A RCT on the effectiveness of nebulized normal saline in infants with acute lower respiratory infection in CED PMGH

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Introduction

- Acute bronchiolitis is the most frequent lower respiratory infection and the most frequent cause of hospitalization in infancy.

➢ *During the colder months in temperate regions and during wet months in tropical regions*

- During the past 3 decades, hospitalization rates for infants with bronchiolitis have more than doubled worldwide costing millions.
  - ➢ *From 1980 to 1996, the rate of hospitalization for bronchiolitis increased in the United States from 12.9 admissions per 1000 children to 31.2 admissions per 1000 children.*
  - ➢ *In PMGH- leading cause of paediatric hospital admissions*
- Despite its widespread prevalence, there are no proven effective therapies for bronchiolitis.
  - ➢ *Supportive therapy has been the cornerstone treatment- adequate oxygenation, hydration and minimal handling*

Literature review

- Several studies have shown that inhaled hypertonic saline to be a promising therapy for infants < 2 years of age.

- A 2008 Cochrane review suggests nebulized *hypertonic saline* use in acute bronchiolitis:
  - *significantly reduces the length of hospital stay*
  - *improve the clinical severity scores*

Literature review

- American Medical Journal *(Todd A. Florin, MD & Susan Wu, MD)* – two studies conducted in ED using 3% hypertonic saline vs. 0.9% normal saline
  - *no significant effect on the Respiratory Distress Scores*
  - *lower admission rates compared to those who received NS*
- SABRE *(Everard ML et al):* nebulised 3% hypertonic saline is not effective in the treatment of acute bronchiolitis than standard care
- Few previous studies comparing normal saline to standard care on degree of respiratory distress, hypoxaemia, or admission and discharge rates.

Aims/Objectives

- To compare the clinical efficacy of inhaled normal saline with standard care treatment on infants with the clinical diagnosis of acute bronchiolitis

- Does nebulised saline given over 4 hours in an emergency department improve respiratory distress scores, improve hypoxaemia and reduce admission rates?

Methodology

Study design

- An open, randomized clinical trial comparing normal saline with standard care on patients between 2- 24 months of age with a primary diagnosis of acute bronchiolitis
- April to July 2018 at the Children's Emergency Department of PMGH

Randomisation and masking

- After parental informed consent was obtained, patients were allocated by simple randomization using a centralised web-based randomization system with a computer generated algorithm *(www.randomisation.org)*.
- This was an open study when blinding was not possible.

Intervention group

- Hourly nebulised with 2mls of normal saline each dose to a maximum of 3 doses

Methodology

Sample size

- 120 in each arm were required to detect a 50% reduction in the proportion of children who are hypoxic at 4 hours (SpO_2<90%), from a background prevalence of 40% in the standard care arm, to 20% in the nebulised saline (intervention) arm.
- Aimed for a total sample size of 240 patients.

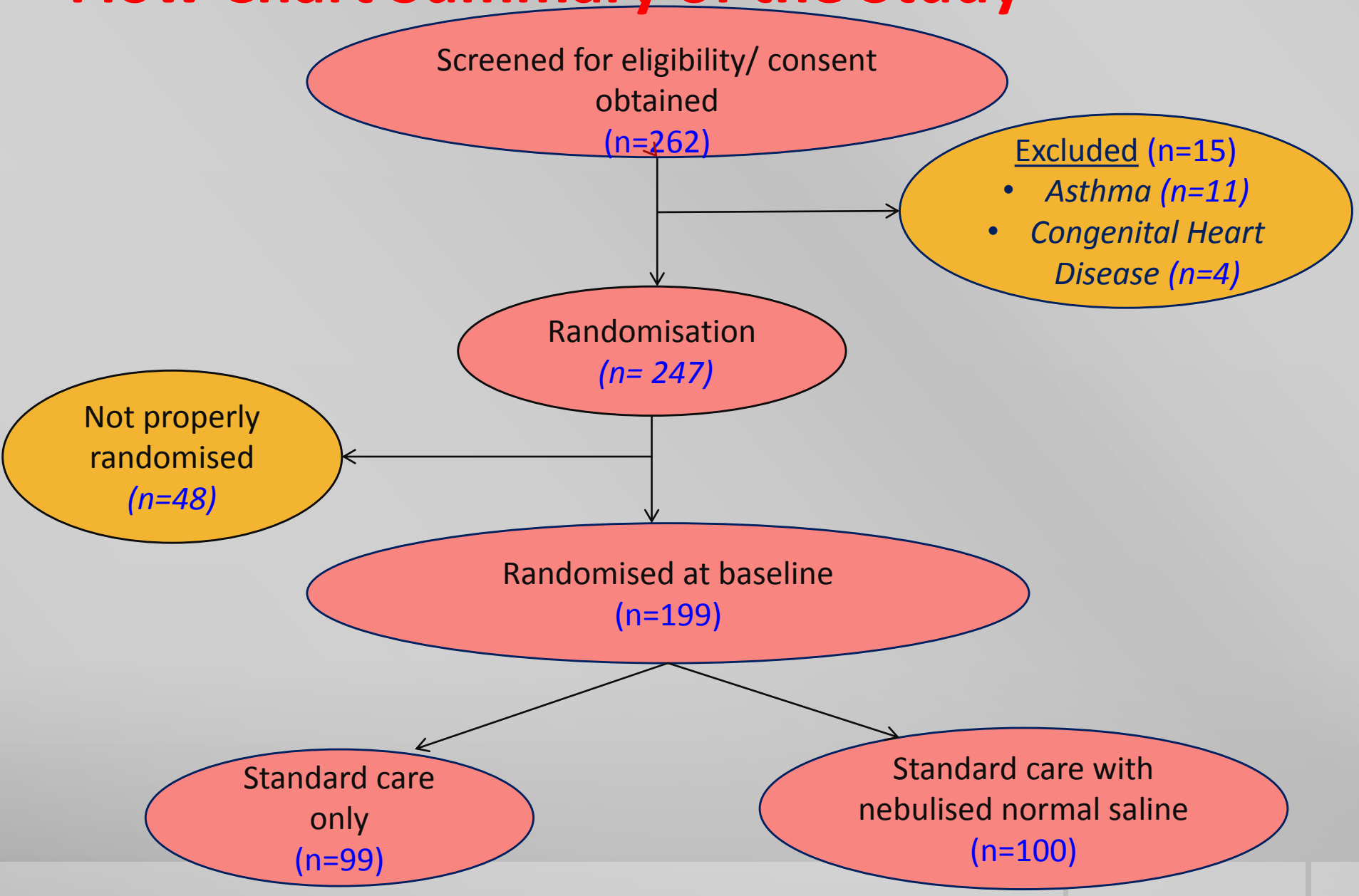
Outcome measures

- *The difference in RDS between 0 and 4 hours*
- *SpO_2 readings between 0 and 4 hours*
- *Admission rates to the wards*

Statistical Analysis

- Data analysis using Excel and Stata version 14

Flow Chart Summary of the Study



Respiratory Distress Score Table- (x/18)

		Mild= 1	Moderate= 2	Severe= 3
1	***Hypoxemia***	Mild **SpO_2 91- 93%**	Moderate **SpO_2 85- 90%**	Severe **SpO_2 <85%**
2	***Chest wall retraction***	None or minimal	Moderate chest wall retraction	Marked chest wall retraction, tracheal tug
3	***Respiratory sounds, audible***	None or minimal external sounds	Intermittent grunting +/- nasal flaring	Grunting with every breath, wheeze, nasal flaring
4	***Respiratory sounds, auscultation***	Good A/E, normal breath sounds or mild wheeze	Moderately reduced A/E. Wheeze and crepitation	Widespread crepitation. Poor A/E.
5	***Respiratory rate/ min***	<40	40- 60	>60
6	***Heart rate/ min***	<140	140- 170	>170

Results: Baseline Characteristics

Characteristic	Standard N=99	Normal saline N=100
Age: mean (SD) in months	8.8 (5.5)	8.9 (5.5)
Weight: mean SD	8.0 (2.4)	7.9 (2.6)
Duration of symptoms	3.5 (1.9)	3.1 (1.8)
Previous admission with pneumonia / bronchiolitis n (%)	49	52
History of apnoea n (%)	15	12
Temperature °C	37.5 (0.85)	37.4 (0.9)
Poor feeding n (%)	33	32
Mean RR (SD)	50.9 (8.9)	51.0 (13.7)
Mean heart rate (SD)	156.7 (20.4)	146.4 (26.9)
Chest indrawing n (%)	97	96
Hepatomegaly n (%)	12	9
Tracheal tugging n (%)	63	50
Grunting n (%)	19	18
Head nodding n (%)	5	5
Cyanosis n (%)	15	16
Severity n (%) Severe pneumonia	20	15
Severity n (%) Moderate pneumonia	79	85
Mean SpO_2 at 0 (SD)	83.5 (6.4)	83.7 (5.8)

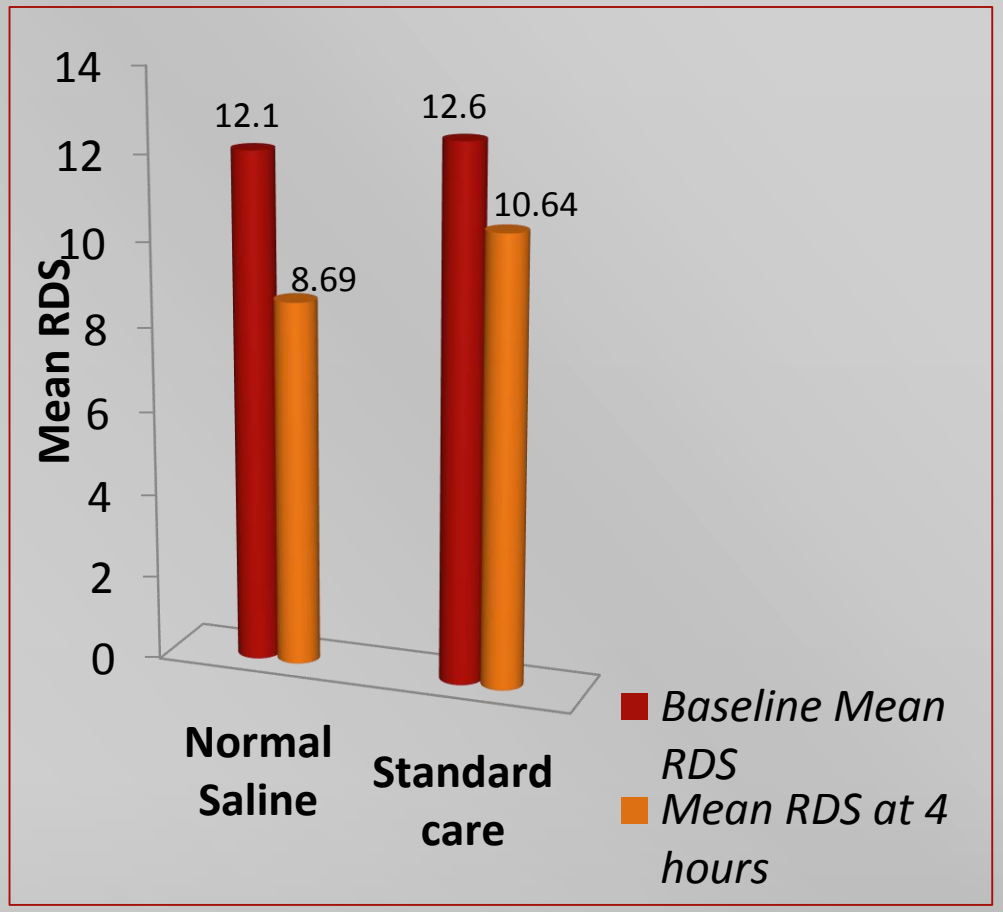
Baseline comparison between the 2 groups

- **Respiratory Distress Score**
  - *Normal saline: 12.1 (95% CI 11.6-12.7)*
  - *Standard: 12.6 (95% CI 12.1-13.2).*
  - *p-value of 0.21: no significant difference between the groups.*

- **Severity of hypoxemia**
  - *Mean SpO_2 in the normal saline group 83.7% (95% CI 82.5-84.8)*
  - *Mean SpO_2 in the standard group 83.5% (95% CI 82.2-84.7)*
  - *p- value of 0.5: no significant difference between the groups*

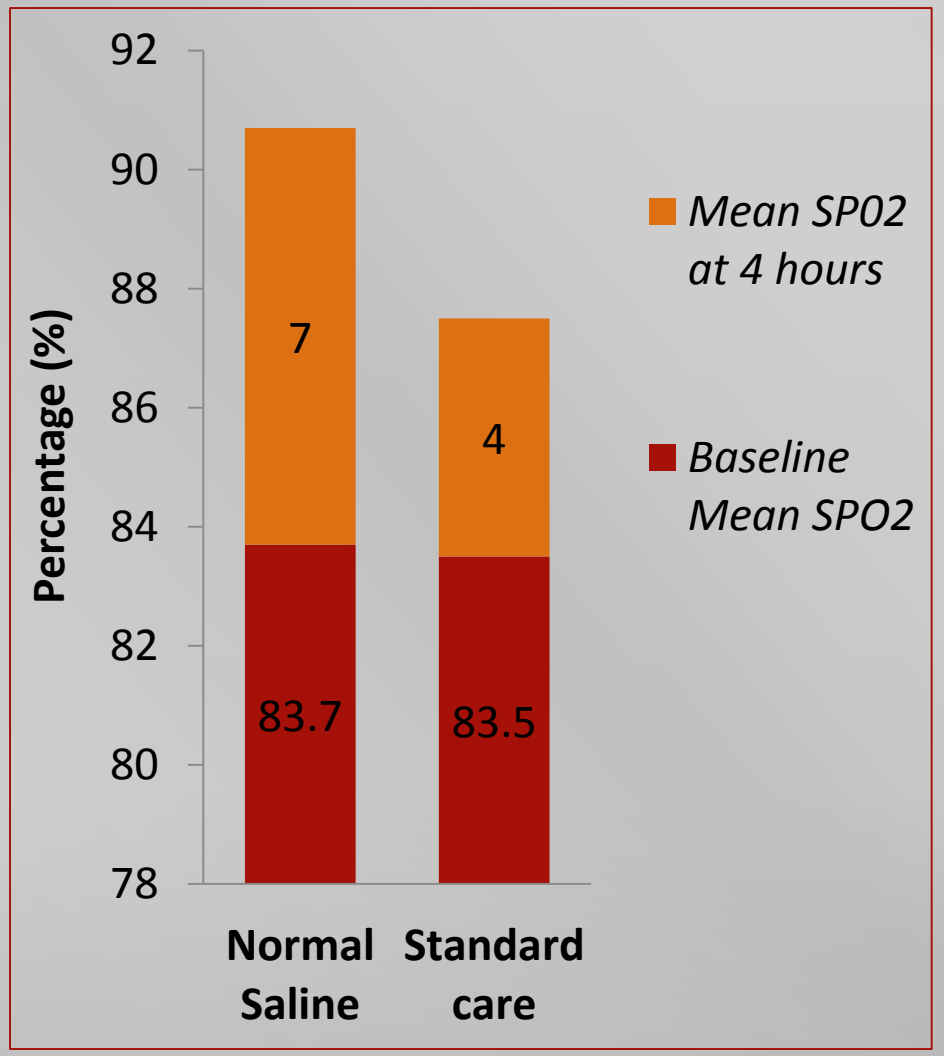
Results: Respiratory Distress Score

- There was a significant difference in the change in RDS at 4 hours between the 2 groups.
  - *Normal saline, the mean RDS reduced by **3.41** (95% CI 3.0-3.8)*
  - *Standard group, the mean RDS reduced by **1.96** (95% CI 1.5-2.4).*
  - *P-value <0.0001.*



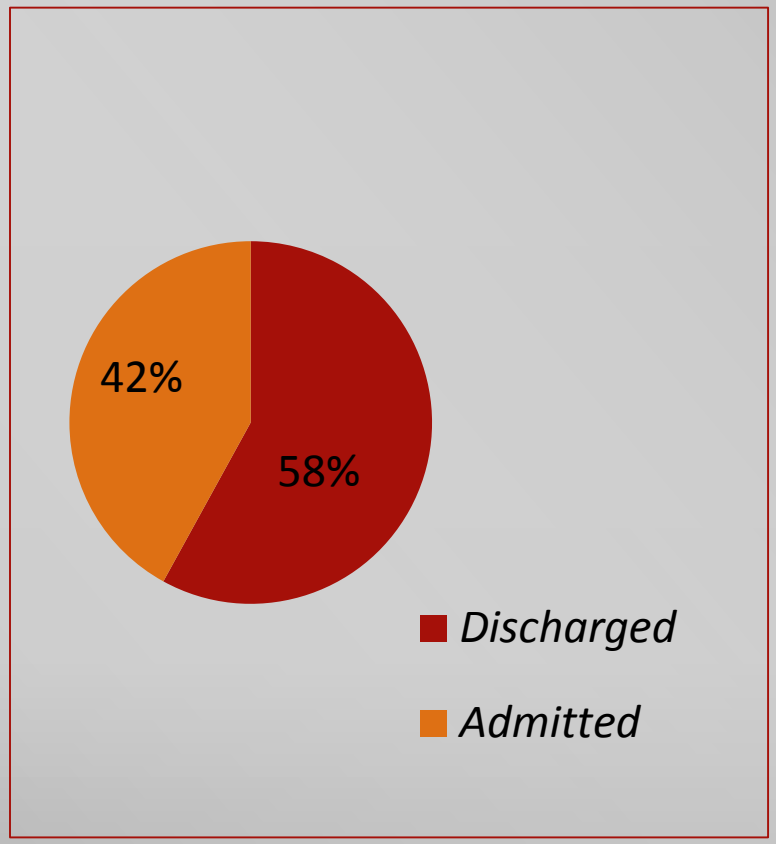
Results: Hypoxemia

- There was a significant difference in the SpO_2 between the 2 groups at 4 hours.
  - *Normal saline: SpO_2 increased by **7%** (95% CI 6.0-7.9) to a mean SpO_2 of 90.7% at 4 hours.*
  - *Standard therapy: SpO_2 increased by **4%** (95% CI 2.8-5.2) to a mean SpO_2 of 87.5% at 4 hours*
  - *P<0.001*

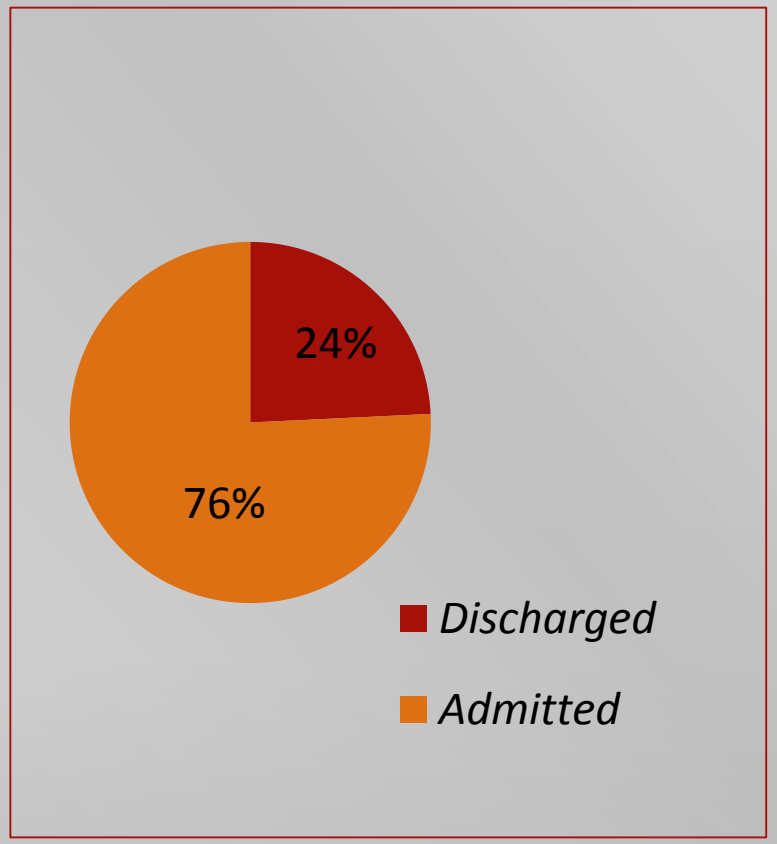


Results: Discharge rates at 4 hours

NORMAL SALINE- *58 OF 100 (58%) WERE DISCHARGED*



STANDARD CARE- *24 OF 99 (24.2%) WERE DISCHARGED*



Results: Decision to discharge

- Change in RDS and hypoxaemia were consistent with the decision to discharge.
  - *In the 82 children who were discharged, the change in SpO_2 was 7.5% (95% CI 6.8-8.3) and the change in RDS was -3.5 (95% CI -3.2 to -3.9).*
  - *Those who were admitted the change in SpO_2 was only 4.1% (95% CI 2.9-5.2) and the change in RDS was only -2.1 (95% CI -1.68 to -2.56).*

Discussion

- This study supports a the short-term use of nebulised saline in the treatment of acute bronchiolitis / moderate pneumonia.

- There were objective clinical benefits of normal saline nebulisation beyond standard care with minimal handling, oxygen (if needed), and antibiotics.

➢ *Benefits in reduced respiratory distress and improved oxygenation*

- The results of this trial may support the conclusions of a Cochrane meta analysis in 2013 that nebulised hypertonic saline improves respiratory clinical scores and reduces length of hospital stay.

Discussion: Potential limitations

- Potential for bias or subjective assessment. The sole investigator made the decision as to whether patient was discharged or kept for admission for IV antibiotics (however SpO_2 and RDS are objective measures).

- Non-blinded study

➢ *Open study as parents were aware what treatment their child was getting.*

➢ *Prevented potential confounders and to determine whether normal saline had a place in routine clinical practice.*

➢ *A number of previous studies have used a randomised blinded approach using distilled water as placebo- 'bronchospasm'.*

- Most patients in the intervention group received 3 doses of nebulised normal saline – no evidence of a benefit of using any more doses.

Discussion: Potential limitations

- Follow-up difficult, while some were followed up many did not return, and this was not included in data collection, therefore longer term outcome assessment not possible

➢ *Most parents were advised on the danger signs and to bring child back to hospital if the child had not improved with treatment at home.*

- Single centre study- results may not be generalizable. This study may need a multicentre design involving a diverse widespread population sample size.

Conclusion

- This study supports the use of nebulised normal saline in the treatment of acute bronchiolitis in addition to standard care.

- Nebulised normal saline given in the ED setting decreases respiratory distress scores, improves hypoxemia and reduces rates of admissions in infants with acute bronchiolitis.

- The respiratory distress score can be used as a tool in the emergency department to monitor patients with acute lower respiratory infection.

References

- Wu Susan MD, et al. ***Nebulized Hypertonic Saline for Bronchiolitis.*** JAMA Paediatrics. 2014;168(7):657-663.
- Florin Todd. A, et al. ***Nebulized Hypertonic Saline for Bronchiolitis in the Emergency Department.*** JAMA Paediatrics. 2014; 168(7): 664-670.
- Everard ML, et al. ***SABRE. Thorax.*** BMJ. 2014;69:1105- 1112.
- Jacobs J, et al***. 7% Hypertonic Saline in Acute Bronchiolitis.*** AAP. 2013; 133(1): 8-13.
- Anil. A, MD, et al. ***High volume normal saline alone is as effective as nebulized salbutamol- normal saline, epinephrine normal saline, and 3 % saline in mild bronchiolitis***. Paediatric Pulmonology 2010; 45: 41- 47.

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