# Factors influencing adherence to secondary prophylaxis among children and adolescents with Rheumatic Heart Disease at Port Moresby General Hospital and Nonga General Hospital: A mixed methods study

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# Background

- Acute rheumatic fever (ARF) develops after infection of the throat or skin with Group A Beta Haemolytic Streptococcus - GAS

- GAS infection can result in permanent damage to the valves of the heart, causing rheumatic heart disease (RHD)

- Worldwide ~ 15.6 million people with RHD with ~ 470 000 new cases of ARF annually & 230 000 deaths related to RHD each year

# Background

- WHO recommends Benzathine penicillin intramuscular injections 4 -weekly for prevention of GAS
- Compliance with secondary prophylaxis reduces the risk of complications
- Factors such as patients knowledge of ARF/RHD , patient staff interactions and the painful nature of benzathine penicillin injections influence compliance
- Single most important challenge to ARF/RHD programs is the poor uptake and adherence to secondary prophylaxis

# Study Aim

- Document patients' and their parents' understanding of rheumatic heart disease and how this influenced their adherence with secondary prophylaxis

# Methodology

**Study type:** Mixed methods study – quantitative and qualitative data

**Study sites**: PMGH & NGH

**Study Time**: February 2016 - July 2018

**Sample size**: 48 patients/ 26 patient interviews

# Methodology

**Inclusion Criteria:**

- Children
  - 5 - 15 years old presenting to PMGH & NGH who fit the 2002–2003 WHO revision of the Jones Criteria for the diagnosis of ARF
  - previously diagnosed with ARF/RHD whose names were on the cardiac register, or were seen in cardiac follow-up clinic
  - on either benzathine penicillin or penicillin V (oral phenoxymethyl penicillin) as secondary prophylaxis

# Methodology

**Data collection**

- Standard ARF & RHD Case Report form completed after verbal consent
- Individual interviews

**Data analysis**

- Data were entered into Microsoft Excel, and analysed using descriptive epidemiology

**Ethical Considerations**

- Ethical approval obtained from UPNG SMHS Research Committee as well as PMGH and NGH Administration

# Results – baseline characteristics

| Variable | Frequency n=48 (%) |
|---|---|
| Age Median (IQR) | 11 years (9 – 13 years) |
| Gender | |
| **Male** | **28 (58.33)** |
| Female | 20 (41.68) |
| Residence | |
| Suburb | 22 (45.83) |
| Settlement | 7 (14.58) |
| Village | 19 (39.58) |
| Presenting Criteria (Major) | |
| **Carditis** | **35 (72.92)** |
| **Migratory polyarthritis** | **23 (47.92)** |
| Sydenham's Chorea | 2 (4.17) |
| Presenting Criteria (Minor) | |
| Fever | 32 (66.67) |
| Polyarthralgia or aseptic monoarthritis | 5 (10.42) |
| Prolonged PR interval on ECG | 10 (20.83) |

# Results – echocardiographic findings

| **Cardiac abnormalities** | **n = 48** | **%** |
|---|---|---|
| **Mod – Severe MR** | **31** | **64.6** |
| Mod – Severe AR | 20 | 41.7 |
| Mild MR | 6 | 12.5 |
| Mild AR | 5 | 8.3 |
| Trivial MR | 0 | 0.00 |
| Trivial AR | 3 | 6.3 |
| Mild MS | 6 | 12.5 |
| Moderate MS | 3 | 6.3 |
| Severe MS | 1 | 2.1 |
| Normal study | 3 | 6.3 |
| Not done | 2 | 4.2 |

# Results - complications

| Complications of Rheumatic Heart Disease | | |
|---|---|---|
| | **n= 48** | **%** |
| Heart Failure | 31 | 64.6 |
| Atrial Fibrillation | 0 | 0.0 |
| Infective Endocarditis | 1 | 2.1 |
| Stroke | 1 | 2.1 |
| None | 15 | 31.3 |

| Heart failure medication for patients in the study population | | |
|---|---|---|
| | n = 31 | % |
| Furosemide | 12 | 38.71 |
| Furosemide, Spironolactone | 13 | 41.94 |
| Furosemide, Spironolactone, Enalapril | 5 | 16.13 |
| Furosemide, Spironolactone, Captopril | 1 | 3.23 |

# Outcomes - deaths

- 4 deaths in the 2 year period of observation (8.3%)
- 2 - Suspected severe anaphylaxis to benzathine penicillin
- 1 - biventricular heart failure
- 1 - stroke

# Results – case study

*'GR was 12 years old when he was first diagnosed with RHD in late 2015. He lived with his mother and grandmother and was brought to the clinic most of the time by his grandmother. On ECHO he was found to have severe mitral and aortic incompetence with mitral stenosis and had signs of heart failure so he was commenced on monthly benzathine injections and frusemide and spironolactone for his heart failure. Unfortunately he often missed several months of his benzathine injections and antifailure treatment because he was not brought to the clinic.*

*In March 2017 GR now almost 14 years old, walked from Korobosea to the PMGH paediatric cardiac clinic for his routine monthly benzathine penicillin injection. He had received his benzathine penicillin injections in the previous 7 months with no issues and appeared fine that morning. As soon as he entered the clinic, he was brought to the procedure bed and the nurse administered his injection as usual. GR then made an attempt to get up but suddenly collapsed afterwards. The medical team present attempted to resuscitate him but were unsuccessful'*

# Changes in practice during the study

- The deaths lead to a change in secondary prophylaxis at PMGH – from predominantly 4-weekly IM benzathine to daily oral penicillin V

- Cause of death and precipitating factors unclear

# Results – secondary prophylaxis

| Secondary Prophylaxis | Comments by patients and parents | Secondary prophylaxis preference |
|---|---|---|
| Benzathine to Penicillin V (n = 19) | (BK M/14): "I prefer monthly injections, its once a month only, It's hard to remember to take tablets everyday"<br><br>Parent of MH:" Even though it's painful, it's once a month. Tablets we forget, when we visit relatives, we leave the tablets at home."<br><br>(JO F/9): I want to drink medicine, the injections are painful<br><br>(PA F/11): Both injection or medicine okay<br><br>Parent of RY: "Both are okay. Injections never did any harm." | Benzathine Penicillin (5, 26.32%)<br><br>Penicillin V (5, 26.32%)<br><br>Either (6, 31.58%)<br><br>Neither (3, 15.79%) |

# Results – secondary prophylaxis

| Secondary Prophylaxis | Comments of Patients | Number of Benzathine Doses Missed |
|---|---|---|
| Benzathine only (n = 5) | (KP M/11) "I don't mind the injections, it's painful but its once a month. I won't be able to remember to take tablets everyday" | 2 (0 missed doses) |
| | (HP F/8): "I want to drink tablets, the injections are painful. I don't like it when the injection is blocked and the nurse tries many times" | 2(< 3 missed doses) |
| | (DT M/13) "I want the tablets, the injections are painful" | 1(> 3 missed doses) |

# Results – secondary prophylaxis

- Preference
  1. Penicillin V (9, 34.6%)
  2. Benzathine Penicillin (8, 30.8%)
  3. Either (6, 23.1%)
  4. Neither ( 3, 11.5%)

- Factors influencing compliance
  - Benzathine injections painful
  - Forget to take Penicillin V everyday

# Results – school participation

| School attendance | n = 48 | % |
|---|---|---|
| Fulltime (miss for reviews only) | 17 | 35.4 |
| Misses some days | 7 | 14.6 |
| Misses several days/weeks | 2 | 4.2 |
| **Not attending** | **21** | **43.8** |
| Not known | 1 | 2.1 |

# Results – school participation

| Parents Comments on School Participation | |
|---|---|
| **Not Attending (n=11)** | **(PAs MUM): She has had several admissions because of her illness. I worry something will happen to her if she goes to school.**<br><br>**NMs DAD: "The teacher told us to keep him at home first because he didn't look well"** |
| **Misses some days (n = 4)** | **(KPs MUM): "He stopped going to school, because he was always unwell. Since getting his injection he is better. He went back to school this year but he has had to repeat a grade".** |

# Discussion

- Low level of awareness of ARF/RHD

- Severe valvular lesions in a very young cohort
  - Nicaragua: Population screening used on 3150 children > children identified with RHD had mild carditis

- Poor school attendance
  - 40 % children not attending school → poor academic performance → economic & socio-developemental consequences

# Discussion – Benzathine Penicillin?

- WHO recommends 4 weekly Benzapen injections as prophylaxis against GAS
- Compliance with daily oral penicillin V a problem
- Systemic review comparing the effectiveness of intramuscular penicillin and oral penicillin > very strong evidence for im penicillin
  - 87 – 96% reduction in RF recurrence
  - 71 – 91% reduction in streptococcal throat infection

# Discussion - Safety of Benzathine Pen

- Widely used for the prevention of recurrent RF for several years , reports of fatal reactions rare
- 1962 report on 3 cases that had fatal reactions to Benzapen all had cardiomegaly and a history of cardiac decompensation
- Children with severe heart failure or arrhythmias possibly more risk of sudden death than children with milder disease
- No reason to believe that Benzapen poses a risk for the vast majority of RHD patients

# Limitations

- Small sample size
- Hospital based study most likely to describe patients with more advanced RHD

# Conclusion

- Rheumatic heart disease is a cause of significant morbidity and mortality in children and adolescents presenting to PMGH & NGH

- Patients often have advanced disease pattern which is a reflection of a high burden of ARF and RHD in the community, late presentation and likely poor secondary prophylaxis adherence.

# Recommendation

- Increase awareness
- Active detection for RHD using population screening
- Role of benzathine penicillin in secondary prophylaxis needs to be made clear, so that the RHD program can be optimally effective

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