute malaria may worsen the severity of malaria. We compared the effect of iron and folate with folate alone on hematologic recovery in children treated for acute malaria. We randomized 82 children 6-60 months of age from Nigeria with smear-positive malaria and anemia (hematocrit < 33%) to receive iron (2 mg/kg/day) plus folate (5 mg/day) or folate alone in addition to antimalarial drugs. The mean ± SD hematocrit at baseline was 28.5% ± 2.9%. At four weeks, the mean hematocrit increased by 2.5% ± 1.6% in the iron plus folate group and by 1.4% ± 1.0% in the folate alone group (P = 0.001). Baseline hematocrit, iron supplementation, weight for height, and weekly meat intake were significant predictors of final hematocrit. The effect of iron was not significantly modified by baseline hematocrit, weekly meat intake, nutritional status, mother's education, sex, or age of the child. Iron supplementation improved hematologic recovery in children with malarial anemia.

Treatment of severe or complicated malaria

(See also Emergency care)

Trans R Soc Trop Med Hyg. 2010 Oct;104(10):684-6. Epub 2010 Jun 17.
Comparison of artesunate and quinine in the treatment of Sudanese children with severe Plasmodium falciparum malaria.
Eltahir HG, Omer AA, Mohamed AA, Adam I.
Source
Faculty of Medicine, University of Khartoum, Khartoum, Sudan.
Abstract
Sixty-six children presenting to Singa hospital, Sudan with different manifestations of severe Plasmodium falciparum malaria were randomly divided into two well-matched groups (33 in each arm) to receive either intravenous artesunate 2·4 mg/kg at 0, 12, and 24 hours, then daily, or intravenous quinine 20mg/kg initially then 10mg/kg three times a day. There was no significant difference in the fever, parasite clearance, and coma resolution times. Three patients died, one in the artesunate and two in the quinine groups. One patient developed hypoglycaemia following quinine infusion. Thus, artesunate can be used for the treatment of severe falciparum malaria.

*** Lancet. 2010 Nov 13;376(9753):1647-57. Epub 2010 Nov 7.
Artesunate versus quinine in the treatment of severe falciparum malaria in African children (AQUAMAT): an open-label, randomised trial.
Dondorp AM, Fanello CI, Hendriksen IC, Gomes E, Seni A, Chhaganlal KD, Bojang K, Olaosebikan R, Anunobi N, Maitland K, Kivaya E, Agbenyega T, Nguah SB, Evans J, Gesase S, Kahabuka C, Mtove G, Nadjm B, Deen J, Mwanga-Amumpaire J, Nansumba M, Karema C, Umulisa N, Uwimana A, Mokuolu OA, Adedoyin OT, Johnson WB, Tshefu AK, Onyamboko

MA, Sakulthaew T, Ngum WP, Silamut K, Stepniewska K, Woodrow CJ, Bethell D, Wills B, Oneko M, Peto TE, von Seidlein L, Day NP, White NJ; AQUAMAT group.
Source
Mahidol Oxford Tropical Medicine Research Unit (MORU), Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand.
Abstract
BACKGROUND: Severe malaria is a major cause of childhood death and often the main reason for paediatric hospital admission in sub-Saharan Africa. Quinine is still the established treatment of choice, although evidence from Asia suggests that artesunate is associated with a lower mortality. We compared parenteral treatment with either artesunate or quinine in African children with severe malaria. METHODS: This open-label, randomised trial was undertaken in 11 centres in nine African countries. Children (<15 years) with severe falciparum malaria were randomly assigned to parenteral artesunate or parenteral quinine. Randomisation was in blocks of 20, with study numbers corresponding to treatment allocations kept inside opaque sealed paper envelopes. The trial was open label at each site, and none of the investigators or trialists, apart from for the trial statistician, had access to the summaries of treatment allocations. The primary outcome measure was in-hospital mortality, analysed by intention to treat. This trial is registered, number ISRCTN50258054. FINDINGS: **5425 children were enrolled; 2712 were assigned to artesunate and 2713 to quinine.** All patients were analysed for the primary outcome. **230 (8·5%) patients assigned to artesunate treatment died compared with 297 (10·9%) assigned to quinine treatment (odds ratio [OR] stratified for study site 0·75, 95% CI 0·63-0·90; relative reduction 22·5%, 95% CI 8·1-36·9; p=0·0022).** Incidence of neurological sequelae did not differ significantly between groups, but the development of coma (65/1832 [3·5%] with artesunate vs 91/1768 [5·1%] with quinine; OR 0·69 95% CI 0·49-0·95; p=0·0231), convulsions (224/2712 [8·3%] vs 273/2713 [10·1%]; OR 0·80, 0·66-0·97; p=0·0199), and deterioration of the coma score (166/2712 [6·1%] vs 208/2713 [7·7%]; OR 0·78, 0·64-0·97; p=0·0245) were all significantly less frequent in artesunate recipients than in quinine recipients. Post-treatment hypoglycaemia was also less frequent in patients assigned to artesunate than in those assigned to quinine (48/2712 [1·8%] vs 75/2713 [2·8%]; OR 0·63, 0·43-0·91; p=0·0134). Artesunate was well tolerated, with no serious drug-related adverse effects. INTERPRETATION: **Artesunate substantially reduces mortality in African children with severe malaria.** These data, together with a meta-analysis of all trials comparing artesunate and quinine, strongly suggest that parenteral artesunate should replace quinine as the treatment of choice for severe falciparum malaria worldwide.

Cochrane Database Syst Rev. 2011 Apr 13;(4):CD004615.
Mannitol and other osmotic diuretics as adjuncts for treating cerebral malaria.
Okoromah CA, Afolabi BB, Wall EC.
Department of Paediatrics and Child Health, College of Medicine, University of Lagos, Idi-Araba, Surulere, Lagos, Lagos, Nigeria, PMB 12003.
Abstract
BACKGROUND: Cerebral oedema occurs with cerebral malaria, and some clinicians think osmotic diuretics, such as mannitol or urea, may improve outcomes. OBJECTIVES: To compare mannitol or urea to placebo or no diuretic for treating children or adults with cerebral malaria. SEARCH STRATEGY: We searched the Cochrane Infectious Diseases Group Specialized Register (Issue 4, 2010), CENTRAL (The Cochrane Library Issue 12, 2010), MEDLINE (1966 to November 2010), EMBASE (1974 to November 2010), LILACS (1982 to

November 2010), and the reference lists of articles. We contacted relevant organizations and researchers. SELECTION CRITERIA: Randomized or quasi-randomized controlled trials comparing mannitol or urea to placebo or no treatment in children and adults with cerebral malaria. Primary outcomes were death, life-threatenining sequelae and major neurological sequelae at six months. DATA COLLECTION AND ANALYSIS: Two authors applied the inclusion criteria, assessed risk of bias, and extracted data independently. MAIN RESULTS: One trial met the inclusion criteria, comparing mannitol 20% to saline placebo in 156 Ugandan children. Allocation was concealed. No difference in mortality, time to regain consciousness, or neurological sequelae were detected. AUTHORS' CONCLUSIONS: There are insufficient data to know what the effects of osmotic diuretics are in children with cerebral malaria. Larger, multicentre trials are needed.

Treatment of vivax malaria

Malar J. 2010 Nov 1;9:308.

Directly-observed therapy (DOT) for the radical 14-day primaquine treatment of Plasmodium vivax malaria on the Thai-Myanmar border.

Takeuchi R, Lawpoolsri S, Imwong M, Kobayashi J, Kaewkungwal J, Pukrittayakamee S, Puangsa-art S, Thanyavanich N, Maneeboonyang W, Day NP, Singhasivanon P.

Source

Department of Tropical Hygiene, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand.

Abstract

BACKGROUND: Plasmodium vivax has a dormant hepatic stage, called the hypnozoite, which can cause relapse months after the initial attack. For 50 years, primaquine has been used as a hypnozoitocide to radically cure P. vivax infection, but major concerns remain regarding the side-effects of the drug and adherence to the 14-day regimen. This study examined the effectiveness of using the directly-observed therapy (DOT) method for the radical treatment of P. vivax malaria infection, to prevent reappearance of the parasite within the 90-day follow-up period. Other potential risk factors for the reappearance of P. vivax were also explored. METHODS: A randomized trial was conducted from May 2007 to January 2009 in a low malaria transmission area along the Thai-Myanmar border. Patients aged ≥ 3 years diagnosed with P. vivax by microscopy, were recruited. **All patients were treated with the national standard regimen of chloroquine for three days followed by primaquine for 14 days. Patients were randomized to receive DOT or self-administered therapy (SAT).** All patients were followed for three months to check for any reappearance of P. vivax. RESULTS: Of the 216 patients enrolled, 109 were randomized to DOT and 107 to SAT. All patients recovered without serious adverse effects. **The vivax reappearance rate was significantly lower in the DOT group than the SAT group (3.4/10,000 person-days vs. 13.5/10,000 person-days, p = 0.021).** Factors related to the reappearance of vivax malaria included inadequate total primaquine dosage received (< 2.75 mg/kg), duration of fever ≤ 2 days before initiation of treatment, parasite count on admission ≥ 10,000/μl, multiple P. vivax-genotype infection, and presence of P. falciparum infection during the follow-up period. CONCLUSIONS: **Adherence to the 14-day primaquine regimen is important for the radical cure of P. vivax malaria infection. Implementation of DOT reduces the reappearance rate of the parasite, and may subsequently decrease P. vivax transmission in the area.**

Malnutrition

(Papers listed in this section refer to the management of protein-energy malnutrition. For other relevant studies of nutrition see also Nutrition, Vitamin A, Vitamin D, Zinc, Maternal health, Anaemia and iron deficiency)

J Nutr. 2010 Nov;140(11):2008-13. Epub 2010 Sep 22.

A lipid-based nutrient supplement but not corn-soy blend modestly increases weight gain among 6- to 18-month-old moderately underweight children in rural Malawi.

Thakwalakwa C, Ashorn P, Phuka J, Cheung YB, Briend A, Puumalainen T, Maleta K.

Source

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Abstract

Although widely used, there is little information concerning the efficacy of corn-soy blend (CSB) supplementation in the treatment of moderate underweight in African children. Lipid-based nutrient supplements (LNS), which have proven to be beneficial treatment for severely wasted children, could offer benefits to less severely affected individuals. We conducted a clinical randomized trial to determine whether LNS or CSB supplementation improves weight gain of moderately underweight children. A total of **182 underweight [weight-for-age Z-score (WAZ) < -2] 6- to 15-mo-old children were randomized to receive for 12 wk a ration of 43 g/d LNS or 71 g/d CSB, providing 1189 and 921 kJ, respectively, or no supplementation (control).** The primary outcome was weight change; secondary outcomes included changes in anthropometric indices, hemoglobin levels, and morbidity. **The body weight increases (mean ± SD) did not differ and were 620 ± 470, 510 ± 350, and 470 ± 350 g in the LNS, CSB, and control groups, respectively (P = 0.11).** Compared with controls, infants and children in the LNS group gained more weight [mean (95% CI) = 150 g (0-300 g); P = 0.05] and had a greater increase in WAZ [0.33 (-0.02-0.65); P = 0.04]. Weight and WAZ changes did not differ between the control and CSB groups. In exploratory stratified analysis, the weight increase was higher in the LNS group compared with the control group among those with lower initial WAZ [250 g (60-430 g; P = 0.01]. **Supplementation with LNS but not CSB modestly increases weight gain among moderately underweight children and the effect appears most pronounced among those with a lower initial WAZ.**

J Pediatr Gastroenterol Nutr. 2010 Nov;51(5):638-44.

Intestinal mucosal permeability of severely underweight and nonmalnourished Bangladeshi children and effects of nutritional rehabilitation.

Hossain MI, Nahar B, Hamadani JD, Ahmed T, Roy AK, Brown KH.

Source

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Abstract

OBJECTIVE: Lactulose/mannitol (L/M) intestinal permeability tests were completed to compare the intestinal function of severely underweight children recovering from diarrhea and other illnesses and of nonmalnourished children from the same communities, and to evaluate the effects of food supplementation, with or without psychosocial stimulation, on the changes in

intestinal function among the underweight children. PATIENTS AND METHODS: Seventy-seven malnourished children completed intestinal permeability studies at baseline and 3 months after receiving 1 of the following randomly assigned treatment regimens: group-C--fortnightly follow-up at community-based follow-up units, including growth monitoring and promotion, health education, and micronutrient supplementation, n = 17; group-SF--same as group-C plus supplementary food (SF) to provide 150 to 300 kcal/day, n = 23; group-PS--same as group-C plus psychosocial stimulation (PS), n = 17; or group-SF + PS--same as group-C plus SF and PS, n = 20. Seventeen nonmalnourished children were included as comparison subjects. RESULTS: The malnourished children's mean ± SD initial age was 13.1 ± 4.0 months, their mean weight-for-age z score was -3.82 ± 0.61, and their median (interquartile range) urinary L/M recovery ratio was 0.16 (0.10-0.28). Eighty-four percent of the children had L/M ≥ 0.07, suggestive of impaired intestinal function. The median L/M of the malnourished children was significantly greater than that of 17 relatively well-nourished children (median 0.09; interquartile range 0.05-0.12; P = 0.001). There were no significant differences in baseline characteristics of the severely malnourished children by treatment group. Following treatment, the L/M ratio improved in all of the groups (P < 0.001), but there were no significant differences in these changes by treatment group. There was a significant positive association between weight gain and the magnitude of improvement in L/M ratio (r = 0.30, P = 0.012). CONCLUSIONS: **Intestinal mucosal function, as measured by sugar permeability, is impaired among severely underweight children. Intestinal permeability improves in relation to weight gain**, but intestinal mucosal recovery is not specifically related to the types or amount of food supplementation or PS provided in this trial.

Indian Pediatr. 2010 Aug 7;47(8):679-86.

Locally made ready to use therapeutic food for treatment of malnutrition a randomized controlled trial.

Singh AS, Kang G, Ramachandran A, Sarkar R, Peter P, Bose A.

Source

Departments of Gastrointestinal Sciences and Community Health, Christian Medical College, Vellore TN 632004, India.

Abstract

OBJECTIVE: To evaluate the effectiveness of a locally made ready-to-use therapeutic food (RUTF) in decreasing mild to moderate malnutrition. DESIGN: A randomized open label, controlled trial. SETTING: Pre-schools run by the Department of Community Health in Kaniyambadi administrative block, Vellore, India; duration of follow-up 3 months from the date of recruitment. PARTICIPANTS: Pupils aged 18 -60 months with Weight-for-Age 2 SD. INTERVENTIONS: **A locally produced energy-dense supplement (RUTF), and the current standard of care [teaching caregivers how to make a fortified cereal-milk supplement called High Calorie Cereal Milk (HCCM)].** MAIN OUTCOME MEASURES: Increase in weight-for-age status; increase in levels of plasma zinc, vitamin B12, serum albumin and haemoglobin. Results: The Mean (SD) weight gain at 3 months was higher in the RUTF group: RUTF (n=51): 0.54 kg; (SE = 0.05; 95% CI = 0.44 - 0.65) vs HCCM (n=45): 0.38 kg;(SE = 0.06; 95% CI = 0.25 - 0.51), P = 0.047. The weight gain per kilogram of body weight was directly proportional to the severity of malnutrition. CONCLUSIONS: **Community-based treatment showed weight gain in both groups, the gain being higher with RUTF.**

Nutr J. 2010 Nov 22;9:56.

Home visits by neighborhood Mentor Mothers provide timely recovery from childhood malnutrition in South Africa: results from a randomized controlled trial.

le Roux IM, le Roux K, Comulada WS, Greco EM, Desmond KA, Mbewu N, Rotheram-Borus MJ.

Source

Philani Child Health and Nutrition Project, Khayelitsha, PO Box 40188, Elonwabeni, Cape Town 7791, South Africa.

Abstract

BACKGROUND: Child and infant malnourishment is a significant and growing problem in the developing world. Malnourished children are at high risk for negative health outcomes over their lifespans. **Philani, a paraprofessional home visiting program, was developed to improve childhood nourishment**. The objective of this study is to evaluate whether the Philani program can rehabilitate malnourished children in a timely manner. METHODS: Mentor Mothers were trained to conduct home visits. Mentor Mothers went from house to house in assigned neighborhoods, weighed children age 5 and younger, and recruited mother-child dyads where there was an underweight child. **Participating dyads were assigned in a 2:1 random sequence to the Philani intervention condition (n = 536) or a control condition (n = 252). Mentor Mothers visited dyads in the intervention condition for one year, supporting mothers' problem-solving around nutrition.** All children were weighed by Mentor Mothers at baseline and three, six, nine and twelve month follow-ups. RESULTS: By three months, children in the intervention condition were five times more likely to rehabilitate (reach a healthy weight for their ages) than children in the control condition. **Throughout the course of the study, 43% (n = 233 of 536) of children in the intervention condition were rehabilitated while 31% (n = 78 of 252) of children in the control condition were rehabilitated.** CONCLUSIONS: Paraprofessional Mentor Mothers are an effective strategy for delivering home visiting programs by providing the knowledge and support necessary to change the behavior of families at risk.

Maternal health

BMC Pregnancy **Childbirth**. 2010 Dec 14;10:82.

Communities, birth attendants and health facilities: a continuum of emergency maternal and newborn care (the Global Network's EmONC trial).

Pasha O, Goldenberg RL, McClure EM, Saleem S, Goudar SS, Althabe F, Patel A, Esamai F, Garces A, Chomba E, Mazariegos M, Kodkany B, Belizan JM, Derman RJ, Hibberd PL, Carlo WA, Liechty EA, Hambidge KM, Buekens P, Wallace D, Howard-Grabman L, Stalls S, Koso-Thomas M, Jobe AH, Wright LL.

Source

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Abstract
BACKGROUND: Maternal and newborn mortality rates remain unacceptably high, especially where the majority of births occur in home settings or in facilities with inadequate resources. The introduction of emergency obstetric and newborn care services has been proposed by several organizations in order to improve pregnancy outcomes. However, the effectiveness of emergency obstetric and neonatal care services has never been proven. Also unproven is the effectiveness of community mobilization and community birth attendant training to improve pregnancy outcomes. METHODS/DESIGN: We have developed a cluster-randomized controlled trial to evaluate the impact of a comprehensive intervention of community mobilization, birth attendant training and improvement of quality of care in health facilities on perinatal mortality in low and middle-income countries where the majority of births take place in homes or first level care facilities. This trial will take place in 106 clusters (300-500 deliveries per year each) across 7 sites of the Global Network for Women's and Children's Health Research in Argentina, Guatemala, India, Kenya, Pakistan and Zambia. The trial intervention has three key elements, community mobilization, home-based life saving skills for communities and birth attendants, and training of providers at obstetric facilities to improve quality of care. The primary outcome of the trial is perinatal mortality. Secondary outcomes include rates of stillbirth, 7-day neonatal mortality, maternal death or severe morbidity (including obstetric fistula, eclampsia and obstetrical sepsis) and 28-day neonatal mortality. DISCUSSION: In this trial, we are evaluating a combination of interventions including community mobilization and facility training in an attempt to improve pregnancy outcomes. If successful, the results of this trial will provide important information for policy makers and clinicians as they attempt to improve delivery services for pregnant women and newborns in low-income countries.

Maternal micronutrients

Afr J Reprod Health. 2010 Jun;14(2):17-26.

Effects of maternal micronutrient supplementation on fetal loss and under-2-years child mortality: long-term follow-up of a randomised controlled trial from Guinea-Bissau.

Andersen GS, Friis H, Michaelsen KF, Rodrigues A, Benn CS, Aaby P, Kaestel P.
Source
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Abstract
A number of trials on maternal multi-micronutrient supplementation (MMS) have found a benefical effect on birth weight, but few have demonstrated a beneficial effect on infant survival. We examined the effect of two different preparations of antenatal MMS on fetal loss and under-2-years child mortality, as compared with iron-folic acid supplementation among 2,100 pregnant women in Guinea-Bissau. Women receiving a 1xRDA MMS preparation (consisting of 14 vitamins and minerals) had a marginally reduced risk of fetal loss (Relative risk (RR) 0.65, 95% CI 0.40; 1.05), and women receiving a 2xRDA MMS preparation had a similar effect (RR 0.67, 95% CI 0.42; 1.08), the pooled effect being 0.66 (95% CI 0.44; 0.99). None of the supplements reduced under-2-years mortality or the combination of fetal loss and under-2-years mortality. There was a marginally negative effect of both the 1xRDA (RR 2.10,

95% CI 0.99; 4.46) and the 2xRDA (RR 2.02, 95% CI 0.95; 4.32) MMS preparation on mortality specifically between 92-365 days of age.

JAMA. 2010 Dec 22;304(24):2716-23.

Prenatal micronutrient supplementation and intellectual and motor function in early school-aged children in Nepal.

Christian P, Murray-Kolb LE, Khatry SK, Katz J, Schaefer BA, Cole PM, Leclerq SC, Tielsch JM.

Source

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Abstract

CONTEXT: Iron and zinc are important for the development of both intellectual and motor skills. Few studies have examined whether iron and zinc supplementation during gestation, a critical period of central nervous system development, affects children's later functioning. OBJECTIVE: To examine intellectual and motor functioning of children whose mothers received micronutrient supplementation during pregnancy. DESIGN, SETTING, AND PARTICIPANTS: **Cohort follow-up of 676 children aged 7 to 9 years in June 2007-April 2009 who had been born to women in 4 of 5 groups of a community-based, double-blind, randomized controlled trial of prenatal micronutrient supplementation between 1999 and 2001 in rural Nepal.** Study children were also in the placebo group of a subsequent preschool iron and zinc supplementation trial. INTERVENTIONS: Women whose children were followed up had been randomly assigned to receive **daily iron/folic acid, iron/folic acid/zinc, or multiple micronutrients containing these plus 11 other micronutrients, all with vitamin A, vs a control group of vitamin A alone from early pregnancy through 3 months postpartum**. These children did not receive additional micronutrient supplementation other than biannual vitamin A supplementation. MAIN OUTCOME MEASURES: Children's intellectual functioning, assessed using the Universal Nonverbal Intelligence Test (UNIT); tests of executive function, including go/no-go, the Stroop test, and backward digit span; and motor function, assessed using the Movement Assessment Battery for Children (MABC) and finger-tapping test. RESULTS: The difference across outcomes was significant (Bonferroni-adjusted P < .001) for iron/folic acid vs control but not for other supplement groups. The mean UNIT T score in the iron/folic acid group was 51.7 (SD, 8.5) and in the control group was 48.2 (SD, 10.2), with an adjusted mean difference of 2.38 (95% confidence interval [CI], 0.06-4.70; P = .04). Differences were not significant between the control group and either the iron/folic acid/zinc (0.73; 95% CI, -0.95 to 2.42) or multiple micronutrient (1.00; 95% CI, -0.55 to 2.56) groups. In tests of executive function, scores were better in the iron/folic acid group relative to the control group for the Stroop test (adjusted mean difference in proportion who failed, -0.14; 95% CI, -0.23 to -0.04) and backward digit span (adjusted mean difference, 0.36; 95% CI, 0.01-0.71) but not for the go/no-go test. The MABC score was lower (better) in the iron/folic acid group compared with the control group but not after adjustment for confounders (mean difference, -1.47; 95% CI, -3.06 to 0.12; P = .07). Finger-tapping test scores were higher (mean difference, 2.05; 95% CI, 0.87-3.24; P = .001) in the iron/folic acid group. CONCLUSION**: Aspects of intellectual functioning including working memory, inhibitory control, and fine motor functioning among offspring were positively associated with prenatal iron/folic acid supplementation in an area where iron deficiency is prevalent.**

Acta Obstet Gynecol Scand. 2010 Nov;89(11):1396-402. Epub 2010 Sep 13.

Maternal calcium supplementation during pregnancy and dental caries of children at 12 years of age: follow-up of a randomized controlled trial.

Bergel E, Gibbons L, Rasines MG, Luetich A, Belizán JM.

Source

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Abstract

OBJECTIVES: To evaluate if calcium supplementation during pregnancy could have any influence on primary dentition measured as the reduction of dental caries of the child. DESIGN: Individual randomized controlled trial. SETTING: One hospital in Rosario, Argentina. POPULATION: Random sample of 195 12-year-old children from a follow-up study of 614 women who were randomized during pregnancy to calcium supplementation or placebo. METHODS: An independent researcher blinded to the group where the mothers were assigned performed a dental examination of the children. MAIN OUTCOME MEASURES: Proportion of children with at least one decayed, missing or filled teeth (DMFT/dmft) and mean number of decayed, missing or filled surfaces (DMFS/dmfs) per children. RESULTS: **Ninety-eight children were assessed in the calcium supplementation group and 97 in the placebo group. 63.3% of the children whose mother took calcium supplementation had at least one DMFT/dmft compared to 86.6% in the placebo group (<0.001).** The children whose mother received the intervention had a 27% reduction in the risk of developing at least one DMFT/dmft (RR: 0.73, CI 95%: [0.62; 0.87]). CONCLUSIONS: This study shows a modeling effect of calcium intake during pregnancy on dental caries of the offspring. **At around 12 years of age children whose mothers received calcium supplementation when pregnant showed a significant reduction in dental caries.**

Am J Clin Nutr. 2011 Jun 15. [Epub ahead of print]

Nutritional supplementation during pregnancy and offspring cardiovascular disease risk in The Gambia.

Hawkesworth S, Walker CG, Sawo Y, Fulford AJ, Jarjou LM, Goldberg GR, Prentice A, Prentice AM, Moore SE.

Source

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Abstract

BACKGROUND: Maternal nutritional intake during pregnancy may have important consequences for long-term health in offspring. OBJECTIVE: The objective was to follow up the offspring in 2 randomized trials of nutrient supplementation during pregnancy to investigate the effect on cardiovascular disease (CVD) risk in offspring. DESIGN: We recruited offspring born during 2 trials in The Gambia, West Africa. **One trial provided protein-energy-dense food supplements (1015 kcal and 22 g protein/d) to pregnant (intervention, from 20 wk gestation until delivery) or lactating (control, for 20 wk from birth) women and was randomized at the village level. The second was a double-blind, individually randomized, placebo-controlled trial of calcium supplementation (1.5 g/d), which was also provided from 20 wk gestation until delivery.** RESULTS: Sixty-two percent (n = 1267) of children (aged 11-17 y) born during the protein-energy trial were recruited and included in the analysis,

and 64% (n = 350) of children (aged 5-10 y) born during the calcium trial were recruited and included in the analysis. Fasted plasma glucose was marginally lower in children born to mothers receiving protein-energy supplements during pregnancy than in those children of the lactating group (adjusted mean difference: -0.05 mmol/L; 95% CI: -0.10, -0.001 mmol/L). **There were no other differences in CVD risk factors, including blood pressure, body composition, and cholesterol, between children born to intervention and control women from the protein-energy trial. Maternal calcium supplementation during pregnancy was unrelated to offspring blood pressure.** CONCLUSION: These data suggest that providing supplements to pregnant women in the second half of pregnancy may have little effect on the CVD risk of their offspring, at least in this setting and at the ages studied here. This trial was registered at www.controlled-trials.com as ISRCTN96502494.

*** Int J Epidemiol. 2011 Apr;40(2):350-62. Epub 2011 Jan 19.

Modifying effects of wealth on the response to nutrient supplementation in pregnancy on birth weight, duration of gestation and perinatal mortality in rural western China: double-blind cluster randomized controlled trial.

Zeng L, Yan H, Cheng Y, Dibley MJ.

Source

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Abstract

BACKGROUND: There have been few reports of differential responses to nutrition interventions in women and children from poor households. Women from poor households have greater nutritional risks and are potentially a target group for programmes. We assessed the modifying effects of household wealth on responses to micronutrient supplements in pregnancy on newborn anthropometry and perinatal mortality. METHODS: A cluster randomized double-blind controlled trial conducted in two rural counties in northwestern China. All pregnant women in villages were randomly allocated from enrolment until delivery to daily supplementation with folic acid (control), iron/folic acid or multiple micronutrients (MMNs) with a recommended allowance of 15 vitamins and minerals. Wealth was based on a score from an inventory of household assets. RESULTS: **In the pregnant women from the poorest one-third of the households, MMN supplements significantly increased birth weight by 68 g [95% confidence interval (CI) 4-131 g], reduced low birth weight by 60% [relative risks (RRs) 0.40, 95% CI 0.21-0.78] and tended to reduce early neonatal mortality by 52% (RR 0.48, 95% CI 0.17-1.36) compared with folic acid. Iron/folic acid significantly increased the duration of gestation by 0.41 weeks (95% CI 0.18-0.65), reduced pre-term birth by 45% (RR 0.55, 95% CI 0.32-0.93) and significantly reduced early neonatal mortality by 90% (RR 0.10, 95% CI 0.01-0.79) compared with folic acid.** Iron/folic acid and MMN supplements had no significant effects in women from wealthier households. CONCLUSIONS: In rural China, women from the poorest households had the largest perinatal outcome responses to micronutrient supplementation. In these women, standard iron/folic acid provided more protection for neonatal survival than MMN supplements.

Acta Obstet Gynecol Scand. 2011 Jan;90(1):47-56. doi: 10.1111/j.1600-0412.2010.01014.x. Epub 2010 Nov 26.

Prevalence of anemia and micronutrient deficiencies in early pregnancy in rural Bangladesh, the MINIMat trial.

Lindström E, Hossain MB, Lönnerdal B, Raqib R, El Arifeen S, Ekström EC.

Source

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Abstract

OBJECTIVE: To describe the prevalence of anemia and micronutrient deficiencies as well as their determinants in early pregnancy. DESIGN: Baseline data from a population-based randomized intervention trial. SETTING: The study was conducted in Matlab, a sub-district in rural Bangladesh from 1 January to 31 December 2002. POPULATION: Pregnant women (n= 740) were enrolled in approximately week 14 in pregnancy. METHODS: Data were collected using questionnaires, physical examinations and laboratory analyses of blood samples for concentrations of hemoglobin, ferritin, zinc, folate and vitamin B-12. MAIN OUTCOME MEASURES: Covariates associated with anemia and micronutrient deficiencies in bivariate analyses were evaluated in multivariate logistic regression models adjusting for potential confounders. RESULTS: **Anemia was present in 28% of the women, 55% were zinc deficient, 46% were vitamin B-12 deficient and 18% were folate deficient.** Anemia was not associated with iron deficiency but rather with vitamin B-12 deficiency. **Infestation with Ascaris was highly prevalent (67%) and associated with both folate and vitamin B-12 deficiency.** Anemia and micronutrient deficiencies all varied significantly with season. CONCLUSIONS: The high prevalences of zinc and vitamin B-12 deficiencies in early pregnancy are a concern, as it could lead to adverse pregnancy outcomes and increased health risks for both mother and child. The prevalence of iron deficiency was low, but as this was during early pregnancy, the women might develop iron deficiency and consequently iron deficiency anemia as the pregnancy progresses.

Maternal mental health

Reprod Health. 2011 May 2;8:9.

Depressed mood in pregnancy: Prevalence and correlates in two Cape Town peri-urban settlements.

Hartley M, Tomlinson M, Greco E, Comulada WS, Stewart J, le Roux I, Mbewu N, Rotheram-Borus MJ.

Source

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Abstract

BACKGROUND: The disability associated with depression and its impact on maternal and child health has important implications for public health policy. While the prevalence of postnatal depression is high, there are no prevalence data on antenatal depression in South Africa. The purpose of this study was to determine the prevalence and correlates of depressed

mood in pregnancy in Cape Town peri-urban settlements. METHODS: This study reports on baseline data collected from the Philani Mentor Mothers Project (PMMP), a community-based, cluster-randomized controlled trial on the outskirts of Cape Town, South Africa. The PMMP aims to evaluate the effectiveness of a home-based intervention for preventing and managing illnesses related to HIV, TB, alcohol use and malnutrition in pregnant mothers and their infants. Participants were 1062 pregnant women from Khayelitsha and Mfuleni, Cape Town. Measures included the Edinburgh Postnatal Depression Scale (EPDS), the Derived AUDIT-C, indices for social support with regards to partner and parents, and questions concerning socio-demographics, intimate partner violence, and the current pregnancy. Data were analysed using bivariate analyses followed by logistic regression. RESULTS: **Depressed mood in pregnancy was reported by 39% of mothers. The strongest predictors of depressed mood were lack of partner support, intimate partner violence, having a household income below R2000 per month, and younger age.** CONCLUSIONS: The high prevalence of depressed mood in pregnancy necessitates early screening and intervention in primary health care and antenatal settings for depression. The effectiveness and scalability of community-based interventions for maternal depression must be developed for pregnant women in peri-urban settlements.

Womens groups

Trials. 2011 Jan 4;12:2.

Project Masihambisane: a cluster randomised controlled trial with peer mentors to improve outcomes for pregnant mothers living with HIV.

Rotheram-Borus MJ, Richter L, Van Rooyen H, van Heerden A, Tomlinson M, Stein A, Rochat T, de Kadt J, Mtungwa N, Mkhize L, Ndlovu L, Ntombela L, Comulada WS, Desmond KA, Greco E.

Source

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Abstract

BACKGROUND: Pregnant women living with HIV (WLH) face daily challenges maintaining their own and their babies' health and mental health. Standard Prevention of Maternal to Child Transmission (PMTCT) programs are not designed to address these challenges. METHODS/DESIGN: As part of a cluster randomized controlled trial, WLH are invited to attend four antenatal and four postnatal small group sessions led by a peer WLH (a Peer Mentor). The WLH and their babies are assessed during pregnancy and at one week, six months, and twelve months post-birth. Mobile phones are used to collect routine information, complete questionnaires and remain in contact with participants over time. Pregnant WLH (N = 1200) are randomly assigned by clinic (N = 8 clinics) to an intervention program, called Masihambisane (n = 4 clinics, n = 600 WLH) or a standard care PMTCT control condition (n = 4 clinics; n = 600 WLH). DISCUSSION: Data collection with cellular phones are innovative and effective in low-resource settings. Standard PMTCT programs are not designed to address the daily challenges faced by WLH; Peer Mentors may be useful in supporting WLH to cope with these challenges.

Neonatal care

Pediatrics. 2010 Dec;126(6):e1485-92.

Effects of traditional swaddling on development: a randomized controlled trial.

Manaseki-Holland S, Spier E, Bavuusuren B, Bayandorj T, Sprachman S, Marshall T.

Source

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Abstract

OBJECTIVE: Evidence of the effects of tight, prolonged binding of infants on development is inconclusive and based on small ethnographic studies. The null hypothesis was that Mongolian infants not swaddled or swaddled tightly in a traditional setting (to >7 months of age) do not have significantly different scores for the Bayley Scales of Infant Development, Second Edition (BSID-II). PATIENTS AND METHODS: In a randomized controlled trial, **1279 healthy newborns in Ulaanbaatar, Mongolia, were allocated at birth to traditional swaddling or nonswaddling.** The families received 7 months of home visits to collect data and monitor compliance. At 11 to 17 months of age, the BSID-II was administered to 1100 children. RESULTS: No significant between-group differences were found in mean scaled mental and psychomotor developmental scores. The unadjusted mean difference between the groups was -0.69 (95% confidence interval [CI]: -2.59 to 1.19) for psychomotor and -0.42 (95% CI: -1.68 to 0.84) for mental scores in favor of the swaddling group. A subgroup analysis of the compliant sample produced similar results. BSID-II-scaled psychomotor and mental scores were 99.98 (95% CI: 99.03-100.92) and 105.52 (95% CI: 104.89-106.14), respectively. Background characteristics were balanced across the groups. CONCLUSIONS: **In the Mongolian context, prolonged swaddling in the first year of life did not have any significant impact on children's early mental or psychomotor development.** Additional studies in other settings need to confirm this finding. The Mongolian infants in this trial had scaled BSID-II mental and psychomotor scores comparable to United States norms.

*** Lancet. 2011 Jan 29;377(9763):403-12. Epub 2011 Jan 14.

Improvement of perinatal and newborn care in rural Pakistan through community-based strategies: a cluster-randomised effectiveness trial.

Bhutta ZA, Soofi S, Cousens S, Mohammad S, Memon ZA, Ali I, Feroze A, Raza F, Khan A, Wall S, Martines J.

Source

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Abstract

BACKGROUND: Newborn deaths account for 57% of deaths in children younger than 5 years in Pakistan. Although a large programme of trained lady health workers (LHWs) exists, the effectiveness of this training on newborn outcomes has not been studied. We aimed to evaluate the effectiveness of a community-based intervention package, principally delivered through LHWs working with traditional birth attendants and community health committees, for reduction of perinatal and neonatal mortality in a rural district of Pakistan. METHODS: We

undertook a cluster randomised trial between February, 2006, and March, 2008, in Hala and Matiari subdistricts, Pakistan. Catchment areas of primary care facilities and all affiliated LHWs were used to define clusters, which were allocated to intervention and control groups by restricted, stratified randomisation. **The intervention package delivered by LHWs through group sessions consisted of promotion of antenatal care and maternal health education, use of clean delivery kits, facility births, immediate newborn care, identification of danger signs, and promotion of careseeking; control clusters received routine care.** Independent data collectors undertook quarterly household surveillance to capture data for births, deaths, and household practices related to maternal and newborn care. Data collectors were masked to cluster allocation; those analysing data were not. The primary outcome was perinatal and all-cause neonatal mortality. Analysis was by intention to treat. This trial is registered, ISRCTN16247511. FINDINGS: 16 clusters were assigned to intervention (23,353 households, 12,391 total births) and control groups (23,768 households, 11,443 total births). LHWs in the intervention clusters were able to undertake 4428 (63%) of 7084 planned group sessions, but were only able to visit 2943 neonates (24%) of a total 12,028 livebirths in their catchment villages. **Stillbirths were reduced in intervention clusters (39·1 stillbirths per 1000 total births) compared with control (48·7 per 1000; risk ratio [RR] 0·79, 95% CI 0·68-0·92; p=0·006). The neonatal mortality rate was 43·0 deaths per 1000 livebirths in intervention clusters compared with 49·1 per 1000 in control groups (RR 0·85, 0·76-0·96; p=0·02).** INTERPRETATION: Our results support the scale-up of preventive and promotive maternal and newborn interventions through community health workers and emphasise the need for attention to issues of programme management and coverage for such initiatives to achieve maximum potential.

THE LANCET
FULL-TEXT ARTICLE

Trop Doct. 2010 Oct;40(4):199-202. Epub 2010 Jul 28.

Effect of Kangaroo Mother Care on physical growth, breastfeeding and its acceptability.

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Source

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Abstract

The aim of this study was to determine whether the implementation of Kangaroo Mother Care (KMC) to low birth weight infants would improve physical growth, breastfeeding and its acceptability. A randomized controlled trial was performed over 16 months in which **110 neonates were randomized into a KMC group and a control group** using a random number table. The KMC group was subjected to KMC for at least 6 h per day. The babies also received KMC after moving from the neonatal intensive care unit and at home. The control group received standard care (incubator or open care system). Weight, length and occipitofrontal circumference (OFC) were measured weekly for three months. The acceptability of KMC by mothers and nursing staff was assessed on day 7 after the start of KMC using a questionnaire incorporating the Likert scale. Breastfeeding rates were calculated based on history at end of three months. The mean gestational age was 35.48 ± 1.20 weeks in the KMC group and 35.04 ± 1.09 weeks in the control group (P > 0.05). KMC was initiated at a mean age of 1.72 ± 0.45 days and the duration of KMC was 9.74 ± 1.48 h/day. The mean birth weight was 1.69 ± 0.11 kg in the KMC group compared to 1.69 ± 0.12 kg in the control group (P > 0.05). **The mean weight gain in gm/day in the KMC group was 21.92 ± 1.44 compared to 18.61 ± 1.28 in the**

control group (P < 0.05). The mean length gain in cm/week was 1.03 ± 0.5 in the KMC group compared to 0.74 ± 0.05 in the control group (P < 0.05). The mean OFC gain in cm/week was 0.59 ± 0.04 in the KMC group compared to 0.47 ± 0.03 in the control group (P < 0.05). **The exclusive breast-feeding rate at end of three months was 88% in the KMC group compared to 72% in the control group (P < 0.05).** KMC improved physical growth, breastfeeding rates and was well accepted by both mothers and nursing staff.

J Clin Nurs. 2010 Dec;19(23-24):3307-13. doi: 10.1111/j.1365-2702.2010.03382.x. Epub 2010 Oct 14.

The effectiveness of structured discharge education on maternal confidence, caring knowledge and growth of premature newborns.

Shieh SJ, Chen HL, Liu FC, Liou CC, Lin YI, Tseng HI, Wang RH.

Source

Department of Nursing, Kaohsiung Medical University Hospital, College of Nursing, Kaohsiung Medical University, Kaohsiung, Taiwan.

Abstract

AIMS: The aim of this study is to evaluate the effectiveness of structured discharge education on maternal confidence and caring knowledge and the growth of premature newborns. BACKGROUND: Parents of premature newborns are usually confronted with great difficulties in caring for their babies after discharge. Building maternal confidence and caring knowledge can help mothers reduce such difficulties of caring for their babies after discharge from hospital. DESIGN: Randomised controlled trial. METHODS: Mothers with premature babies were randomly assigned into experimental (n=29) and control groups (n=30) at a medical centre in southern Taiwan. The mothers of both groups had received a questionnaire concerning maternal confidence and caring knowledge at pretest. After the pretest, a structured discharged education programme was provided to the mothers of the experimental group. The control group only received traditional discharge education. Mothers of experimental and control groups again received the questionnaire of maternal confidence and caring knowledge at the day before discharge and one month after discharge. At that time, the body height and body weight of newborns were measured and recorded. RESULTS: Maternal confidence and caring knowledge of mothers in the experimental group were significantly higher than those of the control group at the day before discharge; however, there were no significant differences between the two groups one month after discharge. Using repeated anova analysis, the time × group interaction was significant for maternal confidence and caring knowledge, indicating that the groups differed significantly in changes in maternal confidence and caring knowledge over the three time points. CONCLUSIONS: Structured discharge education on mothers could significantly increase maternal confidence and caring knowledge at the day before discharge. Furthermore, structured discharge education could significantly increase the percentage of growth on body height of premature newborns. RELEVANCE TO CLINICAL PRACTICE: The results could help clinical nurses design appropriate discharge education programmes for mothers of premature newborns.

J Clin Nurs. 2011 Apr;20(7-8):1008-17. doi: 10.1111/j.1365-2702.2010.03356.x. Epub 2010 Nov 5.

The effects of various interventions to newborns on pain and duration of crying.

Yilmaz F, Arikan D.

Source

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Abstract

AIM AND OBJECTIVE: This study aimed to compare the effects of mother's milk, sucrose and pacifier use to overcome pain during painful interventions to the newborns on the crying time and pain. BACKGROUND: Various non-pharmacological methods are used to overcome the pain associated with painful interventions with newborns. DESIGN: A prospective, randomised, controlled study involved 120 newborns in Turkey. METHODS: The population consisted of healthy newborns hospitalised in the gynaecology clinics of Trabzon Delivery and Children's Diseases hospital between February 2007-January 2008. **The newborns who had blood sampling by heel stick were divided into four groups: mother's milk, sucrose, pacifier and control groups with 30 newborns in each.** Data collection was performed using an information form on the newborn characteristics, which was developed by the researchers in the light of literature, clinical IR ear thermometer ET1 for temperature measurement, OXIMAX N-65 Pulse oxymeter for oxygen saturation and heart rate and neonatal infant pain scale for the measurement of the behavioural. No differences were determined between the responses of newborns. Results. groups for heart rate and oxygen saturation in the newborns during painful interventions ($p > 0{\cdot}05$). Sucrose followed by pacifier was the most effective method of reducing the crying time in the newborns. CONCLUSION: **The results indicate that all three practices reduce the behavioural responses to pain at a higher rate than in the control group.** RELEVANCE TO CLINICAL PRACTICE: Health care personnel should perform painful interventions to the newborns while the babies are held by their mothers and during the procedure use of sucrose should be the primary choice.

Neurocysticercosis

Neurol **India**. 2010 Jul-Aug;58(4):560-4.

Comparison of 1 week versus 4 weeks of albendazole therapy in single small enhancing computed tomography lesion.

Kaur P, Dhiman P, Dhawan N, Nijhawan R, Pandit S.

Source

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Abstract

BACKGROUND: The appropriate duration of albendazole therapy in neurocysticercosis is uncertain. The observation in small uncontrolled randomized trials in children that short-course therapy (1 week) is as effective as the conventional regimen (4weeks) must be tested. OBJECTIVE: To compare the efficacy of 1 and 4 weeks of albendazole therapy in children with single small enhancing computed tomographic lesion (SSECTL). STUDY DESIGN: An open-labeled, randomized, clinical trial. MATERIALS AND METHODS: One hundred twenty

children with SSECTLs presenting with seizure. INTERVENTION: **The subjects were assigned to two groups using random tables: group A (n=58) received albendazole for 1 week and group B (n=62) for 4 weeks.** All the subjects were followed up for 6 months. RESULTS: The proportions of subjects with complete resolution of lesion in the two groups were similar (group A 63.8% versus group B 51.6%). The proportion of subjects in the two groups in whom the lesion calcified on follow up (group A 19% versus group B 24.2%) also did not differ significantly. The incidence of seizure recurrence during the 6-month follow-up period was also similar in both the groups (group A 9.6% versus group B 3.4%, P > 0.05). CONCLUSION: **One week of albendazole therapy is as effective as 4 weeks of therapy in children with SSECTLs**.

Nutrition, micronutrients and breast feeding

(See also maternal health, HIV case management)

Trans R Soc Trop Med Hyg. 2010 Nov;104(11):743-5. Epub 2010 Sep 18.

Preliminary evaluation of the Moyo chart-a novel, low-cost, weight-for-height slide chart for the improved assessment of nutritional status in children.

Sikorski C, Kerac M, Fikremariam M, Seal A.

Source

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Abstract

The Moyo chart is a novel weight-for-height slide chart. We explore the hypothesis that it improves accuracy, speed and ease of nutritional assessment compared with traditional lookup tables. In a crossover randomised controlled trial, 61 medical students in Ethiopia diagnosed hypothetical cases of severe acute malnutrition, moderate acute malnutrition and normal nutrition in children. Mean accuracy of nutritional status diagnosis was 83.2% using the Moyo chart and 76.1% using lookup tables (P = 0.011). There was a trend towards a reduced time per correct diagnosis using the Moyo chart and 78% of participants preferred using it. These preliminary results suggest that the Moyo chart may aid frontline health workers classifying child nutritional status.

Matern **Child** Nutr. 2011 Apr;7 Suppl 2:89-98. doi: 10.1111/j.1740-8709.2011.00313.x.

Impact of fatty acid status on immune function of children in low-income countries.

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Source

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Abstract

In vitro and animal studies point to numerous mechanisms by which fatty acids, especially long-chain polyunsaturated fatty acids (LCPUFA), can modulate the innate and adaptive arms of the immune system. These data strongly suggest that improving the fatty acid supply of young children in low-income countries might have immune benefits. Unfortunately, there have been

virtually no studies of fatty acid/immune interactions in such settings. Clinical trial registers list over 150 randomized controlled trials (RCTs) involving PUFAs, only one in a low-income setting (the Gambia). We summarize those results here. There was evidence for improved growth and nutritional status, but the primary end point of chronic environmental enteropathy showed no benefit, possibly because the infants were still substantially breastfed. In high-income settings, there have been RCTs with fatty acids (usually LCPUFAs) in relation to 18 disease end points, for some of which there have been numerous trials (asthma, inflammatory bowel disease and rheumatoid arthritis). For these diseases, the evidence is judged reasonable for risk reduction for childhood asthma (but not in adults), as yielding possible benefit in Crohn's disease (insufficient evidence in ulcerative colitis) and for convincing evidence for rheumatoid arthritis at sufficient dose levels, though formal meta-analyses are not yet available. This analysis suggests that fatty acid interventions could yield immune benefits in children in poor settings, especially in non-breastfed children and in relation to inflammatory conditions such as persistent enteropathy. Benefits might include improved responses to enteric vaccines, which frequently perform poorly in low-income settings, and these questions merit randomized trials.

Asia Pac J Clin Nutr. 2011;20(1):69-76.

Improved growth of toddlers fed a milk containing synbiotics.

Firmansyah A, Dwipoerwantoro PG, Kadim M, Alatas S, Conus N, Lestarina L, Bouisset F, Steenhout P.

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Abstract

Bifidobacterium longum (BL999), Lactobacillus rhamonosus (LPR), prebiotics (inulin and fructo-oligosaccharides), and long-chain polyunsaturated fatty acids (LCPUFA) are believed to have health benefits. In a randomized, double-blind, controlled trial we compared growth and development of toddlers fed milk containing synbiotics (BL999, LPR, and prebiotics) and LCPUFA or a control milk. Three hundred and ninety three healthy, 12 month-old toddlers were fed approximately 400 mL/day for 12 months. Anthropometric measurements were taken at 12, 14, and 16 months. Toddlers' response to measles and hepatitis A vaccine was measured at 16 months, and Bayley scale for motor, cognitive, and behavioral functions made at 24 months. The primary outcome was weight gain between 12 and 16 months. Secondary outcomes were gain in length, head circumference, and body mass index, gastrointestinal tolerance (stool characteristics), stool bacterial counts, safety, anti-vaccine IgG, and neurodevelopment. Weight gain was greater in the synbiotics group (mean±SD, 7.57±4.13 g/day) compared with the control group (6.64±4.08 g/day). The difference of 0.93 g/day (with a 95% confidence interval of 0.12 to 1.75) is significant (p=0.025). The gain in the synbiotics group resulted in a change in z-score weight-for-age closer to WHO Child Growth Standard. There was a significant increase in lactobacilli and enterococci counts between 12 months and 16 months in the synbiotic group. We conclude that in healthy toddlers milk containing synbiotics and LCPUFA provides better growth and promotes favorable gut colonization, as shown by higher Lactobacillus counts.

Pediatrics. 2011 May;127(5):e1191-7. Epub 2011 Apr 18.

A cluster-randomized evaluation of a responsive stimulation and feeding intervention in Bangladesh.

Aboud FE, Akhter S.
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Abstract

OBJECTIVES: The goal of this study was to determine if a responsive stimulation and feeding intervention improved developmental and nutritional outcomes compared with a regular information-based parenting program. The hypothesis was that mothers in the intervention would exhibit better parenting skills and children would exhibit better developmental and nutritional outcomes than controls. METHODS: A cluster-randomized field trial was conducted with 302 children aged 8 to 20 months and their mothers in rural Bangladesh who were randomly assigned according to village to 1 of 3 groups. **The control mothers received 12 informational sessions on health and nutrition. The intervention groups received an additional 6 sessions delivered by peer educators who included modeling and coached practice in self-feeding and verbal responsiveness with the child during play. A second intervention group received, along with the sessions, 6 months of a food powder fortified with minerals and vitamins.** Developmental outcomes included the Home Observation for Measurement of the Environment (HOME) Inventory, mother-child responsive talk, and language development. Nutritional outcomes included weight, height, self-feeding, and mouthfuls eaten. We used analysis of covariance to compare the 3 groups at the posttest and at follow-up, covarying the pretest levels and confounders. RESULTS: At follow-up, responsive stimulation-feeding groups had better HOME inventory scores, responsive talking, language, mouthfuls eaten, and hand-washing. Micronutrient fortification resulted in more weight gain. CONCLUSIONS: A brief behavior-change program that focused on modeling and practice in stimulation and feeding was found to benefit children's nutrition and language development. Micronutrients benefited children's weight but not length.

J Nutr. 2010 Nov;140(11):2002-7. Epub 2010 Sep 15.

Maternal dietary counseling in the first year of life is associated with a higher healthy eating index in childhood.

Vitolo MR, Rauber F, Campagnolo PD, Feldens CA, Hoffman DJ.
Source
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Abstract

Food preferences are established in early childhood and track later in life. Therefore, it is important to promote healthy feeding practices as early as possible. A randomized field trial was conducted with 500 mother-child pairs from a low-income area of São Leopoldo, State of Rio Grande do Sul, Brazil, to evaluate the impact of a nutritional intervention in the first year of life on the dietary quality of 3- to 4-y-old children. **Mother-child pairs were randomized either to intervention and control groups and dietary counseling was provided for mothers in the intervention group during 10 home visits in the course of the first year of life**. These visits were carried out by fieldworkers who counseled the mothers about the Ten Steps for Healthy Feeding from Birth to Two Years of Age, based on the WHO guidelines. Dietary intake was

assessed at 3-4 y of age for 345 children using two 24-h food recalls. Overall diet quality was determined by the Healthy Eating Index**. The prevalence of poor diet in the intervention group was lower compared with the control group [relative risk (RR) = 0.30; 95% CI = 0.13-0.71). The number of children who achieved the 75th percentile for the vegetable and fruit component score was higher in the intervention than in control group (RR = 1.95; 95% CI = 1.31-2.89 and RR = 1.49; 95% CI = 1.07-2.07, respectively).** Such data provide evidence that dietary counseling for mothers during the first year of life improves the overall dietary quality of children in a low-income population.

Micronutients and food fortification

(see also Anaemia, Zinc, Maternal nutrition, Vitamin A)

J Acquir Immune Defic Syndr. 2011 Feb 1;56(2):166-75.

Provision of micronutrient-fortified food from 6 months of age does not permit HIV-exposed uninfected Zambian children to catch up in growth to HIV-unexposed children: a randomized controlled trial.

Filteau S, Baisley K, Chisenga M, Kasonka L, Gibson RS; CIGNIS Study Team.
Filteau S, Kasonka L, Gibson R, Gompels UA, Jaffar S, Kafwembe E, Monze M, Sinkala M, Tomkins A, Zulu R, Chisenga M, Siame J, Mabuda HB, Baisley K, Dale H, Rehman A, Bates M, Mullen A, Bwalya HK, Chileshe M, Kowa PK, Kumwenda M, Likando M, Mambwe S, Muzyamba M, Mwale A, Nyaywa L, Kapambwe M, Bima H, Gosset L, Hackett L, Jackson A, Njunju E, Mwanza S, Shampwaya N, Kabanga C, Soko P, Chobo J, Kapumba W, Musonda C.
Source
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Abstract
BACKGROUND: HIV-exposed, uninfected (HIV-EU) children represent a large proportion of children in southern Africa. The reasons for their poorer growth and higher morbidity and mortality than their HIV-unexposed peers are unclear. OBJECTIVE: We compared anthropometry of 125 HIV-EU with 382 HIV-unexposed young Zambian children participating in a trial of micronutrient-fortified complementary/replacement food. DESIGN: **The randomized controlled trial provided children from age 6 to 18 months with a porridge flour containing either a basal or a rich level of micronutrients.** Weight and length were measured 3 monthly and head and arm circumferences and triceps and subscapular skinfolds 6 monthly. RESULTS: **There were no significant anthropometric differences between the 2 treatment groups.** In unadjusted analyses, most anthropometric Z scores of HIV-EU children were lower than those of HIV-unexposed children; after adjustment for treatment arm, socioeconomic factors, breastfeeding and sex, head and arm circumference Z scores remained lower. Subscapular skinfold Z scores were lower among HIV-EU than HIV-unexposed children at 6 months but not 18 months. CONCLUSIONS: Socioeconomic factors accounted for some but not all of the impaired growth of HIV-EU children. Micronutrient malnutrition may not be the socioeconomic factor responsible for the growth faltering. Factors acting earlier in life had irreversible effects.

J Nutr. 2011 Feb;141(2):237-42. Epub 2010 Dec 22.

A micronutrient powder with low doses of highly absorbable iron and zinc reduces iron and zinc deficiency and improves weight-for-age Z-scores in South African children.

Troesch B, van Stuijvenberg ME, Smuts CM, Kruger HS, Biebinger R, Hurrell RF, Baumgartner J, Zimmermann MB.

Source

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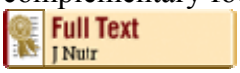
Abstract

Micronutrient powders (MNP) are often added to complementary foods high in inhibitors of iron and zinc absorption. Most MNP therefore include high amounts of iron and zinc, but it is no longer recommended in malarial areas to use untargeted MNP that contain the Reference Nutrient Intake for iron in a single serving. The aim was to test the efficacy of a low-iron and -zinc (each 2.5 mg) MNP containing iron as NaFeEDTA, ascorbic acid (AA), and an exogenous phytase active at gut pH. **In a double-blind controlled trial, South African school children with low iron status (n = 200) were randomized to receive either the MNP or the unfortified carrier added just before consumption to a high-phytate maize porridge 5 d/wk for 23 wk**; primary outcomes were iron and zinc status and a secondary outcome was somatic growth. Compared with the control, the MNP increased serum ferritin ($P < 0.05$), body iron stores ($P < 0.01$) and weight-for-age Z-scores ($P < 0.05$) and decreased transferrin receptor ($P < 0.05$). **The prevalence of iron deficiency fell by 30.6% ($P < 0.01$) and the prevalence of zinc deficiency decreased by 11.8% ($P < 0.05$).** Absorption of iron from the MNP was estimated to be 7-8%. Inclusion of an exogenous phytase combined with NaFeEDTA and AA may allow a substantial reduction in the iron dose from existing MNP while still delivering adequate iron and zinc. In addition, the MNP is likely to enhance absorption of the high native iron content of complementary foods based on cereals and/or legumes.



Am J Clin Nutr. 2011 Mar;93(3):636-43. Epub 2011 Jan 26.

Long-term effects of iron and zinc supplementation during infancy on cognitive function at 9 y of age in northeast Thai children: a follow-up study.

Pongcharoen T, DiGirolamo AM, Ramakrishnan U, Winichagoon P, Flores R, Martorell R.

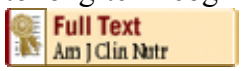
Source

Nutrition and Health Sciences Program, Graduate Division of Biological and Biomedical Sciences, Emory University, Atlanta, GA 30322, USA.

Abstract

BACKGROUND: Iron and zinc are important micronutrients for child growth and development. One would expect that iron and zinc supplementation in infancy would affect long-term cognitive development and school achievement, but this has not been evaluated. OBJECTIVE: We investigated the effect of iron or zinc supplementation or both during infancy on cognitive performance 8 y later. DESIGN: A follow-up study was performed in 560 children aged 9 y or 92% of those who had participated in a randomized controlled trial involving 4 groups who received daily iron, zinc, iron plus zinc, or a placebo at 4-6 mo of age for 6 mo. Cognitive performance was assessed by using the Wechsler Intelligence Scale for Children-Third Edition (Thai version), the Raven's Colored Progressive Matrices (CPM), and school performance tests. General linear mixed models were used to assess long-term effects. RESULTS: No significant differences in any of the outcomes at 9 y of age were observed at follow-up between the 4

groups. Mean intelligence quotients ranged across groups from 92.9 to 93.7 for full scale, 93.9-95.4 for verbal, and 93.1-94.0 for performance. The Raven's CPM score ranged from 21.4 to 22.4. CONCLUSION: Supplementation with iron or zinc or both during infancy does not lead to long-term cognitive improvement in 9-y-old children.



Int J Food Sci Nutr. 2011 Feb;62(1):1-16. Epub 2010 Aug 12.

Point-of-use micronutrient fortification: lessons learned in implementing a preschool-based pilot trial in South Africa.

Ogunlade AO, Kruger HS, Jerling JC, Smuts CM, Covic N, Hanekom SM, Mamabolo RL, Kvalsvig J.

Source

Centre of Excellence for Nutrition, North-West University (Potchefstroom Campus), Potchefstroom, South Africa.

Abstract

This current pilot trial assessed the feasibility of implementing a point-of-use (PoU) micronutrient fortification in preschool settings. Preschool children (n = 151) aged 36-79 months were randomized into intervention (n = 76) and control (n = 75) groups, both receiving breakfast maize-porridge with added micronutrient or placebo powder for 52 school days. Process evaluation and early childhood development indicators were used to assess trial feasibility. Process evaluation results showed that the implementation components were feasible and could be delivered with high fidelity. The improvement in hemoglobin concentration in intervention and control groups were not significantly different (P = 0.250). There was medium likelihood for practical significance for the two global cognitive scores assessed: non-verbal index (intervention effects: 7.20; 95% confidence interval: 2.60, 11.81; P = 0.002, effect size: 0.55) and mental processing index (intervention effects: 2.73; 95% confidence interval: 0.25, 5.70; P = 0.072, effect size: 0.36) on the Kaufman Assessment Battery for Children, Second Edition. The lessons from this trial could help in planning/implementing future PoU micronutrient fortification trial among South African preschool children.

Isr Med Assoc J. 2010 Jun;12(6):342-7.

Efficacy of multiple micronutrient supplementations on child health: study design and baseline characteristics.

Bilenko N, Belmaker I, Vardi H, Fraser D.

Source

Department of Epidemiology and Health Services Evaluation, Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer Sheva, Israel. natalya@bgu.ac.il

Abstract

BACKGROUND: The rates of anemia in children in southern Israel are high despite the current prevention strategy. A daily dose of "Sprinkles" (SuppleForte, Heinz, Canada), a micronutrient home supplementation, was proven effective for the treatment of anemia worldwide. OBJECTIVES: To assess the efficacy of Sprinkles, a novel supplementation formulation, in the

primary prevention of anemia in infants who have free access to health care services. METHODS: A two-arm open-labeled cluster randomized controlled clinical trial was performed in 6 month old Bedouin and Jewish infants. The Sprinkles arm received sachets with iron, vitamins A and C, folic acid and zinc, and the control arm received standard treatment (liquid iron and vitamins A and D). The infants were from families attending Mother and Child Health clinics during 2005-2007. Intervention and follow-up were conducted for babies aged 6-12 months. Health outcomes (hematologic and nutritional indicators, growth parameters, morbidity rates) were evaluated at 12 and 18 months. RESULTS: The final study population numbered 621 infants (328 Bedouin and 293 Jewish); of the parents approached 88.5% agreed to participate. Hemoglobin > 11 g/dl was found in 55% of Bedouin and 40% of Jewish infants ($P < 0.01$). Bedouin infants had significantly lower serum concentration of iron, folic acid and zinc. All background, hematologic and micronutrient indicators were similar in the two study arms except for a slightly but not clinically significant difference in hemoglobin and hematocrit levels in Bedouins. CONCLUSIONS: Our findings indicate the need to improve the micronutrient status of infants living in the Negev. A cluster randomized trial in MCH clinics is a feasible option.

Am J Clin Nutr. 2010 Dec;92(6):1406-15. Epub 2010 Oct 20.

The effects of iron fortification on the gut microbiota in African children: a randomized controlled trial in Cote d'Ivoire.

Zimmermann MB, Chassard C, Rohner F, N'goran EK, Nindjin C, Dostal A, Utzinger J, Ghattas H, Lacroix C, Hurrell RF.

Source

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Abstract

BACKGROUND: Iron is essential for the growth and virulence of many pathogenic enterobacteria, whereas beneficial barrier bacteria, such as lactobacilli, do not require iron. Thus, increasing colonic iron could select gut microbiota for humans that are unfavorable to the host. OBJECTIVE: The objective was to determine the effect of iron fortification on gut microbiota and gut inflammation in African children. DESIGN: In a 6-mo, randomized, double-blind, controlled trial, **6-14-y-old Ivorian children (n = 139) received iron-fortified biscuits, which contained 20 mg Fe/d, 4 times/wk as electrolytic iron or nonfortifoed biscuits.** We measured changes in hemoglobin concentrations, inflammation, iron status, helminths, diarrhea, fecal calprotectin concentrations, and microbiota diversity and composition (n = 60) and the prevalence of selected enteropathogens. RESULTS: At baseline, there were greater numbers of fecal enterobacteria than of lactobacilli and bifidobacteria ($P < 0.02$). Iron fortification was ineffective; there were no differences in iron status, anemia, or hookworm prevalence at 6 mo. The fecal microbiota was modified by iron fortification as shown by a significant increase in profile dissimilarity ($P < 0.0001$) in the iron group as compared with the control group. **There was a significant increase in the number of enterobacteria ($P < 0.005$) and a decrease in lactobacilli ($P < 0.0001$) in the iron group after 6 mo.** In the iron group, there was an increase in the mean fecal calprotectin concentration ($P < 0.01$), which is a marker of gut inflammation, that correlated with the increase in fecal enterobacteria ($P < 0.05$). CONCLUSIONS: **Anemic African children carry an unfavorable ratio of fecal enterobacteria to bifidobacteria and lactobacilli, which is increased by iron fortification.**

Thus, iron fortification in this population produces a potentially more pathogenic gut microbiota profile, and this profile is associated with increased gut inflammation.

Comment

The risks of iron supplementation are controversial, a meta-analysis of studies in 2002 showed no increased risk of infectious diseases with iron supplementation, but subsequent studies showed increased risk of malaria. In some populations, especially severely malnourished children with environmental enteropathy, and in low birth weight newborns, iron fortification or supplementation may increase the risk of enteric bacterial sepsis, through gut inflammation and promotion of growth of Gram negative bacteria.

Eur J Clin Nutr. 2010 Oct;64(10):1101-7. Epub 2010 Aug 4.

Helicobacter pylori infection does not influence the efficacy of iron and vitamin B(12) fortification in marginally nourished Indian children.

Thankachan P, Muthayya S, Sierksma A, Eilander A, Thomas T, Duchateau GS, Frenken LG, Kurpad AV.

Source

Division of Nutrition, St John's Research Institute, St John's National Academy of Health Sciences, Bangalore, India. prashanth@sjri.res.in

Abstract

BACKGROUND/OBJECTIVES: Helicobacter pylori infection and iron and vitamin B(12) deficiencies are widespread in economically disadvantaged populations. There is emerging evidence that H. pylori infection has a negative effect on the absorption of these micronutrients. The aim of this study was to evaluate the effect of H. pylori infection on the efficacy of micronutrient (including iron and vitamin B(12))-fortified foods supplied for 1 year in marginally nourished children. SUBJECTS/METHODS: In all, **543 Indian children, aged 6-10 years, participated in a double-blind, randomized controlled intervention trial, receiving foods fortified with either high (100% Recommended Dietary Allowances (RDA)) or low (15% RDA) amounts of iron, vitamin B(12) and other micronutrients.** The presence of H. pylori infection was diagnosed by the (13)C-labeled urea breath test at 11 months after the start of the intervention. Blood hemoglobin, serum ferritin (SF), total body iron and plasma vitamin B(12) were estimated at baseline and 12 months, and differences between these time points were assessed using an independent t-test. RESULTS: Overall, the prevalence of H. pylori infection in this group of children was 79%. Baseline hemoglobin, SF, body iron and vitamin B(12) concentrations were not associated with H. pylori infection. The response to the intervention (either high or low amounts of iron and vitamin B(12) fortification) in terms of change in iron markers and vitamin B(12) status did not differ between children with and without H. pylori infection. CONCLUSIONS: **This study shows that the presence of H. pylori infection did not affect the efficacy of long-term iron and vitamin B(12) fortification in these marginally nourished children.**

Breastfeeding and Complementary feeding

BMC Pediatr. 2011 Jan 13;11:4.

Complementary feeding: a Global Network cluster randomized controlled trial.

Krebs NF, Hambidge KM, Mazariegos M, Westcott J, Goco N, Wright LL, Koso-Thomas M, Tshefu A, Bose C, Pasha O, Goldenberg R, Chomba E, Carlo W, Kindem M, Das A, Hartwell T, McClure E; Complementary Feeding Study Group.

Source

University of Colorado Denver, Aurora, CO, USA. nancy.krebs@ucdenver.edu

Abstract

BACKGROUND: Inadequate and inappropriate complementary feeding are major factors contributing to excess morbidity and mortality in young children in low resource settings. Animal source foods in particular are cited as essential to achieve micronutrient requirements. The efficacy of the recommendation for regular meat consumption, however, has not been systematically evaluated. METHODS/DESIGN: A cluster randomized efficacy trial was designed to test the hypothesis that 12 months of daily intake of beef added as a complementary food would result in greater linear growth velocity than a micronutrient fortified equi-caloric rice-soy cereal supplement. The study is being conducted in 4 sites of the Global Network for Women's and Children's Health Research located in Guatemala, Pakistan, Democratic Republic of the Congo (DRC) and Zambia in communities with toddler stunting rates of at least 20%. Five clusters per country were randomized to each of the food arms, with 30 infants in each cluster. The daily meat or cereal supplement was delivered to the home by community coordinators, starting when the infants were 6 months of age and continuing through 18 months. All participating mothers received nutrition education messages to enhance complementary feeding practices delivered by study coordinators and through posters at the local health center. Outcome measures, obtained at 6, 9, 12, and 18 months by a separate assessment team, included anthropometry; dietary variety and diversity scores; biomarkers of iron, zinc and Vitamin B12 status (18 months); neurocognitive development (12 and 18 months); and incidence of infectious morbidity throughout the trial. The trial was supervised by a trial steering committee, and an independent data monitoring committee provided oversight for the safety and conduct of the trial. DISCUSSION: Findings from this trial will test the efficacy of daily intake of meat commencing at age 6 months and, if beneficial, will provide a strong rationale for global efforts to enhance local supplies of meat as a complementary food for young children.

Food Nutr Bull. 2010 Sep;31(3):418-30.

The effectiveness of quality protein maize in improving the nutritional status of young children in the Ethiopian highlands.

Akalu G, Taffesse S, Gunaratna NS, De Groote H.

Source

Ethiopian Health and Nutrition Research Institute (EHNRI), Addis Ababa, Ethiopia.

Abstract

BACKGROUND: Undernutrition is a persistent problem in Africa, especially in rural areas where the poor largely depend on staples and have limited access to a diverse diet. Quality protein maize (QPM) consists of maize varieties biofortified with increased lysine and tryptophan levels. Several studies in controlled settings have indicated the positive impact of QPM on the nutritional status of children. OBJECTIVE: Two 1-year, randomized, controlled studies were undertaken to measure the effect of QPM on the nutritional status of children consuming typical maize-based diets when QPM was cultivated by their households in the western Ethiopian highlands. METHODS: The first study used a cluster-randomized design with 151 children aged 5 to 29 months; the second study used a completely randomized design with 211 children aged 7 to 56 months. In both studies, half of the households were provided with QPM seed and the other half with seed of an improved conventional maize variety. RESULTS: Undernutrition was pervasive, and maize was the dominant food in the children's complementary diets. In the first study a positive effect of QPM was observed for weight but not height, with children in the QPM group recovering from a drop in weight-for-height. **In the second study, children consuming conventional maize progressively faltered in their growth, whereas children consuming QPM did not change significantly in height-for-age and had a marginal increase in weight-for-age.** CONCLUSIONS: These studies indicate that in major maize-producing and -consuming areas of Africa, home cultivation and use of QPM in children's diets could reduce or prevent growth faltering and may in some cases support catch-up growth in weight.

Oncology

Pediatr Blood Cancer. 2011 Feb;56(2):234-8. doi: 10.1002/pbc.22778. Epub 2010 Sep 14.

Anti-emetic effect of ginger powder versus placebo as an add-on therapy in children and young adults receiving high emetogenic chemotherapy.

Pillai AK, Sharma KK, Gupta YK, Bakhshi S.

Source

College of Nursing, All India Institute of Medical Sciences, New Delhi, India.

Abstract

PURPOSE: Chemotherapy-induced nausea and vomiting (CINV) are major adverse effects of chemotherapy. Ginger has been used in postoperative and pregnancy-induced nausea and vomiting. Data on its utility in reducing CINV in children and young adults are lacking. PATIENTS AND METHODS: **Sixty chemotherapy cycles of cisplatin/doxorubicin in bone sarcoma patients were randomized to ginger root powder capsules or placebo capsules as an additional antiemetic to ondensetron and dexamethasone in a double-blind design.** Acute CINV was defined as nausea and vomiting occurring within 24 hr of start of chemotherapy (days 1-4) and delayed CINV as that occurring after 24 hr of completion of chemotherapy (days 5-10). CINV was evaluated as per Edmonton's Symptom Assessment Scale and National Cancer Institute criteria respectively. RESULTS: **Acute moderate to severe nausea was observed in 28/30 (93.3%) cycles in control group as compared to 15/27 (55.6%) cycles in experimental group (P = 0.003). Acute moderate to severe vomiting was significantly more in the control group compared to the experimental group [23/30 (76.7%) vs. 9/27 (33.33%) respectively (P= 0.002)].** Delayed moderate to severe nausea was observed in 22/30 (73.3%) cycles in the control group as compared to 7/27 (25.9%) in the experimental group (P < 0.001). Delayed moderate to severe vomiting was significantly more in the control group compared to the experimental group [14/30 (46.67%) vs. 4/27 (14.81%) (P =

0.022)]. CONCLUSION: **Ginger root powder was effective in reducing severity of acute and delayed CINV as additional therapy to ondensetron and dexamethasone in patients receiving high emetogenic chemotherapy.**

Ophthalmology

Ophthalmic Epidemiol. 2010 Aug;17(4):203-10.

A randomized controlled trial assessing the effectiveness of strategies delivering low vision rehabilitation: design and baseline characteristics of study participants.

Christy B, Keeffe JE, Nirmalan PK, Rao GN.

Source

Dr P R K Prasad Center for Rehabilitation of the Blind and Visually Impaired, Hyderabad, India. beula@lvpei.org

Abstract

PURPOSE: To design a randomized controlled trial (RCT) to compare the effectiveness of four different strategies to deliver low vision rehabilitation services. METHODS: The four arms of the RCT comprised-center based rehabilitation, home based rehabilitation, a mix of center based and home based rehabilitation, and center based rehabilitation with home based non interventional supplementary visits by rehabilitation workers. Outcomes were assessed 9 months after baseline and included measuring changes in adaptation to age-related vision loss, quality of life, impact of vision impairment and effectiveness of low vision rehabilitation training. The socio-demographic and vision characteristics of the sample in each of the 4 arms were compared to ensure that outcomes are not associated with differences between the groups. RESULTS: Four hundred and thirty six individuals were enrolled in the study; 393 individuals completed the study. One-fifth of participants were children aged 8 to 16 years. At baseline, socio-demographic and clinical characteristics were similar between individuals in the four arms of the trial. Socio-demographic and clinical characteristics did not differ significantly, except for age, between the 393 individuals who completed the trial and the 43 individuals who dropped out of the study. Twenty six (60.46%) of the forty three drop outs were from the center based arm of the trial. CONCLUSIONS: Information from this trial has the potential to shape policy and practice pertaining to low vision rehabilitation services.

Trachoma

PLoS Negl Trop Dis. 2010 Nov 2;4(11):e861.

Trachoma prevalence and associated risk factors in the Gambia and Tanzania: baseline results of a cluster randomised controlled trial.

Harding-Esch EM, Edwards T, Mkocha H, Munoz B, Holland MJ, Burr SE, Sillah A, Gaydos CA, Stare D, Mabey DC, Bailey RL, West SK; PRET Partnership.

Source
Clinical Research Unit, Department of Infectious and Tropical Diseases, London School of Hygiene & Tropical Medicine, London, United Kingdom. emma.harding-esch@lshtm.ac.uk
Abstract
BACKGROUND: Blinding trachoma, caused by ocular infection with Chlamydia trachomatis, is targeted for global elimination by 2020. Knowledge of risk factors can help target control interventions. METHODOLOGY/PRINCIPAL FINDINGS: As part of a cluster randomised controlled trial, we assessed the baseline prevalence of, and risk factors for, active trachoma and ocular C. trachomatis infection in randomly selected children aged 0-5 years from 48 Gambian and 36 Tanzanian communities. Both children's eyes were examined according to the World Health Organization (WHO) simplified grading system, and an ocular swab was taken from each child's right eye and processed by Amplicor polymerase chain reaction to test for the presence of C. trachomatis DNA. **Prevalence of active trachoma was 6.7% (335/5033) in The Gambia and 32.3% (1008/3122) in Tanzania. The countries' corresponding Amplicor positive prevalences were 0.8% and 21.9%.** After adjustment, risk factors for follicular trachoma (TF) in both countries were ocular or nasal discharge, a low level of household head education, and being aged ≥ 1 year. Additional risk factors in Tanzania were flies on the child's face, being Amplicor positive, and crowding (the number of children per household). The risk factors for being Amplicor positive in Tanzania were similar to those for TF, with the exclusion of flies and crowding. In The Gambia, only ocular discharge was associated with being Amplicor positive. CONCLUSIONS/SIGNIFICANCE: These results indicate that although the prevalence of active trachoma and Amplicor positives were very different between the two countries, the risk factors for active trachoma were similar but those for being Amplicor positive were different. **The lack of an association between being Amplicor positive and TF in The Gambia highlights the poor correlation between the presence of trachoma clinical signs and evidence of C. trachomatis infection in this setting.** Only ocular discharge was associated with evidence of C. trachomatis DNA in The Gambia, suggesting that at this low endemicity, this may be the most important risk factor.

Ophthalmic Epidemiol. 2011 Feb;18(1):20-9.
Design and baseline data of a randomized trial to evaluate coverage and frequency of mass treatment with azithromycin: the Partnership for Rapid Elimination of Trachoma (PRET) in Tanzania and The Gambia.
Stare D, Harding-Esch E, Munoz B, Bailey R, Mabey D, Holland M, Gaydos C, West S.
Source
Dana Center for Preventive Ophthalmology, Johns Hopkins University, Baltimore, MD, USA. dstare1@jhmi.edu
Abstract
OBJECTIVES: Trachoma is the principal cause of infectious blindness. As part of its strategy to eliminate trachoma, the World Health Organization recommends annual mass antibiotic treatment for at least 3 years with an 80% population coverage target. However, to date, ideal population coverage and mass treatment duration have not been determined and further evaluation of treatment recommendations in areas of varying endemicity is warranted. The studies presented here **evaluate the impact of coverage level and frequency of mass treatment with single dose azithromycin on trachoma and ocular C. trachomatis infection**. METHODS: The Partnership for the Rapid Elimination of Trachoma supervises 2 randomized,

community-based clinical trials in Tanzania and The Gambia. Although each trial is a stand-alone effort, protocols, data collection, and analytic approaches have been harmonized to permit generalizations. Communities in each site were randomized using a 2X2 factorial design to standard (80%-90.0%) versus high (over 90.0%) treatment coverage; communities were further randomized to annual treatment for 3 years versus a "graduation" rule where evidence indicates an absence of follicular trachoma or infection and annual treatment is halted. RESULTS: **Average prevalence of follicular trachoma in children age less than 5 years was 32.2% in Tanzania and 5.96% in The Gambia**. Randomization appeared to be effective, as prevalence was not statistically different between the arms within each country. CONCLUSIONS: There are challenges in harmonizing 2, large trials in Africa. Study outcomes will provide critical data to national trachoma control programs on treatment methodology and resource allocation toward elimination of the disease.

Arch Ophthalmol. 2011 Apr;129(4):512-3.

Slow resolution of clinically active trachoma following successful mass antibiotic treatments.

Keenan JD, Lakew T, Alemayehu W, Melese M, House JI, Acharya NR, Porco TC, Gaynor BD, Lietman TM.

Trachoma, caused by infection with ocular strains of chlamydia, is the leading infectious cause of blindness worldwide. The World Health Organization recommends that in districts where the prevalence of clinically active trachoma exceeds 10% in children aged 1 to 9 years, communities should receive 3 annual mass antibiotic distributions followed by clinical reassessment; any communities with persistent trachoma should continue receiving annual mass antibiotic treatments until the prevalence of clinically active trachoma in children aged 1 to 9 years falls below 5%. Although trachoma treatment decisions are based on the prevalence of clinically active trachoma, it is unclear how quickly the clinical signs of trachoma resolve once infection has been cleared, especially in areas with severe trachoma. **We recently performed a series of cluster-randomized clinical trials for trachoma in an area of Ethiopia with hyperendemic trachoma. In these trials, infection was brought to a low level in 24 villages randomized to receive mass azithromycin treatments every 6 months.** This provided an opportunity to determine the rate of resolution of the clinical signs of trachoma given little to no chlamydial reinfection.

Trans R Soc Trop Med Hyg. 2011 Jan;105(1):7-16. Epub 2010 Oct 30.

Randomised trial of face-washing to develop a standard definition of a clean face for monitoring trachoma control programmes.

King JD, Ngondi J, Kasten J, Diallo MO, Zhu H, Cromwell EA, Emerson PM.

Source

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Abstract

Surgery, antibiotics, facial cleanliness and environmental improvements (SAFE) are recommended for trachoma control. Programmes assess clean faces in children, but no standard definition of a clean face exists. We conducted a randomised controlled trial of face-washing to

develop a valid and repeatable definition of a clean face. A total of 424 children were randomised to washed and unwashed groups after a first observation. Three additional observations were made throughout the day. Photographs were taken at each observation. No difference was observed in wet nasal discharge, dust, food or flies on the face between the face washed and unwashed groups at baseline or after washing. A difference was observed in the presence of ocular discharge ($P < 0.001$) and dry nasal discharge ($P < 0.001$) after washing. Agreement among observers was highest for flies (Kappa = 0.89, 95% CI = 0.87-0.91), followed by nasal (Kappa = 0.64, 0.62-0.66) and ocular (Kappa = 0.48, 0.46-0.50) discharge. The ability of any definition to identify whether a face had been washed decreased at each observation. This study suggests that the absence of ocular and dry nasal discharge can be used as an indicator of 'clean face', although it is not a good predictor of whether a face has been washed and is difficult to recommend.

Int Ophthalmol. 2011 Feb;31(1):3-8. Epub 2010 Dec 31.

Laser photocoagulation (810 nm diode) for threshold retinopathy of prematurity: a prospective randomized pilot study of treatment to ridge and avascular retina versus avascular retina alone.

Uparkar M, Sen P, Rawal A, Agarwal S, Khan B, Gopal L.

Source

Shri Bhagwan Mahavir Department of Vitreo-Retinal Services, Medical Research Foundation, Sankara Nethralaya, 18 College Road, Nungambakkam, Chennai, 600006, India. uparkar@gmail.com

Abstract

The purpose of this study was to compare the structural outcome of laser treatment to avascular retina and ridge versus laser treatment to avascular retina alone in cases with threshold retinopathy of prematurity (ROP). A prospective, randomized, interventional, comparative study of consecutive cases referred to a single tertiary center was considered here. 50 infants with bilateral symmetrical threshold ROP were recruited into this study over a period of 3 years. Threshold ROP was defined as per CRYO-ROP study. Perinatal history details for all patients including significant maternal history were recorded. One eye of each patient was randomized (Microsoft Excel 2000) to one of the two treatment groups--laser treatment to avascular retina (Group A) or laser treatment to avascular retina and ridge (Group B). Laser treatment was performed with a 810 nm diode laser (Iris Medical Instruments, Inc. Mountain View, CA, USA). Treatment was continued until regression of ROP. Structural outcome was assessed at a minimum follow-up of 6 months and was considered favorable or unfavorable as per the CRYO-ROP study criteria. An unfavorable outcome consisted of either (1) a retinal fold involving the macula; (2) any retinal detachment involving zone 1; or (3) a retrolental mass that obscured visualization of the posterior pole. Secondary outcome measures included the difference in time to regression of ROP and complications of treatment between the two treatment groups. 100 eyes of 50 infants received laser photocoagulation for threshold ROP after randomization (50 eyes in each group). Of these 50 infants, 20 (40%) were female and 30 (60%) were male. A significant proportion of the children (46%) were conceived as twins. The average birth weight was 1360 ± 326 g (range 750-2200 g). The mean gestational age at birth was 30.72 ± 1.6 weeks (range 26-36 weeks). Zone I disease was present in 14 (14%) eyes and zone II in the remaining 86 eyes (86%). Threshold stage retinopathy (CRYO-ROP criteria) extending 360° (12 clock hours) was present in 21 infants (42%), 5 contiguous clock hours of stage 3+ in 14 infants (28%) and intermediate range in the remaining 15 infants (30%). At 6 months follow-up, 3 eyes (6%) in group A and 1 eye (2%) in group B had an adverse structural outcome; however, the time to regression of retinopathy 2.98 ± 1.5 weeks in group A and 3.12 ± 1.1 in group B (P =

0.889) and the rate of complications such as retinal hemorrhage, 3 eyes in group A and 4 eyes in group B, was comparable. Zone I eyes showed equal incidence of favorable anatomical outcome (85.7%) in each group. **Laser treatment to ridge was found to be safe and effective in the treatment of threshold ROP in this short-term pilot study; however, it needs to be ascertained whether this treatment has long-term advantages over conventional laser treatment to avascular retina, as well as the long-term benefits of treatment to ridge.**

Oral health / dentistry

BMC Oral Health. 2011 Mar 22;11:11.

Effectiveness of the bucco-lingual technique within a school-based supervised toothbrushing program on preventing caries: a randomized controlled trial.

Frazão P.

Source

Public Health School, University of São Paulo, São Paulo, Brazil. pafrazao@usp.br

Abstract

BACKGROUND: Supervised toothbrushing programs using fluoride dentifrice have reduced caries increment. However there is no information about the effectiveness of the professional cross-brushing technique within a community intervention. The aim was to assess if the bucco-lingual technique can increase the effectiveness of a school-based supervised toothbrushing program on preventing caries. METHODS: A randomized double-blinded controlled community intervention trial to be analyzed at an individual level was conducted in a Brazilian low-income fluoridated area. Six preschools were randomly assigned to the test and control groups and 284 five-year-old children presenting at least one permanent molar with emerged/sound occlusal surface participated. In control group, oral health education and dental plaque dying followed by toothbrushing with fluoride dentifrice supervised directly by a dental assistant, was developed four times per year. At the remaining school days the children brushed their teeth under indirect supervising of the teachers. In test group, children also underwent a professional cross-brushing on surfaces of first permanent molar rendered by a specially trained dental assistant five times per year. Enamel and dentin caries were recorded on buccal, occlusal and lingual surfaces of permanent molars during 18-month follow-up. Exposure time of surfaces was calculated and incidence density ratio was estimated using Poisson regression model. RESULTS: Difference of 21.6 lesions per 1,000 children between control and test groups was observed. Among boys whose caries risk was higher compared to girls, incidence density was 50% lower in test group (p = 0.016). CONCLUSION: Modified program was effective among the boys. It is licit to project a relevant effect in a larger period suggesting in a broader population substantial reduction of dental care needs.

J Indian Soc Pedod Prev Dent. 2010 Jul-Sep;28(3):179-82.

Efficacy of a probiotic and chlorhexidine mouth rinses: a short-term clinical study.

Harini PM, Anegundi RT.

Source

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Abstract

INTRODUCTION: Probiotic technology represents a breakthrough approach to maintaining oral health by utilizing natural beneficial bacteria commonly found in healthy mouths to provide a natural defense against those bacteria thought to be harmful to teeth and gums. However, data are still sparse on the probiotic action in the oral cavity. The review article on probiotics in children published by Twetman and Stecksen- Blicks in 2008 showed only one study of dental interest on probiotics in children. AIM AND OBJECTIVES: The present study evaluated clinically the efficacy of a probiotic and chlorhexidine mouth rinses on plaque and gingival accumulation in children. The trial design is a double-blind parallel group, 14 days comparative study between a probiotic mouth rinse and a chlorhexidine mouth rinse, which included 45 healthy children in the age group of 6-8 years. RESULTS: **The Probiotic and Chlorhexidine groups had less plaque accumulations compared with the Control group at the end of 14 years (P < 0.001 and P < 0.001, respectively). But, unlike the plaque score, there was a significant difference in the Gingival Index between the Probiotic and the Chlorhexidine groups (P = 0.009), Probiotic group being better than the Chlorhexidine group (mean = 0.2300 and 0.6805, respectively).** CONCLUSION: The Probiotic mouth rinse was found effective in reducing plaque accumulation and gingival inflammation. Therefore, probiotic mouth rinse obviously has a potential therapeutic value and further long-term study is recommended to determine its efficacy.

Parasites – other

Tungiasis – sand flea disease

PLoS Negl Trop Dis. 2010 Nov 9;4(11):e879.

Control of tungiasis through intermittent application of a plant-based repellent: an intervention study in a resource-poor community in Brazil.

Buckendahl J, Heukelbach J, Ariza L, Kehr JD, Seidenschwang M, Feldmeier H.

Source

Department of Microbiology and Hygiene, Campus Benjamin Franklin, Charité University Medicine, Berlin, Germany.

Abstract

BACKGROUND: Tungiasis, an ectoparasitosis caused by the female sand flea Tunga penetrans, is an important health problem in many impoverished communities in the tropics. Sand flea disease is associated with a broad spectrum of clinical pathology and severe sequels are frequent. Treatment options are limited. METHODOLOGY/PRINCIPAL FINDINGS: We assessed the **effectiveness of the intermittent application of the plant-based repellent**

Zanzarin to reduce infestation intensity and tungiasis-associated morbidity in a resource-poor community in Brazil, characterized by a very high attack rate. The study population was randomized into three cohorts. Initially, during a period of four weeks, the repellent was applied twice daily to the feet of all cohort members. This reduced the number of embedded sandfleas to 0 in 98% of the participants. **Thereafter members of cohort A applied the repellent every second week twice daily for one week, members of cohort B every fourth week for one week, and members of cohort C served as controls**. Infestation intensity and tungiasis-associated morbidity were monitored during five months. The intermittent application of Zanzarin for one week every second week significantly reduced infestation intensity from a median 4 lesions (IQR 1-9) during the whole transmission season. In contrast, in cohort B (application of the repellent every fourth week) the infestation intensity remained twice as high (median 8 lesions, IQR 9-16; p = 0.0035), and in the control cohort C 3.5 times as high (median 14 lesions; IQR 7-26; p = 0.004 during the transmission season). Tungiasis-related acute pathology remained very low in cohort A (median severity score 2; IQR 1-4) as compared to cohort B (median severity score 5; IQR 3-7; p<0.001), and control cohort C (median severity score 6.5; IQR 4-8; p<0.001). CONCLUSIONS/SIGNIFICANCE: **Our study shows that in a setting with intense transmission, tungiasis-associated morbidity can be minimized through the intermittent application of a plant-based repellent**.

Renal disease

Clin J Am Soc Nephrol. 2011 Jan;6(1):63-9. Epub 2010 Sep 16.

Daily corticosteroids reduce infection-associated relapses in frequently relapsing nephrotic syndrome: a randomized controlled trial.

Gulati A, Sinha A, Sreenivas V, Math A, Hari P, Bagga A.

Source

Division of Nephrology, Department of Pediatrics, All India Institute of Medical Sciences, Ansari Nagar, New Delhi, India.

Abstract

BACKGROUND AND OBJECTIVES: Relapses of nephrotic syndrome often follow minor infections, commonly of the upper respiratory tract. Daily administration of maintenance prednisolone during intercurrent infections was examined to determine whether the treatment reduces relapse rates in children with frequently relapsing nephrotic syndrome. DESIGN, SETTING, PARTICIPANTS, & MEASUREMENTS: In a randomized controlled trial (nonblind, parallel group, tertiary-care hospital), **100 patients with idiopathic, frequently relapsing nephrotic syndrome eligible for therapy with prolonged low-dose, alternate-day prednisolone with or without levamisole were randomized to either receive their usual dose of alternate-day prednisolone daily for 7 days during intercurrent infections (intervention group) or continue alternate-day prednisolone** (controls). Primary outcome was assessed by comparing the rates of infection-associated relapses at 12-month follow-up. Secondary outcomes were the frequency of infections and the cumulative amount of prednisolone received in both groups. RESULTS: Patients in the intervention group showed significantly lower infection-associated (rate difference, 0.7 episodes/patient per year; 95% confidence intervals [CI] 0.3, 1.1) and lower total relapse rates (0.9 episodes/patient per year, 95% CI 0.4, 1.4) without increase in steroid toxicity. **Poisson regression, adjusted for occurrence of infections, showed that daily administration of prednisolone during**

infections independently resulted in 59% reduction in frequency of relapses (rate ratio, 0.41; 95% CI 0.3, 0.6). For every six patients receiving this intervention, one showed a reduction of relapse frequency to less than three per year. CONCLUSIONS: **Daily administration of maintenance doses of prednisolone, during intercurrent infections, significantly reduces relapse rates and the proportion of children with frequently relapsing nephrotic syndrome.**

School health

(See also Nutrition, Opthalmology)

Trials. 2010 Oct 7;11:93.

Improving educational achievement and anaemia of school children: design of a cluster randomised trial of school-based malaria prevention and enhanced literacy instruction in Kenya.

Brooker S, Okello G, Njagi K, Dubeck MM, Halliday KE, Inyega H, Jukes MC.

Source

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Abstract

BACKGROUND: Improving the health of school-aged children can yield substantial benefits for cognitive development and educational achievement. However, there is limited experimental evidence on the benefits of school-based malaria prevention or how health interventions interact with other efforts to improve education quality. This study aims to evaluate the impact of school-based malaria prevention and enhanced literacy instruction on the health and educational achievement of school children in Kenya. DESIGN: A factorial, cluster randomised trial is being implemented in 101 government primary schools on the coast of Kenya. **The interventions are (i) intermittent screening and treatment of malaria in schools by public health workers and (ii) training workshops and support for teachers to promote explicit and systematic literacy instruction. Schools are randomised to one of four groups: receiving either (i) the malaria intervention alone; (ii) the literacy intervention alone; (iii) both interventions combined; or (iv) control group where neither intervention is implemented.** Children from classes 1 and 5 are randomly selected and followed up for 24 months. **The primary outcomes are educational achievement and anaemia, the hypothesised mediating variables through which education is affected.** Secondary outcomes include malaria parasitaemia, school attendance and school performance. A nested process evaluation, using semi-structured interviews, focus group discussion and a stakeholder analysis will investigate the community acceptability, feasibility and cost-effectiveness of the interventions. DISCUSSION: **Across Africa, governments are committed to improve health and education of school-aged children, but seek clear policy and technical guidance as to the optimal approach to address malaria and improved literacy.** This evaluation will be one of the first to simultaneously evaluate the impact of health and education interventions in the improvement of educational achievement. Reflection is made on the practical issues encountered in conducting research in schools in Africa.

J Pediatr. 2011 May;158(5):796-801.e1. Epub 2011 Jan 17.

Health promotion intervention in low socioeconomic kindergarten children.

Nemet D, Geva D, Eliakim A.

Source

Child Health and Sports Center, Pediatric Department, Meir Medical Center, Kfar-Saba, Sackler School of Medicine, Tel-Aviv University, Tel Aviv, Israel. dnemet@gmail.com

Abstract

OBJECTIVE: To prospectively examine the effects of a randomized school-based intervention on nutrition and physical activity knowledge and preferences, anthropometric measures, and fitness in low socioeconomic kindergarten children. STUDY DESIGN: A total of 376 children completed a school-year combined dietary-behavioral-physical activity intervention and were compared with 349 control subjects (age 3.8 to 6.8 years). RESULTS: The prevalence of overweight and obesity among the kindergarten children was 27.7%. Even though the intervention was not associated with between group differences in body mass index changes, it was associated with significantly ($P < .05$) greater increase in nutrition knowledge and preferences, physical activity knowledge and preferences, and improvement in fitness. There was a greater ($P < .05$) decrease in the number of overweight children in the intervention group (-31.9%) compared with the controls (-17.5%). CONCLUSIONS: A kindergarten dietary-physical activity intervention applied by the kindergarten teachers, had no effect on body mass index changes between the groups, but improved nutrition and physical activity knowledge and preferences, improved fitness, and decreased the percent of overweight children. This intervention may play an important role in health promotion, prevention and treatment of childhood obesity.

Biomed Environ Sci. 2010 Jun;23(3):180-7.

Report on childhood obesity in China (8): effects and sustainability of physical activity intervention on body composition of Chinese youth.

Li YP, Hu XQ, Schouten EG, Liu AL, Du SM, Li LZ, Cui ZH, Wang D, Kok FJ, Hu FB, Ma GS.

Source

National Institute for Nutrition and Food Safety, Chinese Center for Disease Control and Prevention, Beijing, China. liyanping72@yahoo.com

Abstract

OBJECTIVES: To determine whether a large-scale physical activity intervention could affect body composition in primary school students in Beijing, China. METHODS: The study design was one-year cluster randomized controlled trial of physical activity intervention (20 min of daily exercise in the classroom) with an additional year of follow-up among 4 700 students aged 8-11 years at baseline. RESULTS: After the one-year intervention, BMI increased by 0.56 kg/m(2) (SD 1.15) in the intervention group and by 0.72 kg/m(2) (SD 1.20) in the control group, with a mean difference of -0.15 kg/m(2) (95% CI: -0.28 to -0.02). BMI z score decreased by -0.05 (SD 0.44) in the intervention group, but increased by 0.01 (SD 0.46) in the control group, with a mean difference of -0.07 (-0.13 to -0.01). After another year of follow up, compared to the control group, children in the intervention group had significantly lower BMI (-0.13, -0.25 to -0.01), BMI z score (-0.05, -0.10 to -0.01), fat mass (-0.27 kg, -0.53 to -0.02) and percent body fat (-0.53, -1.00 to -0.05). The intervention had a more pronounced effect on weight, height, BMI, BMI z score, and body composition among obese children than among normal weight or overweight children. Compared to the control group, the intervention group had a significantly

higher percentage of children who maintained or reduced their BMI z score at year 1 (P=0.008) and year 2 (P=0.04). CONCLUSIONS: These findings suggest that 20 min of daily moderate to vigorous physical activity during the school year is a feasible and effective way to prevent excessive gain of body weight, BMI, and body fatness in primary school students.

J Sch Nurs. 2010 Dec;26(6):473-82. Epub 2010 Sep 23.

A controlled evaluation of a school-based obesity prevention in Turkish school children.

Toruner EK, Savaser S.

Source

Gazi University Health Sciences Faculty, Nursing Department, Ankara, Turkey.

Abstract

This research was conducted to assess the effect of a weight management program in Turkish school children with overweight and obesity. Forty one students formed the intervention group while 40 students formed the control group in two elementary schools. Students in intervention group were given seven training sessions in a period of 2.5 months. Concurrently, parents were given two trainings and consultancy. The Body Mass Indices (BMIs) of the intervention group at the third measurement were decreased ($p < .05$) significantly when compared to the control group. The findings suggest use of school-based weight management programs starting from elementary school.

Skin disease

Indian J Dermatol Venereol Leprol. 2010 Sep-Oct;76(5):591.

A study to evaluate the efficacy and safety of hydrocortisone aceponate 0.127% lipophilic cream in steroid responsive dermatoses in Indian patients.

Mukhopadhyay AK, Baghel V.

Source

Galderma India Pvt Ltd, Andheri, Mumbai, India.

Abstract

BACKGROUND: Topical corticosteroids (CSs) are the mainstay of therapy in various steroid responsive dermatoses. Newer CSs are more efficacious and safer than the older ones. There is no published data on the efficacy and safety of a new steroid hydrocortisone aceponate in the Indian population. AIM: **To evaluate the efficacy and safety of hydrocortisone aceponate (0.127%) lipophilic cream in the treatment of steroid responsive dermatoses in Indian patients**. METHODS: Four hundred and fifteen patients with clinically diagnosed steroid responsive dermatoses enrolled in this study. They were advised to apply hydrocortisone aceponate (0.127%) lipophilic cream as a thin film to all the affected areas twice daily. Cleansing was done prior to the application with either soap-free cleanser or soap (that would not affect the study result). Use of oral antihistamines and/or antibiotics was permissible. However, other oral/topical steroid use was not permitted during the study. Patients were evaluated at day 0 and at day 21. Data were recorded regarding clinical improvement and side-effects, if any. They were then analyzed to determine the efficacy and safety of the cream. RESULTS: Physician's global evaluation of therapy showed that lesions were cleared in 82 (22.10%), excellent result in 200 (53.91%), good result in 72 (19.41%), fair response in 15 (4.04%) and no change in 2 (0.54%) patients. There was no history of exacerbation in any

patient. CONCLUSION: **The study showed that hydrocortisone aceponate (0.127%) lipophilic cream is an effective therapeutic agent with a very good safety profile in various steroid responsive dermatoses in the Indian patient population**.
http://www.neurologyindia.com/article.asp?issn=0028-3886;year=2010;volume=58;issue=4;spage=560;epage=564;aulast=Kaur

Surgical problems

Mymensingh Med J. 2010 Jul;19(3):348-52.

Comparison of post operative morbidity between laparoscopic and open appendectomy in children.

Saha N, Saha DK, Rahman MA, Islam MK, Aziz MA.

Source

Dr Nirupama Saha, Assistant Professor, Department of Peadiatric Surgery, Mymensingh Medical College & Hospital, Mymensingh.

Abstract

This prospective comparative study was conducted in the department of Pediatric Surgery, Dhaka Shishu (children) Hospital during the period of June 2007 to September 2008 with the children of <12 years, diagnosed as acute Appendicitis. Patient selection was done by simple random technique by means of lottery. For open Appendectomy (OA) conventional method & for Laparoscopic Appendectomy (LA) 3 trocher technique was applied. Data was analyzed with the help of SPSS version 10. In this study 60 cases with acute Appendicitis including both gender were studied by two groups, **group-A include 30 cases for laparoscopic and group-B include 30 cases for open appendectomy.** Postoperative pain was assessed in both groups by using FLACC scale and compared at 1st 6-hours, 24 hours, 72 hours, 96 hours & at day 7. At 1st 6-hours, most of the children 24(80%) of group A had moderate pain whereas 17(56.7%) children of group B had severe pain (p<0.001). **At 24 hours most of the patient 17 (56.7%) of group A had mild pain compared to 27 (90%) patients of group B had moderate pain (p<0.0001).** At 48 hours in group A most of the children 23(76.7%) had mild pain compared to moderate pain in 18(60%) children of group B (p<0.0001). Subsequently at 72 hours and at 96 hours most of the patients of LA group were free of pain compared to OA group. At final follow-up on day 7, 29(96.7%) children of group A had no pain compared to 26(86.7%) of group B. Regarding analgesics requirement both qualitative & quantitative requirements of analgesics were less in LA group than OA group. About post operative wound infection in group A only 1(3.3%) case had developed post operative wound infection whereas in group B 7(23.3 %) cases had. The mean (+/-SD) of post operative length of hospital stay was 52.00+/-11.62 (range 48-96) hours for group A and 76.00+/-12.74 (range 48-96) hours for group B children (p<0.001). **Laparoscopic Appendectomy is more effective, preferable & superior procedure than that of open** Appendectomy to reduce the post operative morbidity in children undergone appendectomy for acute appendicitis.

Burns. 2011 Mar;37(2):203-7. Epub 2010 Nov 13.

A comparative analysis of cetirizine, gabapentin and their combination in the relief of post-burn pruritus.

Ahuja RB, Gupta R, Gupta G, Shrivastava P.

Source

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Abstract

Post-burn pruritis is a very distressing symptom having a reported incidence between 80 and 100%. The mainstay of management of post-burn itch has been with antihistaminics and emollients but the treatment is ineffective in a very large percentage of patients. With the recognition of a distinct itch specific neuronal pathway, which has a complex interaction with pain pathway, a fresh approach to itch management has surfaced with the use of gabapentin. **Gabapentin is an antiepileptic drug which has been successfully used to manage neuropathic pain**, and is reporting to be successful in management of all forms of itch. With a paucity of randomized trials evaluating the role of gabapentin in post-burn itch management the current study was undertaken to individually evaluate gabapentin, cetirizine and their combination in relieving itch. **Twenty patients were randomly recruited in each of the three groups and administered the respective drug(s) in doses determined by initial VAS (visual analog scale) scores.** There was no significant difference in all the three groups with respect to mean age, sex distribution, mean percentage of TBSA burn and mean VAS score on day 0. **VAS scores were evaluated over next 28 days (days 3, 7, 14, 21 and 28), and no emollients were prescribed for the study period.** The initial mean VAS score reduced 95% in gabapentin group compared to 52% for the cetirizine group, which was highly significant ($p<0.01$). There was a 94% reduction in mean VAS score in the combination group which was comparable to the relief observed with gabapentin alone ($p>0.05$). Even the onset of action with gabapentin was significantly faster than the cetirizine group as evident from the mean VAS scores on day 3, which decreased 74% in gabapentin group compared to 32% in cetirizine group ($p<0.01$). Whereas all patients receiving gabapentin (either as monotherapy or in combination with cetirizine) reached an itch free status (VAS score 0-1) by day 28 only 3/20 patients reached this level with cetirizine alone. It is quite evident from this study that **gabapentin is significantly better than cetirizine as monotherapy in relieving post-burn itch** and it also has a faster action. The hypothetical combination of a centrally acting drug with a peripherally acting agent did not result in any better control of post-burn itch than monotherapy with gabapentin. No side effects were reported with gabapentin administration but all patients receiving cetirizine reported sedation. There is now a need to relook at the antipruritic protocols in burn management.

J Burn Care Res. 2011 Mar-Apr;32(2):200-9.

Comparisons of the effects of biological membrane (amnion) and silver sulfadiazine in the management of burn wounds in children.

Mostaque AK, Rahman KB.

Source

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Abstract

This prospective study was conducted on 102 children with second-degree thermal burns to assess qualitative differences between topical silver sulfadiazine (SD) and oven-dried, radiation-

sterilized human amnion as wound dressing. The patients were divided into silver SD and amniotic membrane (AM) group by random sampling technique. The variables compared 1) the number of days admitted in the hospital, 2) the number of dressing changes, 3) time needed for epithelialization, 4) comfort and pain of the patients during dressing, 5) comfort and pain of the patients between dressings, 6) activities during treatment, 7) acceptability of the modules by the patients or attending guardians, and 8) comfort of the doctor during application. Patients' ages ranging from 1 day to 12 years and admitted to inpatient burn unit within 72 hours of occurrence were included in this study. Fifty-one burned children enrolled in each group. The mean hospital stay is significantly lower in AM group (P < .01). The number of dressing changes in AM group was significantly low (P < .001). The mean time taken for epithelial coverage of superficial second-degree burns is significantly lower in AM than in SD group (P < .001) and also those of deep second-degree burns (P < .001). Application was painless in AM than SD group (P < .001). State of pain in-between application shows significant difference (P < .001). Application of AM was comfortable to the attending doctor (P < .001). Significant activity of the patients was observed during treatment (P < .01) with AM. AM was accepted by the patients or parents (P < .001). This study indicates that radiation-sterilized, oven-dried AM is a better treatment option because its use reduces hospital stay and the number of dressing changes. Epithelialization of the wound is quicker. The use of AM is painless and odorless. The procedure is easy and comfortable to the doctor, and it is well accepted. Most of the patients remain ambulatory during treatment.

Iowa Orthop J. 2010;30:7-14.

Ponseti clubfoot management: changing surgical trends in Nigeria.

Adegbehingbe OO, Oginni LM, Ogundele OJ, Ariyibi AL, Abiola PO, Ojo OD.

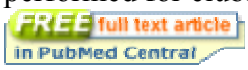
Source

Obafemi Awolowo University, Faculty of Clinical Sciences, Department of Orthopaedic Surgery & Traumatology, Ile Ife Osun State, Nigeria. olayinkaadegbehingbe@yahoo.co.uk

Abstract

BACKGROUND: Congenital clubfoot treatment continues to be controversial particularly in a resource-constrained country. Comparative evaluation of clubfoot surgery with Ponseti methods has not been reported in West Africa. OBJECTIVES: To determine the effects of Ponseti techniques on clubfoot surgery frequency and patterns in Nigeria. METHODS: This was a prospective hospital-based intention-to-treat comparative study of clubfoot managed with Ponseti methods (PCG) and extensive soft tissue surgery (NPCG). The first step was a nonselective double-blind randomization of clubfoot patients into two groups using Excel software in a university teaching hospital setting. The control group was the NPCG patients. The patients' parents gave informed consent, and the medical research and ethics board approved the study protocol. Biodata was gathered, clubfoot patterns were analyzed, Dimeglio-Bensahel scoring was done, the number of casts applied was tallied, and patterns of surgeries were documented. The cost of care, recurrence and outcomes were evaluated. Kruskal-Wallis analysis and Mann-Whitney U technique were used, and an alpha error of < 0.05 at a CI of 95% were taken to be significant. RESULTS: We randomized 153 clubfeet (in 105 clubfoot patients) into two treatment groups. **Fifty NPCG patients (36.2%) underwent manipulation and extensive soft tissue surgery and 55 PCG patients (39.9%) were treated with Ponseti methods.** Fifty-two patients of the Ponseti group had no form of surgery (94.5% vs. 32%, p<0.000). Extensive soft tissue surgery was indicated in 17 (34.0%) of the NPCG group, representing 8.9% of the total of 191 major orthopaedic surgeries within the study period. Thirty-five patients (70.0%) from the NPCG group required more than six casts compared to thirteen patients (23.6%) of the PCG (p<0.000). The mean care cost was high within the NPCG when compared to the Ponseti

group (48% vs. 14.5%, p<0.000). **The Ponseti-treated group had fewer treatment complications (p<0.003), a lower recurrence rate (p<0.000) and satisfactory early outcome (p<0.000).** CONCLUSION: Major clubfoot surgery was not commonly indicated among patients treated with the Ponseti method. The Ponseti clubfoot technique has reduced total care costs, cast utilization, clubfoot surgery frequency and has also changed the patterns of surgery performed for clubfoot in Nigeria.



Comment

The Ponsetti technique involves weekly stretching of the deformity followed by application of a long-leg cast. Most deformities (excet the equinas component) correct within 4-5 weeks. The technique and results are well described in Pediatrics 2004; Vol. 113 pp. 376 -380 (doi: 10.1542/peds.113.2.376) http://pediatrics.aappublications.org/content/113/2/376.long

Tuberculosis

N Engl J Med. 2011 Jul 7;365(1):21-31.

Primary isoniazid prophylaxis against tuberculosis in HIV-exposed children.

http://www.nejm.org/doi/full/10.1056/NEJMoa1011214

Madhi SA, Nachman S, Violari A, Kim S, Cotton MF, Bobat R, Jean-Philippe P, McSherry G, Mitchell C; P1041 Study Team.

Source

Department of Science and Technology/National Research Foundation: Vaccine Preventable Diseases and the Medical Research Council: Respiratory and Meningeal Pathogens Research Unit, University of the Witwatersrand, Johannesburg, South Africa. madhis@rmpru.co.za

Abstract

BACKGROUND: The dual epidemic of human immunodeficiency virus (HIV) and tuberculosis is a major cause of sickness and death in sub-Saharan Africa. We conducted a double-blind, randomized, placebo-controlled trial of preexposure isoniazid prophylaxis against tuberculosis in HIV-infected children and uninfected children exposed to HIV during the perinatal period. METHODS: **We randomly assigned 548 HIV-infected and 804 HIV-uninfected infants (91 to 120 days of age) to isoniazid (10 to 20 mg per kilogram of body weight per day) or matching placebo for 96 weeks**. All patients received bacille Calmette-Guérin (BCG) vaccination against tuberculosis within 30 days after birth. HIV-infected children had access to antiretroviral therapy. The primary outcome measures were tuberculosis disease and death in HIV-infected children and latent tuberculosis infection, tuberculosis disease, and death in HIV-uninfected children within 96 to 108 weeks after randomization. RESULTS: Antiretroviral therapy was initiated in 98.9% of HIV-infected children during the study. **Among HIV-infected children, protocol-defined tuberculosis or death occurred in 52 children (19.0%) in the isoniazid group and 53 (19.3%) in the placebo group (P=0.93).** Among HIV-uninfected children, there was no significant difference in the combined incidence of tuberculosis infection, tuberculosis disease, or death between the isoniazid group (39 children, 10%) and the placebo group (45 children, 11%; P=0.44). The rate of tuberculosis was 121 cases per 1000 child-years (95% confidence interval [CI], 95 to 153) among HIV-infected children as compared with 41 per 1000 child-years (95% CI, 31 to 52) among HIV-uninfected children. There were no significant differences in clinical or severe laboratory toxic effects between treatment groups. CONCLUSIONS: Primary isoniazid prophylaxis did not improve tuberculosis-disease-free survival among HIV-infected children or tuberculosis-infection-free survival among HIV-

uninfected children immunized with BCG vaccine. Despite access to antiretroviral therapy, the burden of tuberculosis remained high among HIV-infected children.

J Infect Dis. 2010 Oct 15;202(8):1265-72.

Interferon γ responses to mycobacterial antigens protect against subsequent HIV-associated tuberculosis.

Lahey T, Sheth S, Matee M, Arbeit R, Horsburgh CR, Mtei L, Mackenzie T, Bakari M, Vuola JM, Pallangyo K, von Reyn CF.

Source

Dartmouth Medical School, Lebanon, New Hampshire, USA.

Abstract

BACKGROUND: The cellular immune responses that protect against tuberculosis have not been identified. METHODS: We assessed baseline interferon γ (IFN γ) and lymphocyte proliferation assay (LPA) responses to antigen 85 (Ag85), early secretory antigenic target 6 (ESAT 6), and Mycobacterium tuberculosis whole cell lysate (WCL) in human immunodeficiency virus (HIV)-infected and bacille Calmette Guérin (BCG)-immunized adults with CD4 cell counts of >or= 200 cells/μL who received placebo in the DarDar tuberculosis vaccine trial in Tanzania. Subjects were followed prospectively to diagnose definite or probable tuberculosis. RESULTS: Tuberculosis was diagnosed in 92 of 979 subjects during a mean follow up of 3.2 years. The relative risk of tuberculosis among subjects with positive IFNγ responses to Ag85 was 0.51 (95% confidence interval [CI], 0.26-0.99; P = .049), to ESAT 6 was 0.44 (95% CI, 0.23-0.85; P = .004), and to WCL was 0.67 (95% CI, 0.49-0.88; P = .002). The relative risk of tuberculosis was not significantly associated with baseline LPA responses. In a multivariate Cox regression model, subjects with IFNγ responses to ESAT 6 and WCL had a lower hazard of developing tuberculosis, with a hazard ratio for ESAT 6 of 0.35 (95% CI, 0.16–0.77; P = .009) and a hazard ratio for WCL of 0.30 (95% CI, 0.16-0.56; P < .001). CONCLUSIONS: Baseline IFN γ responses to ESAT-6 and WCL were associated with protection from subsequent tuberculosis among HIV-infected subjects with childhood BCG immunization in a region of high tuberculosis prevalence. Trial registration.

Typhoid

PLoS Negl Trop Dis. 2011 Jan 4;5(1):e929.

Temporal fluctuation of multidrug resistant salmonella typhi haplotypes in the mekong river delta region of Vietnam.

Holt KE, Dolecek C, Chau TT, Duy PT, La TT, Hoang NV, Nga TV, Campbell JI, Manh BH, Vinh Chau NV, Hien TT, Farrar J, Dougan G, Baker S.

Source

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Abstract
BACKGROUND: typhoid fever remains a public health problem in Vietnam, with a significant burden in the Mekong River delta region. Typhoid fever is caused by the bacterial pathogen Salmonella enterica serovar Typhi (S. Typhi), which is frequently multidrug resistant with reduced susceptibility to fluoroquinolone-based drugs, the first choice for the treatment of typhoid fever. We used a GoldenGate (Illumina) assay to type 1,500 single nucleotide polymorphisms (SNPs) and analyse the genetic variation of S. Typhi isolated from 267 typhoid fever patients in the Mekong delta region participating in a randomized trial conducted between 2004 and 2005. PRINCIPAL FINDINGS: the population of S. Typhi circulating during the study was highly clonal, with 91% of isolates belonging to a single clonal complex of the S. Typhi H58 haplogroup. The patterns of disease were consistent with the presence of an endemic haplotype H58-C and a localised outbreak of S. Typhi haplotype H58-E2 in 2004. H58-E2-associated typhoid fever cases exhibited evidence of significant geo-spatial clustering along the Sông H u branch of the Mekong River. Multidrug resistance was common in the established clone H58-C but not in the outbreak clone H58-E2, however all H58 S. Typhi were nalidixic acid resistant and carried a Ser83Phe amino acid substitution in the gyrA gene. SIGNIFICANCE: the H58 haplogroup dominates S. Typhi populations in other endemic areas, but the population described here was more homogeneous than previously examined populations, and the dominant clonal complex (H58-C, -E1, -E2) observed in this study has not been detected outside Vietnam. IncHI1 plasmid-bearing S. Typhi H58-C was endemic during the study period whilst H58-E2, which rarely carried the plasmid, was only transient, suggesting a selective advantage for the plasmid. These data add insight into the outbreak dynamics and local molecular epidemiology of S. Typhi in southern Vietnam.

Vaccines and immunization

Immunization coverage

Trop Med Int Health. 2011 Mar;16(3):334-42. doi: 10.1111/j.1365-3156.2010.02698.x. Epub 2010 Dec 15.

Randomized controlled trial to improve childhood immunization adherence in rural Pakistan: redesigned immunization card and maternal education.

Usman HR, Rahbar MH, Kristensen S, Vermund SH, Kirby RS, Habib F, Chamot E.
Source
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Abstract
OBJECTIVE: A substantial dropout from the first dose of diphtheria-tetanus-pertussis (DTP1) to the 3rd dose of DTP (DTP3) immunization has been recorded in Pakistan. We conducted a randomized controlled trial to assess the effects of providing a substantially redesigned immunization card, centre-based education, or both interventions together on DTP3 completion at six rural expanded programme on immunization (EPI) centres in Pakistan. METHODS: **Mother-child pairs were enrolled at DTP1 and randomized to four study groups: redesigned card, centre-based education, combined intervention and standard care. Each child was followed up for 90 days to record the dates of DTP2 and DTP3 visits. The study**

outcome was DTP3 completion by the end of follow-up period in each study group. RESULTS: We enrolled 378 mother-child pairs in redesigned card group, 376 in centre-based education group, 374 in combined intervention group and 378 in standard care group. By the end of follow-up, 39% of children in standard care group completed DTP3. **Compared to this, a significantly higher proportion of children completed DTP3 in redesigned card group (66%) (crude risk ratio [RR] = 1.7; 95% CI = 1.5, 2.0), centre-based education group (61%) (RR = 1.5; 95% CI = 1.3, 1.8) and combined intervention group (67%) (RR = 1.7; 95% CI = 1.4, 2.0).** CONCLUSIONS: Improved immunization card alone, education to mothers alone, or both together were all effective in increasing follow-up immunization visits. The study underscores the potential of study interventions' public health impact and necessitates their evaluation for complete EPI schedule at a large scale in the EPI system.

Comment

The authors described that the new immunization card acted as a constant reminder to others of the next immunization visit and to make it easy for them to locate and read the date of the next immunization. It was larger than the existing EPI card (15.5 x 11.5 cm when folded), bright yellow in colour, placed in a plastic jacket and provided with a hanging string. On its outer sides, the card showed only the next immunization date in a large font (Times New Roman 42 pt) using pre-printed stickers. Boxes on the inner sides of the card recorded the name of the EPI centre, card number, card's date of issue, child's name and address, complete immunization schedule dates and instructions to the mothers. The cost of each card including the plastic jacket was US$ 0.05 (Pakistani Rupees 3).

Non-specific effects

Vaccine. 2011 Jan 10;29(3):487-500. Epub 2010 Nov 18.

Diphtheria-tetanus-pertussis vaccine administered simultaneously with measles vaccine is associated with increased morbidity and poor growth in girls. A randomised trial from Guinea-Bissau.

Agergaard J, Nante E, Poulstrup G, Nielsen J, Flanagan KL, Østergaard L, Benn CS, Aaby P.

Source

Bandim Health Project, Indepth Network, Apartado 861, 1004 Bissau Codex, **Guinea**-Bissau. heja@dadlnet.dk

Abstract

BACKGROUND: Combined vaccination with diphtheria-tetanus-pertussis (DTP) and measles vaccine (MV) has been associated with increased mortality in observational studies. Among children missing MV and a dose of DTP and oral polio vaccine (OPV), we conducted a randomised trial of providing MV+DTP+OPV simultaneously, as currently recommended, or MV+OPV only, and examined the effect on morbidity and growth. We hypothesised that the MV+OPV group would experience less morbidity and grow better. Due to previous observations of sex differences in the non-specific effects of vaccinations, we analysed all data stratified by sex. METHODS: At the Bandim Health Project in Guinea-Bissau, **568 children who were due to receive MV and who were missing either DTP3 or DTP booster were enrolled in the study. A subgroup of 332 children was followed intensively to register adverse events and infections in the first month after vaccination. A subgroup of 276 children was followed every third month for a year to monitor growth. All children were followed for one year for infectious diseases, consultations, and hospitalisations.** RESULTS: As expected, adverse events were more common in the MV+DTP+OPV group;

diarrhoea and use of medication were increased among girls but not among boys (both p=0.02, test of interaction between DTP and sex). Febrile disease with vesicular rash, as well as consultations and hospitalisations tended to be more common in the MV+DTP+OPV group than in the MV+OPV group; the hazard ratio (HR) for febrile disease with vesicular rash was 1.86 (1.00; 3.47). The strongest tendencies for more febrile diseases and hospitalisations in the MV+DTP+OPV group were found in girls. Overall, growth did not differ by randomisation group. However, results differed by sex. Girls in the MV+DTP+OPV group had a consistent pattern of worse z-scores for weight, height, and mid-upper-arm-circumference (MUAC) than girls in the MV+OPV group. The effect was opposite for boys, with boys in the MV+OPV group faring worse than those in the MV+DTP+OPV group, the interaction test for sex and DTP being significant for weight at 6 and 9 months, for MUAC at 12 months and for weight-for-height at 3 and 9 months after randomisation. CONCLUSION: This is the first randomised trial of the non-specific effects of DTP and supports that these effects may be sex-differential and of clinical and anthropometric importance. Combined vaccination with DTP+MV+OPV may be detrimental for girls.

BCG vaccine

2010 Aug 15;185(4):2620-8. Epub 2010 Jul 19.

Delaying bacillus Calmette-Guérin vaccination from birth to 4 1/2 months of age reduces postvaccination Th1 and IL-17 responses but leads to comparable mycobacterial responses at 9 months of age.

Burl S, Adetifa UJ, Cox M, Touray E, Ota MO, Marchant A, Whittle H, McShane H, Rowland-Jones SL, Flanagan KL.

Source

Medical Research Council (United Kingdom), The Gambia, Fajara, The Gambia, West Africa. sburl@mrc.gm

Abstract

Bacillus Camette-Guérin (BCG) vaccine is the only licensed vaccine against tuberculosis, yet its protective efficacy is highly variable between different geographical regions. We hypothesized that exposure to nontuberculous mycobacteria attenuates BCG immunogenicity by inducing mycobacterial-specific regulatory T cells (Tregs). **Gambian neonates were recruited at birth and randomized to receive BCG vaccination either at birth or at 4 1/2 mo.** Mycobacterial immune responses were assessed at birth, 4 1/2, and 9 mo of age. At 4 1/2 mo of age the BCG naive individuals had detectable mycobacterial responses, including increased IL-10 production suggesting environmental priming. **Vaccination at birth significantly enhanced Th1, Th2, IL-6, IL-17, and Treg responses in mycobacterial cultures at 4 1/2 mo compared with the BCG naive group. Analyzing results at 4 1/2 mo postvaccination revealed lower IFN-gamma, IL-6, and IL-17 responses in the delayed BCG vaccine group compared with those vaccinated at birth, but this did not relate to Treg levels prevaccination.** When comparing responses pre- and post-BCG vaccination in the delayed vaccine group, there was no priming of mycobacterial IL-17. Mycobacterial responses waned over 9 mo in those vaccinated at birth, leading to comparable mycobacterial immunity in both groups at 9 mo of age. Overall, these data suggest that vaccination at birth induces a broad Th1/Th2/IL-17/Treg mycobacterial response but the Th1/Th-17 response was reduced when delaying the vaccine. The evidence did not suggest that mycobacterial specific naturally occurring Tregs accounted for this attenuated immunogenicity.

Diptheria – Tetanus – Pertussus - Haemophilus influenzae vaccine

BMC Infect Dis. 2010 Oct 15;10:297.

Primary and booster vaccination in Latin American children with a DTPw-HBV/Hib combination: a randomized controlled trial.

Espinoza F, Tregnaghi M, Gentile A, Abarca K, Casellas J, Collard A, Lefevre I, Jacquet JM.

Source

Universidad Nacional Autonoma de Leon, Leon, Nicaragua.

Abstract

BACKGROUND: Diphtheria-tetanus-whole-cell pertussis (DTPw)-based combination vaccines are an attractive option to rapidly achieve high coverage and protection against other important pathogens, such as hepatitis B virus (HBV) and Haemophilus influenzae type B (Hib). To ensure adequate antigen supply, GlaxoSmithKline Biologicals has introduced a new DTPw antigen source and developed a new DTPw-HBV/Hib combination vaccine containing a reduced amount of Hib polyribosylribitol phosphate (PRP). This study was undertaken to compare the immunogenicity and reactogenicity of this new DTPw-HBV/Hib vaccine with a licensed DTPw-HBV/Hib vaccine (Tritanrix™-HBV/Hib). METHODS: This was a randomized, partially-blind, multicenter study in three countries in Latin America (Argentina, Chile and Nicaragua). **Healthy children received either the new DTPw-HBV/Hib vaccine (1 of 3 lots; n = 439; double-blind) or Tritanrix™-HBV/Hib (n = 146; single-blind) co-administered with oral poliovirus vaccine (OPV) at 2, 4 and 6 months, with a booster dose at 18-24 months.** RESULTS: **One month after the end of the 3-dose primary vaccination course, the new DTPw-HBV/Hib vaccine was non-inferior to Tritanrix™-HBV/Hib in terms of seroprotection/vaccine response rates for all component antigens; ≥97.3% and ≥93.9% of subjects in the two groups, respectively, had seroprotective levels of antibodies against diphtheria, tetanus, hepatitis B and Hib and a vaccine response to the pertussis component.** Persistence of antibodies against all vaccine antigens was comparable between groups, with marked increases in all antibody concentrations after booster administration in both groups. Both vaccines were generally well-tolerated as primary and booster doses. CONCLUSIONS: Results confirm the suitability of this new DTPw-HBV/Hib vaccine comprising antigens from a new source and a reduced PRP content for inclusion into routine childhood vaccination programs.

Vaccine. 2011 Mar 16;29(13):2359-64. Epub 2011 Feb 1.

A phase III randomized, controlled study to assess the immunogenicity and tolerability of DTPw-HBV-Hib, a liquid pentavalent vaccine in Indian infants.

Sharma H, Yadav S, Lalwani S, Gupta V, Kapre S, Jadhav S, Chakravarty A, Parekh S, Palkar S.

Source

Serum Institute of India Ltd., 212/2, Hadapsar, Pune 411028, India. drhjs@seruminstitute.com

Abstract

Immunogenicity and tolerability of two liquid pentavalent vaccines, Pentavac(®) (new vaccine), and Easyfive(®) (available in the market) was assessed in a multicentre study in India. In all, 484 infants aged 6-8 weeks were enrolled, and their blood samples were assessed prior to the

first dose and one month after the third dose. A 100% seroprotection rate was achieved with both vaccines' antigens, except pertussis for which the response was 95% and 96%, respectively, for the two vaccines. A diary-based recording of adverse events showed that the two most common events were pain at the injection site and restricted limb movements and were less frequent ($p<0.001$) among the recipients of the new vaccine. The new vaccine meets all criteria of childhood vaccination. Its low reactogenicity and low cost are valid reasons to recommend this vaccine for general use.

Hum Vaccin. 2010 Aug;6(8):664-72.

Immunogenicity, reactogenicity and safety of three-dose primary and booster vaccination with combined diphtheria-tetanus-whole-cell pertussis-hepatitis B-reduced antigen content Haemophilus influenzae type b vaccine in Filipino children.

Gatchalian SR, Ramakrishnan G, Bock HL, Lefevre I, Jacquet JM.

Source

Research Institute for Tropical Medicine, DOH Compound, Alabang, Muntinlupa City, Philippines. sally.r.gatchalian@gsk.com

Abstract

OBJECTIVES: To evaluate the immunogenicity, reactogenicity and safety of primary and booster vaccination with DTPw-HBVLT/Hib2.5 vaccine containing low thiomersal and reduced quantities of Hib polysaccharide (PRP). BACKGROUND: Combined DTP vaccines have high global coverage. Thus, the addition of new antigens to existing DTP vaccines is the most effective way to ensure high coverage. METHODS: **192 healthy infants were randomized to receive the investigational DTPw-HBVLT/Hib2.5 vaccine or licensed DTPw-HBV/Hib10 at 6, 10, 14 weeks.** Immune memory to the Hib antigen was assessed through administration of plain PRP challenge at 10 months in 50% of subjects. Challenged and unchallenged subjects respectively received a DTP-HBV or DTPa-HBV/Hib booster at 15-18 months of age. Antibody responses were measured using enzyme-linked immunosorbent assay (ELISA) and reactogenicity was assessed using diary cards. RESULTS: **One month post-primary vaccination, 100% and ≥ 93.7% of subjects in both groups had anti-PRP antibody concentrations ≥ 0.15 µg/mL and ≥ 1.0 µg/mL, respectively.** Robust responses to PRP were observed after the 10 month plain PRP challenge and booster responses were observed in unchallenged subjects after the booster dose at 15-18 months of age. Post-primary and post-booster responses to the other vaccine antigens were at least as high in the DTPw-HBVLT/Hib2.5 group versus the DTPw-HBV/Hib10 group. The reactogenicity profile of the DTPw-HBVLT/Hib2.5 vaccine was acceptable. CONCLUSION: The DTPw-HBVLT/Hib2.5 combination vaccine with reduced thiomersal and Hib content had equivalent immunogenicity and tolerability versus the full standard DTPw-HBV/Hib10 vaccine. DTPw-HBVLT/Hib2.5 or DTPw-HBV/Hib10 vaccines can contribute to reducing childhood diseases through ensuring high vaccine coverage in mass vaccination programs. ClinicalTrials.gov identifiers: NCT 01061541, NCT00158808.

Hepatitis B vaccine

Vaccine. 2011 Mar 9;29(12):2302-7. Epub 2011 Jan 28.

Antibody levels and immune memory 23 years after primary plasma-derived hepatitis B vaccination: results of a randomized placebo-controlled trial cohort from China where endemicity is high.

Wu Q, Zhuang GH, Wang XL, Wang LR, Li N, Zhang M.

Source

Department of Epidemiology and Biostatistics, Xi'an Jiaotong University College of Medicine, Xi'an, Shaanxi 710061, PR China.

Abstract

The duration of protection of hepatitis B vaccine remains incompletely understood. To assess the long-term protection provided by a primary vaccine series, the current study again recruited all subjects of a previous randomized placebo-controlled trial cohort 23 years after vaccination. Two hundred and sixty-one healthy children aged 5-9 years living in a highly HBV-endemic country were enrolled in the primary trial and received three doses of plasma-derived vaccine or placebo. The primary placebo receivers who did not receive any immunization against hepatitis B were used as non-vaccinated controls in the current study. After eliminating the interference of an early booster dose and vaccines outside the study, 48.1% (39/81) vaccinees still maintained anti-HBs titers ≥ 10 mI U/mL at Year 23, higher than 34.7% (26/75) in non-vaccinated controls (P=0.088). **75-100% of vaccinees with anti-HBs titer <10 mI U/mL at Year 23 in different sub-groups divided according to early immune backgrounds developed a rapid and robust antibody anamnestic response after a booster dose, highly significantly different from non-vaccinated controls who received the same dose of vaccine (7.5%, P<0.01). No case of clinically significant HBV infection was found in the primary cohort during the whole 23 years, but 10 transient HBsAg seroconversions in the primary placebo group and one in the primary vaccine group were determined.** Anti-HBc positive rate obviously tended to be lower in vaccinees compared with non-vaccinated controls at Year 23. These results suggest a persisting immune memory and certain protection for 23 years after primary vaccination in children living in highly HBV-endemic areas. Clinically insignificant infections, which cannot be avoided and may often occur in vaccinees, play a positive role in the maintaining of immunity to HBV. **Booster doses should be unnecessary for more than 20 years after a full primary immunization in children (as catch-up vaccination) and, also likely, in newborns living in highly HBV-endemic areas.**

HPV vaccine

JAMA. 2011 Apr 13;305(14):1424-31.

Immunogenicity and reactogenicity of alternative schedules of HPV vaccine in Vietnam: a cluster randomized noninferiority trial.

Neuzil KM, Canh do G, Thiem VD, Janmohamed A, Huong VM, Tang Y, Diep NT, Tsu V, LaMontagne DS.

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Abstract
CONTEXT: Human papillomavirus (HPV) vaccine programs may decrease the morbidity and mortality due to cervical cancer seen among women in low-resource countries. However, the 3-dose schedule over a 6-month period is a potential barrier to vaccine introduction in such settings. OBJECTIVE: To determine the immunogenicity and reactogenicity of different dosing schedules of quadrivalent HPV vaccine in adolescent girls in Vietnam. DESIGN, SETTING, AND PARTICIPANTS: Open-label, cluster randomized, noninferiority study (conducted between October 2007 and January 2010) assessing 4 schedules of an **HPV vaccine delivered in 21 schools to 903 adolescent girls (aged 11-13 years at enrollment) living in northwestern Vietnam.** INTERVENTION: **Intramuscular injection of 3 doses of quadrivalent HPV vaccine delivered on a standard dosing schedule (at 0, 2, and 6 months) and 3 alternative dosing schedules (at 0, 3, and 9 months; at 0, 6, and 12 months; or at 0, 12, and 24 months).** MAIN OUTCOME MEASURES: Serum anti-HPV geometric mean titers (GMT) measured 1 month after the third dose of the HPV vaccine was administered; GMT was determined by type-specific competitive immunoassay. Noninferiority of each alternative vaccination dosing schedule was achieved if the lower bound of the multiplicity-adjusted confidence interval (CI) of the type-specific GMT ratio for HPV-16 and HPV-18 was greater than 0.5 (primary outcome). Safety outcomes were immediate reactions, local reactions, fever within 7 days after each dose, and serious adverse events up to 30 days following the last dose. RESULTS: In the intention-to-treat analysis, 809 girls who received at least 1 HPV vaccine dose had valid serum measurements 1 month after the third dose. After the third dose, the GMTs for those in the standard schedule group who received doses at 0, 2, and 6 months were 5808.0 (95% CI, 4961.4-6799.0) for HPV-16 and 1729.9 (95% CI, 1504.0-1989.7) for HPV-18; 5368.5 (95% CI, 4632.4-6221.5) and 1502.3 (95% CI, 1302.1-1733.2), respectively, for those whose received doses at 0, 3, and 9 months; 5716.4 (95% CI, 4876.7-6700.6) and 1581.5 (95% CI, 1363.4-1834.6), respectively, for those who received doses at 0, 6, and 12 months; and 3692.5 (95% CI, 3145.3-4334.9) and 1335.7 (95% CI, 1191.6-1497.3), respectively, for those who received doses at 0, 12, and 24 months. Noninferiority criteria were met for the alternative schedule groups that received doses at 0, 3, and 9 months (HPV-16 GMT ratio: 0.92 [95% CI, 0.71-1.20]; HPV-18 GMT ratio: 0.87 [95% CI, 0.68-1.11]) and at 0, 6, and 12 months (HPV-16 GMT ratio: 0.98 [95% CI, 0.75-1.29]; HPV-18 GMT ratio: 0.91 [95% CI, 0.71-1.17]). Prespecified noninferiority criteria were not met for the alternative schedule group that received doses at 0, 12, and 24 months (HPV-16 GMT ratio: 0.64 [95% CI, 0.48-0.84]; HPV-18 GMT ratio: 0.77 [95% CI, 0.62-0.96]). Pain at the injection site was the most common adverse event. CONCLUSIONS: **Among adolescent girls in Vietnam, administration of the HPV vaccine on standard and alternative schedules was immunogenic and well tolerated.** The use of 2 alternative dosing schedules (at 0, 3, and 9 months and at 0, 6, and 12 months) compared with a standard schedule (at 0, 2, and 6 months) did not result in inferior antibody concentrations.


J Korean Med Sci. 2010 Aug;25(8):1197-204. Epub 2010 Jul 21.
Vaccination with a human papillomavirus (HPV)-16/18 AS04-adjuvanted cervical cancer vaccine in Korean girls aged 10-14 years.
Kim YJ, Kim KT, Kim JH, Cha SD, Kim JW, Bae DS, Nam JH, Ahn WS, Choi HS, Ng T, Bi D, OK JJ, Descamps D, Bock HL.

Source
Department of Obstetrics and Gynecology, Hanyang University Hospital, [corrected] Seoul, Korea.

Abstract
The human papillomavirus (HPV)-16/18 AS04-adjuvanted cervical cancer vaccine has been demonstrated to be highly efficacious and immunogenic with a favorable safety profile. This study assessed the immunogenicity and safety of the HPV-16/18 AS04-adjuvanted vaccine in healthy Korean girls aged 10-14 yr. This multi-center, observer-blind trial randomly assigned **321 healthy girls to receive three doses (0, 1, 6-month schedule) of HPV-16/18 AS04-adjuvanted vaccine or hepatitis A vaccine.** Immunogenicity against vaccine antigens was assessed one month post-Dose 3. Solicited and unsolicited adverse events (AEs) and serious AEs (SAEs) were recorded. In the according-to-protocol analysis, all initially seronegative subjects vaccinated with the HPV-16/18 AS04-adjuvanted vaccine had seroconverted at Month 7, with a peak geometric mean titer (GMT) that was 600-fold higher than the natural infection titer of 29.8 EU/mL for HPV-16 and a peak GMT that was 400-fold higher than the natural infection titer of 22.6 EU/mL for HPV-18. The vaccine was well tolerated with no increase in reactogenicity with subsequent doses and no reports of vaccine-related SAEs. **In conclusion, the HPV-16/18 AS04-adjuvanted vaccine is shown to be highly immunogenic and generally well-tolerated in Korean girls aged 10-14 yr.**

Japanese Encephalitis Virus vaccine

Pediatr Infect Dis J. 2010 Dec;29(12):1111-7.

Safety and immunogenicity of a single administration of live-attenuated Japanese encephalitis vaccine in previously primed 2- to 5-year-olds and naive 12- to 24-month-olds: multicenter randomized controlled trial.

Chokephaibulkit K, Sirivichayakul C, Thisyakorn U, Sabchareon A, Pancharoen C, Bouckenooghe A, Gailhardou S, Boaz M, Feroldi E.
Source
Division of Infectious Diseases, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand.

Abstract
BACKGROUND: Safe and effective Japanese encephalitis (JE) vaccines are needed to protect populations living in or visiting endemic areas. A live-attenuated JE-chimeric virus vaccine (JE-CV) has been developed with a single-dose regimen. METHODS: In an open-label, crossover study, 100 children aged 2 to 5 years with a history of 2-dose primary vaccination with mouse-brain derived inactivated JE vaccine according to the Thai Expanded Program for Immunization schedule, and 200 JE vaccination-naive 12- to 24-month-old toddlers were randomized 1:1 to receive JE-CV, containing ≥4 log10 plaque forming units, 1 month before or after hepatitis A control vaccine. Neutralizing antibody titers were assessed using PRNT50 (titers expressed in inverse of dilution) before and 28 days after JE-CV, and at months 7 and 12. RESULTS: All 2- to 5-year-olds and 96% of 12- to 24-month-olds were seroprotected (titer ≥10) 28 days after JE-CV administration, and geometric mean titers (GMT) (95% confidence interval) in these age groups were 2634 (1928-3600) and 281 (219-362), respectively. One year later, seroprotection rates in the 2 age groups were 97% and 84% and GMTs were 454 and 62.3, respectively.

Vaccine-induced antibodies neutralized a panel of wild-type JE isolates. There were no vaccine-related serious adverse events. Reactogenicity of JE-CV was comparable with that of the inactivated hepatitis A vaccine. CONCLUSIONS: **A single administration of JE-CV has a good safety profile and elicits a protective immune response in both JE-naive toddlers and JE-primed young children.**

Polio vaccine

Zhongguo Yi Miao He Mian Yi. 2010 Jun;16(3):193-6.

Study on safety and immunogenicity of oral poliomyelitis attenuated live vaccine (human diploid cell).

Guo SH, Tao H, Ying ZF.

Source

Beijing Tiantan Biological Products Co., Ltd., Beijing 100024, China.

Abstract

OBJECTIVE: To evaluate the safety and Immunogenicity of the Poliomyelitis vaccine (Human Diploid Cell) in > or =2 month-old children. METHODS: A random, blind and control trial, 1200 healthy children of 2-5 months old in Jiangsu province were administered OPV (HDC) vaccine and control vaccines. The antibody was tested by neutralization test. RESULTS: After 3 doses of the OPV (HDC) vaccine, the systemic reactions were mild. After 1 month of vaccination with 3 doses of the OPV (HDC) vaccine, the immune success rates of I, II, III type were 98.28%, 99.45%, and 95.71% respectively, the GMTs of I, II, III type in susceptible children were 1:1243.72, 1:234.38 and 1:273.10 respectively. CONCLUSIONS: The OPV (HDC) vaccine was safe and immunogenicity for the children > or =2 months old.

Shigella vaccine

Vaccine. 2011 Feb 1;29(6):1347-54. Epub 2010 Oct 30.

Safety, dose, immunogenicity, and transmissibility of an oral live attenuated Shigella flexneri 2a vaccine candidate (SC602) among healthy adults and school children in Matlab, Bangladesh.

Rahman KM, Arifeen SE, Zaman K, Rahman M, Raqib R, Yunus M, Begum N, Islam MS, Sohel BM, Rahman M, Venkatesan M, Hale TL, Isenbarger DW, Sansonetti PJ, Black RE, Baqui AH.

Source

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Abstract

In double-blind trials in Bangladesh, 88 adults, and 79 children (8-10 years) were randomized to receive either a single oral dose of 1 × 10(4), 1 × 10(5) or 1 × 10(6)CFU of SC602 (a live, attenuated Shigella flexneri 2a strain vaccine) or placebo. In the adult outpatient 1 × 10(6) CFU group, severe joint pain and body aches were reported by one and two vaccinees respectively. In the adult inpatient trial, SC602 was isolated from 3 volunteers, pre-vaccination antibody titers were high, and fourfold increases in serum IgG anti-LPS responses were observed in 2 of 5 subjects of the 1 × 10(6)CFU group. None of the volunteers developed diarrhea. Overall, SC602

was found to be associated with minimal vaccine shedding, minimal reactogenicity, no transmission risk, and low immune stimulation.

Typhoid vaccine

PLoS One. 2010 Jul 26;5(7):e11778.

A randomised trial evaluating the safety and immunogenicity of the novel single oral dose typhoid vaccine M01ZH09 in healthy Vietnamese children.

Tran TH, Nguyen TD, Nguyen TT, Ninh TT, Tran NB, Nguyen VM, Tran TT, Cao TT, Pham VM, Nguyen TC, Tran TD, Pham VT, To SD, Campbell JI, Stockwell E, Schultsz C, Simmons CP, Glover C, Lam W, Marques F, May JP, Upton A, Budhram R, Dougan G, Farrar J, Nguyen VV, Dolecek C.

Source

The Hospital for Tropical Diseases, Ho Chi Minh City, Vietnam.

Abstract

BACKGROUND: The emergence of drug resistant typhoid fever is a major public health problem, especially in Asia. An oral single dose typhoid vaccine would have major advantages. M01ZH09 is a live oral single dose candidate typhoid vaccine containing Salmonella enterica serovar Typhi (Ty2 aroC(-)ssaV(-)) ZH9 with two independently attenuating deletions. Studies in healthy adults demonstrated immunogenicity and an acceptable safety profile.

OBJECTIVES: **We conducted a randomised placebo controlled, single-blind trial to evaluate the safety and immunogenicity of M01ZH09 in healthy Vietnamese children aged 5 to 14 years.** METHODS: Subjects were randomly assigned to receive either a nominal dose of 5x10(9) CFU of M01ZH09 or placebo and were followed up for 28 days. The primary safety outcome was the proportion of subjects with any adverse event attributed to M01ZH09. The primary immunogenicity endpoint was the proportion of subjects who showed a positive immune response to M01ZH09 in the Salmonella Typhi lipopolysaccharide (LPS) specific serum IgA and IgG ELISA. PRINCIPAL FINDINGS: **One hundred and fifty-one children were enrolled, 101 subjects received M01ZH09 and 50 subjects received placebo.** An intention to treat analysis was conducted. There were no serious adverse events and no bacteraemias. **In the M01ZH09 group, 26 (26%; 95% CI, 18-5%) of 101 subjects experienced adverse events compared to 11 (22%; 95% CI, 12-36%) of 50 subjects in the placebo group (odds ratio (OR) [95%CI] = 1.23 [0.550-2.747]; p = 0.691). Faecal shedding of S. Typhi (Ty2 aroC(-)ssaV(-)) ZH9 was detected in 51 (51%; 95% CI, 41-61%) of 100 M01ZH09 subjects. No shedding was detected beyond day 3. A positive immune response, defined as 70% increase (1.7 fold change) in LPS specific serum IgG (day 14 or 28) and/or 50% increase (1.5 fold change) in LPS specific serum IgA (day 7 or 14) from baseline was detected in 98 (97%; 95% CI, 92-99%) of 101 M01ZH09 recipients and 8 (16%; 95% CI, 7-29%) of 50 placebo recipients.** Twenty-eight (100%; 95% CI, 88-100%) of 28 vaccine recipients who were evaluated in the LPS specific IgA ELISPOT assay showed a positive response compared to none of the 14 placebo recipients tested. CONCLUSIONS: This was the first phase II trial of a novel oral candidate typhoid vaccine in children in an endemic country. M01ZH09 had an appropriate safety profile and was immunogenic in children.

Rotavirus vaccine

J Infect Dis. 2010 Sep 1;202 Suppl:S93-100.

Comparison of 2 different regimens for reactogenicity, safety, and immunogenicity of the live attenuated oral rotavirus vaccine RIX4414 coadministered with oral polio vaccine in South African infants.

Steele AD, Reynders J, Scholtz F, Bos P, de Beer MC, Tumbo J, Van der Merwe CF, Delem A, De Vos B.

Source

MRC Diarrhoeal Pathogens Research Unit, University of Limpopo, Pretoria, Republic of South Africa. dsteele@path.org

Abstract

BACKGROUND: A phase II, randomized, double-blind, placebo-controlled study was conducted in South Africa during 2003-2004 to evaluate the safety, reactogenicity, and immunogenicity of 2 regimens of the live attenuated oral human rotavirus vaccine RIX4414 when coadministered with the Expanded Program on Immunization childhood vaccines, including oral polio vaccine. METHODS: **Healthy infants were randomized (2:2:1) to receive either 2 doses of RIX4414 (n = 190; at 10 and 14 weeks, with placebo at 6 weeks), 3 doses of RIX4414 (n = 189; at 6, 10, and 14 weeks), or 3 doses of placebo (n = 96), all with concomitant routine vaccinations.** The antirotavirus IgA seroconversion rate was assessed using enzyme-linked immunosorbent assay at 2 months after the last dose of RIX4414 or placebo. Antipolio types 1, 2, and 3 antibodies were measured using a virus neutralization assay. Solicited symptoms were recorded for 15 days after each dose. RESULTS: **The antirotavirus IgA seroconversion rates were similar in the RIX4414 2- and 3-dose groups (44.3% and 44.4%, respectively; P = .544, by 1-sided Fisher exact test) and antirotavirus IgA geometric mean concentrations were also comparable. Seroprotection rates for antipolio types 1, 2, and 3 antibodies were high (93%-100%) and were not significantly different among groups.** Solicited symptoms reported within 15 days after vaccination were similar in all groups. CONCLUSIONS: **The immune seroconversion response to the RIX4414 vaccine with 3 doses was not superior to the 2-dose regimen**. There was no interference by either regimen with antibody response to oral polio vaccine, and RIX4414 was well tolerated when given with routine vaccinations.

Cholera vaccine

Vaccine. 2011 Feb 24;29(10):1855-8. Epub 2011 Jan 12.

Evaluation of a probiotics, Bifidobacterium breve BBG-01, for enhancement of immunogenicity of an oral inactivated cholera vaccine and safety: a randomized, double-blind, placebo-controlled trial in Bangladeshi children under 5 years of age.

Matsuda F, Chowdhury MI, Saha A, Asahara T, Nomoto K, Tarique AA, Ahmed T, Nishibuchi M, Cravioto A, Qadri F.
Source
Graduate School of Medicine, Kyoto University, Kyoto, Japan.
Abstract
To evaluate the probiotic, Bifidobacterium breve strain Yakult (BBG-01), for safety and enhancement of immunogenicity in an oral inactivated cholera vaccine, a randomized double-blind placebo-controlled study was performed. Bangladeshi children under 5-year-old received BBG-01 or placebo for 4 weeks with two doses of oral cholera vaccine. Serum/fecal antibodies and fecal bacterial flora in the study participants were monitored. All adverse events were mild and transient and had no significant difference between the two groups. Immunological responses were similar comparing the two groups. A negative correlation between Bifidobacterium and Enterobacteriaceae in the probiotic group suggests a possible involvement of BBG-01 in alteration of the enteric bacterial flora. In conclusion, BBG-01 is well tolerated by Bangladeshi children although the post vaccinal immunostimulatory effect of BBG-01 was not evident.

Rabies vaccine

Vaccine. 2011 Mar 24;29(15):2679-81. Epub 2011 Feb 3.
Safety and immunogenicity of two freeze-dried Vero cell rabies vaccines for human use in post-exposure prophylaxis.
Wang LY, Sun MP, Zhang XC, Suo LD, Xu RH, Zou YJ, Zuo LB, Qi H.
Source
Beijing Center for Diseases Prevention and Control, Beijing 100013, China. Lingyunbj@126.com
Abstract
To provide basis for human rabies vaccination in China, the safety and immunogenicity of two freeze-dried Vero cell rabies vaccines for human use were assessed. A total of 250 volunteers were enrolled and divided into two groups: volunteers in Group A (n=200) were vaccinated five doses of Speeda Vero cell rabies vaccine manufactured by Liaoning Chengda Biotechnology Co. Ltd. on day 0, 3, 7, 14, 28 after exposure. Volunteers in Group B (n=50) were treated with Verorab Vero cell rabies vaccine manufactured by Sanofi Pasteur on the same schedule. The local and systematic adverse reactions were observed. Serum neutralizing antibody levels of 80 individuals in Group A and 50 individuals in Group B were tested with RFFIT on day 7, 14, 45, 180, 360 after the first dose. The seroconversion rates in Groups A and B were 40.3% and 37.0% on day 7 after the first dose, 95.5% and 97.7% on day 14, 100% and 100% on day 45, 100% and 100% on day 180, 89.1% and 89.5% on day 360 respectively, indicating no significant differences between the two groups. And no significant differences were found between the neutralizing antibody geometric mean titers (GMTs) of the two groups on day 7, 14, 45, 180 and 360 after the first dose, with the GMTs of day 14, 45, 180 and 360 all higher than 0.5IU/ml. Antibody levels of the two groups peaked around 2 weeks after the full vaccination program, followed by a 55% decrease up to day 180 and another 76% decrease up to day 360. Both groups experienced occasions of transient fever, rash, edema, and scleroma after vaccination. Neither group had any severe adverse reactions. It was concluded that both

vaccines showed satisfactory safety and immunogenicity. Booster vaccination is recommended following another exposure after six months since the full vaccination program.

Influenza vaccine

Clin Infect Dis. 2010 Dec 15;51(12):1370-9. Epub 2010 Nov 10.

Protective efficacy of seasonal influenza vaccination against seasonal and pandemic influenza virus infection during 2009 in Hong Kong.

Cowling BJ, Ng S, Ma ES, Cheng CK, Wai W, Fang VJ, Chan KH, Ip DK, Chiu SS, Peiris JS, Leung GM.

Source

Infectious Disease Epidemiology Group, School of Public Health, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong Special Administrative Region, China. bcowling@hku.hk

Abstract

BACKGROUND: The relationship between seasonal influenza vaccine and susceptibility to 2009 pandemic A/H1N1 virus infection is not fully understood. METHODS: **One child 6-15 years of age from each of 119 households was randomized to receive 1 dose of inactivated trivalent seasonal influenza vaccine (TIV) or saline placebo in November 2008.** Serum samples were collected from study subjects and their household contacts before and 1 month after vaccination (December 2008), after winter (April 2009) and summer influenza (September-October 2009) seasons. Seasonal and pandemic influenza were confirmed by serum hemagglutinination inhibition, viral neutralization titers, and reverse-transcription polymerase chain reaction performed on nasal and throat swab samples collected during illness episodes. RESULTS: . **In multivariable analysis, those infected with seasonal influenza A during the study had a lower risk of laboratory-confirmed pandemic A/H1N1 infection (adjusted odds ratio [OR], 0.35; 95% confidence interval [CI], 0.14-0.87), and receipt of seasonal TIV was unassociated with risk of pandemic A/H1N1 infection (adjusted OR, 1.11; TIV recipients had lower rates of serologically confirmed seasonal A/H1N1 infection (TIV group, 8%; placebo group, 21%; P=.10) and A/H3N2 infection (7% vs 12%; P=A9), but higher rates of pandemic A/H1N1 infection (32% vs 17%; 95% CI, 0.54-2.26).** CONCLUSIONS: TIV protected against strain-matched infection in children. Seasonal influenza infection appeared to confer cross-protection against pandemic influenza. Whether prior seasonal influenza vaccination affects the risk of infection with the pandemic strain requires additional study.

Meningococcal vaccine

N Engl J Med. 2011 Jun 16;364(24):2293-304.

Immunogenicity and safety of a meningococcal A conjugate vaccine in Africans.

Sow SO, Okoko BJ, Diallo A, Viviani S, Borrow R, Carlone G, Tapia M, Akinsola AK, Arduin P, Findlow H, Elie C, Haidara FC, Adegbola RA, Diop D, Parulekar V, Chaumont J, Martellet

L, Diallo F, Idoko OT, Tang Y, Plikaytis BD, Kulkarni PS, Marchetti E, LaForce FM, Preziosi MP.
Source
Centre pour le Développement des Vaccins, Bamako, Mali.
Abstract
BACKGROUND: Group A meningococci are the source of major epidemics of meningitis in Africa. An affordable, highly immunogenic meningococcal A conjugate vaccine is needed. METHODS: We conducted two studies in Africa to evaluate a new MenA conjugate vaccine (PsA-TT). In study A, 601 children, 12 to 23 months of age, were randomly assigned to receive PsA-TT, a quadrivalent polysaccharide reference vaccine (PsACWY), or a control vaccine (Haemophilus influenzae type b conjugate vaccine [Hib-TT]). Ten months later, these children underwent another round of randomization within each group to receive a full dose of PsA-TT, a one-fifth dose of PsACWY, or a full dose of Hib-TT, with 589 of the original participants receiving a booster dose. In study B, 900 subjects between 2 and 29 years of age were randomly assigned to receive PsA-TT or PsACWY. Safety and reactogenicity were evaluated, and immunogenicity was assessed by measuring the activity of group A serum bactericidal antibody (SBA) with rabbit complement and performing an IgG group A-specific enzyme-linked immunosorbent assay. RESULTS: **In study A, 96.0% of the subjects in the PsA-TT group and 63.7% of those in the PsACWY group had SBA titers that were at least four times as high as those at baseline; in study B, 78.2% of the subjects in the PsA-TT group and 46.2% of those in the PsACWY group had SBA titers that were at least four times as high as those at baseline.** The geometric mean SBA titers in the PsA-TT groups in studies A and B were greater by factors of 16 and 3, respectively, than they were in the PsACWY groups ($P<0.001$). In study A, the PsA-TT group had higher antibody titers at week 40 than the PsACWY group and had obvious immunologic memory after receiving a polysaccharide booster vaccine. Safety profiles were similar across vaccine groups, although PsA-TT recipients were more likely than PsACWY recipients to have tenderness and induration at the vaccination site. Adverse events were consistent with age-specific morbidity in the study areas; no serious vaccine-related adverse events were reported. CONCLUSIONS: **The PsA-TT vaccine elicited a stronger response to group A antibody than the PsACWY vaccine.** (Funded by the Meningitis Vaccine Project through a grant from the Bill and Melinda Gates Foundation; Controlled-Trials.com numbers, ISRCTN78147026 and ISRCTN87739946.).
NEJM FREE FULL TEXT

Vitamin A

(See also Maternal health, nutrition and micronutrient supplementation, HIV prevention of mother to child transmission)

J Infect Dis. 2010 Sep 1;202 Suppl:S243-51.
The effect of high-dose vitamin A supplementation given with bacille Calmette-Guérin vaccine at birth on infant rotavirus infection and diarrhea: a randomized prospective study from Guinea-Bissau.

Diness BR, Christoffersen D, Pedersen UB, Rodrigues A, Fischer TK, Andersen A, Whittle H, Yazdanbakhsh M, Aaby P, Benn CS.
Source
Bandim Health Project, INDEPTH Network, Guinea-Bissau. Birgitte@Diness.dk

Abstract
BACKGROUND: Prophylactic vitamin A supplementation (VAS) reduces mortality and may reduce morbidity associated with diarrhea in children >6 months of age. Rotavirus is the most common cause of acute dehydrating diarrhea among children worldwide. METHODS: In a randomized placebo-controlled study of 50,000 IU of vitamin A versus placebo given with bacille Calmette-Guérin vaccine at birth, 287 infants were followed up with weekly interviews and stool sample obtainment to test the hypothesis that VAS reduced the risk of rotavirus infection. RESULTS: **VAS was associated with increased risk of rotavirus infection and diarrhea (incidence rate ratio [IRR] of infection, 1.72 [95% confidence interval (CI), 1.04-2.85]; IRR of diarrhea, 3.74 [95% CI, 1.40-9.98]) among children <6 months of age.** There was no effect in older children. VAS had a beneficial effect on nonrotavirus diarrhea in boys <6 months of age (IRR, 0.51; 95% CI, 0.27-0.95) and a detrimental effect in girls >6 months of age (IRR, 1.84; 95% CI, 0.96-3.55). CONCLUSION: VAS at birth did not reduce rotavirus morbidity. The effect of VAS on nonrotavirus diarrhea may differ by sex, being more beneficial in boys. Clinical trials registration. NCT00168597.

Comment
A previous trial in India (Basu S, Postgrad Med J 2003;79: 397–402) showed marked reductions in number of episodes and duration of diarrhoea among infants of breast-feeding mothers who were given Vitamin A immediately after birth. The finding in the above trial, that vitamin A increases rotavirus disease, would need to be substantiated in larger trials, and balanced against the other benefits of vitamin A supplementation, including in this study above, from non-rotavirus diarrhoea.

Vitamin D and calcium

Singapore Med J. 2010 May;51(5):440-5.
Combination of bolus dose vitamin D with routine vaccination in infants: a randomised trial.
Shakiba M, Sadr S, Nefei Z, Mozaffari-Khosravi H, Lotfi MH, Bemanian MH.
Source
Paediatric Department, Shahid Sadoughi University of Medical Sciences, Avicenna Street, Yazd 89168-56331, Iran. shakiba@ssu.ac.ir
Abstract
INTRODUCTION: The present study was designed to compare two methods of vitamin D supplementation in infants: every two months as a routine vaccination versus a daily dose. METHODS: A randomised clinical trial was performed on 120 healthy breastfed infants between January and September 2007 in Yazd, Iran. **The infants were randomly divided into three groups with different doses of vitamin D3 supplementation: 200 IU daily, 400 IU daily and a bolus of 50,000 IU every two months.** A blood sample was taken and evaluated for 25-hydroxy vitamin D and calcium levels when the infants were six months old. The data was reported as the mean and standard deviation. RESULTS: **No significant differences were observed between the serum level of 25-hydroxy vitamin D in the groups administered with 200 IU and 400 IU vitamin D daily.** However, the serum level of 25-hydroxy vitamin D

reached significance in the third group (p is less than 0.001). All the blood calcium measured was below 11 mg/dl in the bolus group. A few complications such as diarrhoea and agitation, all of which were self-limited, were seen in the bolus group. No other significant side effects were reported in the other groups. CONCLUSION: **This study demonstrates that a bolus of 50,000 IU of vitamin D every two months with a routine child vaccination program provides the ideal serum level of vitamin D.** This method produces no serious side effects and offers a highly convenient way to supply vitamin D, especially among non-compliant parents.

Asia Pac J Clin Nutr. 2010;19(4):465-72.

Vitamin D supplementation and bone mass accrual in underprivileged adolescent Indian girls.

Khadilkar AV, Sayyad MG, Sanwalka NJ, Bhandari DR, Naik S, Khadilkar VV, Mughal MZ.

Source

Hirabai Cowasji Jehangir Medical Research Institute, Jehangire Hosptial, Pune, India.

Abstract

Vitamin D deficiency is common among children and adolescents in India, in spite of abundant sunshine. We conducted a pilot; double blind randomised controlled trial to investigate the effect of vitamin D supplementation on bone mineral content in underprivileged adolescent girls, in Pune, India. **Fifty post-menarcheal girls aged 14 to 15 years were randomised to receive 300,000 IU (7.5 mg) of ergocalciferol or placebo orally, 4 times/year.** All participants received 250 mg elemental calcium (calcium carbonate) daily. Outcome measures included change in serum 25-hydroxyvitamin D, size adjusted bone area and bone mineral content at total body and lumbar spine. Post supplementation, the median serum concentration of 25-hydroxyvitamin D was 75.2 (64.2-85.5) nmol/L in the intervention group and 28.1 (16.7-34.0) nmol/L in the placebo group. Increment in bone outcome measures was not different in the two groups. However, there was a positive effect of intervention in the size adjusted total body bone area ($p<0.05$), total body bone mineral content ($p<0.05$) and lumbar spine bone mineral content ($p<0.05$), and positive trend in lumbar spine bone area ($p=0.07$) in girls who were within 2 years of menarche. **We conclude that vitamin D supplementation did not have a beneficial effect on skeletal mineralization in girls who were more than 2 years post menarcheal. However, there was a significant positive effect of the intervention on size adjusted total body and lumbar spine bone mineral content and a positive trend in lumbar spine bone area, in girls who were <= 2 years of menarche.**

Eur J Clin Nutr. 2011 Apr;65(4):440-6. Epub 2011 Jan 19.

A pilot randomized controlled trial of oral calcium and vitamin D supplementation using fortified laddoos in underprivileged Indian toddlers.

Ekbote VH, Khadilkar AV, Chiplonkar SA, Hanumante NM, Khadilkar VV, Mughal MZ.

Source

Growth and Endocrine Unit, HCJMRI, Jehangir Hospital, Pune, India.

Abstract

BACKGROUND/OBJECTIVES: Low habitual dietary calcium intake and vitamin D deficiency are common among Indian children. Using 'laddoo', an Indian snack, as a vehicle for administering calcium and vitamin D supplements, a randomized double-blind controlled trial was conducted for 12 months to assess its efficacy on total body less head (TBLH) bone mineral

content (BMC) in underprivileged toddlers. SUBJECTS/METHODS: A total of 60 toddlers (mean age 2.7±0.52 years, boys=31) were randomized to two groups**, (i) study group receiving one calcium fortified laddoo (cereal-legume snack) containing 405 mg calcium per day and (ii) control receiving a non-fortified laddoo, containing 156 mg of indigenous calcium. Both groups also received a laddoo fortified with 30,000 IU of vitamin D(3) per month.** Outcome measures included TBLH bone area (BA) and TBLH BMC by GE-Lunar DPX Pro Pencil Beam Dual-Energy X-ray absorptiometry. RESULTS: At baseline, mean energy, protein and calcium intakes were 71, 72 and 47% of Indian Recommended Dietary allowances. In all, 87 and 83% toddlers were hypocalcaemia and vitamin D deficient, respectively. Mean TBLH BMC was 289.5±45.8 g. Post supplementation, mean TBLH BMC of study group showed a significantly greater (P<0.01) increase of 35% as against 28% in controls and the difference remained significant after adjusting for vitamin D status, calcium intake, height and TBLH BA. CONCLUSIONS: **Daily supplementation with calcium fortified laddoo, and monthly vitamin D supplement resulted in a significant increase in TBLH BMC of underprivileged toddlers.** We believe that such strategies have the potential of addressing nutritional problems in developing countries.

Am J Clin Nutr. 2010 Oct;92(4):741-7. Epub 2010 Jul 28.

Effect of maternal calcium supplementation on offspring blood pressure in 5- to 10-y-old rural Gambian children.

Hawkesworth S, Sawo Y, Fulford AJ, Goldberg GR, Jarjou LM, Prentice A, Moore SE.

Source

Medical Research Council International Nutrition Group, London School of Hygiene and Tropical Medicine, London, United Kingdom. sophie.hawkesworth@lshtm.ac.uk

Abstract

BACKGROUND: Evidence suggests that increased maternal calcium intake during pregnancy may result in lower offspring blood pressure, prompting calls for more robust data in this field, particularly in settings of habitually low calcium intake. OBJECTIVE: The objective was to investigate the effect of maternal calcium supplementation on blood pressure in offspring by recruiting children born after a randomized, double-blind, placebo-controlled trial of calcium supplementation during pregnancy. DESIGN: **Children (n = 389) from a rural area of The Gambia (mean age: 7.4 ± 1.2 y; range: 5-10 y), whose mothers received a calcium supplement (1500 mg Ca/d from 20 wk of gestation until delivery) or placebo, were followed up in West Africa.** Blood pressure was assessed under standardized conditions with use of the Omron 705IT automated oscillometric device (Morton Medical Ltd, London, United Kingdom), and anthropometric and body composition (bioelectrical impedance) measurements were also made. RESULTS: The analysis was restricted to 350 children born at term, which represented 64% of original trial births. **There was no difference in systolic (adjusted mean difference: -0.04 mm Hg; 95% CI: -1.78, 1.69 mm Hg) or diastolic (adjusted mean difference: 0.25 mm Hg; 95% CI: -1.27, 1.77 mm Hg) blood pressure between children whose mothers had received calcium and those who received placebo.** No interaction between childhood body mass index (in kg/m(2); mean: 14.0) and maternal calcium supplementation was observed in this study. CONCLUSION: Calcium supplementation in the second half of pregnancy in Gambian women with very low habitual calcium intakes may not result in lower offspring blood pressure at 5-10 y of age.

Zinc

(see also: Acute respiratory infection, Diarrhoea, Vitamin A, Cholera vaccine)

J Nutr. 2010 Sep;140(9):1677-82. Epub 2010 Jul 14.

Two weeks of zinc administration to Nepalese children with pneumonia does not reduce the incidence of pneumonia or diarrhea during the next six months.

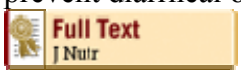
Chandyo RK, Shrestha PS, Valentiner-Branth P, Mathisen M, Basnet S, Ulak M, Adhikari RK, Sommerfelt H, Strand TA.

Source

Centre for International Health, University of Bergen, Bergen, Norway.

Abstract

Diarrhea and pneumonia are the 2 main causes of death in children under 5 y of age. Short courses of zinc administration are now recommended for treatment of childhood diarrhea and some studies have also shown its beneficial effect on treatment of pneumonia. **The objective of our study was to assess the efficacy of zinc administration (10 mg/d for children 2-11 mo and 20 mg/d for >or= 12 mo of age) for 14 d on preventing diarrheal and respiratory illnesses for 6 mo of follow-up**. This was a randomized, double-blind, placebo-controlled trial in children 2-35 mo of age with community-acquired pneumonia. The number of illness episodes and time until the first episode of various illnesses were compared between the 2 study groups. After 14 d of zinc supplementation, plasma zinc was significantly higher in the group receiving zinc. However, this difference was not detectable at 1 and 2.5 mo after the end of zinc administration. Of 2628 enrolled cases, a total of 2599 (99%) were available for assessment after the completion of zinc supplementation. **The number of hospital visits and the median number of days until the first episode of pneumonia, diarrhea, and dysentery was similar in the 2 groups.** The hazard ratios (95% CI) were 1.02 (0.92, 1.14) for nonsevere pneumonia, 1.11 (0.72, 1.73) for severe pneumonia, 1.07 (0.91, 1.26) for diarrhea, and 0.96 (0.69, 1.34) for dysentery. A short course of zinc supplementation given during an episode of pneumonia did not prevent diarrheal or respiratory illness over the next 6 mo.



Comment

*The above trial is in contrast to other studies that have suggested that a similar course of zinc, given as treatment during an **episode of diarrhoea** (not pneumonia), prevents subsequent diarrhoeal episodes (Pediatrics. 2008 121 (5):e1279-85), and may improve growth in some populations (J Pediatr Gastroenterol Nutr. 2009 48(1):89-93).*

*This year there were two studies from India of the effect of zinc **treatment for pneumonia** failed to find a clinical benefit.*

BMC Pediatr. 2010 Sep 21;10:68.

Zinc status in HIV infected Ugandan children aged 1-5 years: a cross sectional baseline survey.

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Source

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Abstract

BACKGROUND: Low concentrations of serum zinc have been reported in HIV infected adults and are associated with disease progression and an increased risk of death. Few studies have been conducted in HIV infected children in Africa. We determined serum zinc levels and factors associated with zinc deficiency in HIV infected Ugandan children. METHODS: We measured the baseline zinc status of 247 children aged 1-5 years enrolled in a randomised trial for multiple micronutrient supplementation at paediatric HIV clinics in Uganda (http://ClinicalTrials.gov NCT00122941). Zinc status was determined using inductively coupled atomic emission spectrophotometry (ICP-AES). Clinical and laboratory characteristics were compared among zinc deficient (zinc < 10.0 μmol/L) and non deficient children. Logistic regression was used to determine predictors of low serum zinc. RESULTS: **Of the 247 children, 134 (54.3%) had low serum zinc (< 10.0 μmol/L). Of the 44 children on highly active antiretroviral therapy (HAART), 13 (29.5%) had low zinc compared to 121/203 (59.6%) who were not on HAART.** Overall, independent predictors of low zinc were fever (OR 2.2; 95%CI 1.1-4.6) and not taking HAART (OR 3.7; 95%CI 1.8-7.6). CONCLUSION: Almost two thirds of HAART naïve and a third of HAART treated HIV infected children were zinc deficient. **Increased access to HAART among HIV infected children living in Uganda might reduce the prevalence of zinc deficiency.**