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Penicillin use and its Impact for the Secondary Prevention of Rheumatic Fever/Rheumatic Heart Disease in a Tertiary Hospital in South Africa

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Abstract

Introduction: Acute rheumatic fever (ARF) is a post infectious, non-suppurative sequela of pharyngeal infection with streptococcal pyogens, or group a beta haemolytic streptococcus. Rheumatic heart disease (RHD) is a condition of global health importance. It is estimated that 15.6-19.6 million people are living with RHD, with almost 80% of those residing in low and middle income countries.

Methods: This was a retrospective review of records of paediatric patients with rheumatic fever and rheumatic heart disease at a tertiary hospital in South Africa; from January 2008 to December 2015. Records were analyzed for the evidence of use of secondary prophylaxis with enzathine penicillin and recurrence of rheumatic fever.

Results: Total of 60 patients was seen over the period of 8 years. Fifty seven patients presented with chronic rheumatic heart disease. Only 3 patients presented with acute rheumatic fever. All the patients in the cohort were on secondary prophylaxis with either oral or intramuscular benzathine penicillin according to the protocol. Of the 60 patients over the period of 8 years, none of the patients developed recurrent rheumatic fever on secondary prophylaxis. Twenty four were operated for rheumatic valvular heart disease.

Conclusion: Secondary prophylaxis with benzathine penicillin is effective in preventing recurrent rheumatic fever/rheumatic heart disease. In our cohort none of the patients who were on prophylaxis developed recurrent rheumatic fever.

Keywords: Rheumatic fever; Rheumatic heart disease; Secondary prophylaxis of rheumatic heartfever; Benzathine penicillin G

Introduction

Acute rheumatic fever (ARF) is a post infectious, non-suppurative sequela of pharyngeal infection with streptococcal pyogens, or group a beta hemolytic streptococcus. Rheumatic heart disease (RHD) is a condition of global health importance. It is estimated that 15.6-19.6 million people are living with RHD, with almost 80% of those residing in low and middle income countries.

Acute rheumatic fever is predominantly a disease of children aged 5-14 years and generally does not affect children less than 3 years old [1]. However, people can have recurrent episodes well into their forties. Rheumatic fever steadily worsens in people who have multiple episodes of ARF [2].

Recurrence of ARF accelerates progression of cardiac valve damage, culminating in heart failure, arrhythmias, and often fatalities [1]. Antibiotics are essential for prophylaxis to prevent recurrences of ARF (secondary prophylaxis) and for treatment of symptomatic group a streptococcus (GAS) infections (primary prevention). Benzathine penicillin G (BPG) is effective for primary and secondary prevention of ARF because its long half-life provides prolonged bactericidal protection from GAS infection [3]. Alternative regimens for the individuals with severe penicillin allergy or intolerance are addressed

in most RF/RHD treatment guidelines [4]. Guidelines for the secondary prophylaxis of rheumatic fever (Table 1) [4].

Methods

This was a retrospective review of records of pediatric patients presenting with acute rheumatic fever and rheumatic heart disease in a tertiary hospital in South Africa; from January 2008 to December 2015.

Demographic data such as age, gender, geographical origin, surgical interventions and outcomes and secondary prophylaxis were analyzed. Record of secondary prophylaxis in all patients was recorded and documentation of administration route (intramuscular or oral penicillin) was made according to the Pediatric Cardiac Clinic protocol of Dora Nginza Hospital. Records were analyzed for evidence of recurrence of acute rheumatic fever and rheumatic heart disease in the patients who were already diagnosed with either acute rheumatic fever/rheumatic heart disease.

Statistical analysis and ethical clearance

Variables were reported as a mean (± standard deviation) or median (range). Nominal Variables were compared using t test. Statistical significance was determined by using P<0.05. Ethical clearance was obtained from chief executive officer of Dora Nginza Hospital and the Health Research Ethics and Biosafety Committee of Walter Sisulu University. All the information obtained from the patient's files was

treated with strict confidentiality and no patients were prejudiced in any form.

Benzathine penicillin-regular single dose IM	<30 kg: 600,000 IU, >30 kg: 1, 2 million IU
Phenoxymethylpenicillin, oral course if IM not acceptable/possible	250 mg q12 h
Erythromycin-for patients sensitive to penicillin	250 mg q12 h
Duration of prophylaxis	For 5 years after the last attack of RF or until 18 years of age (whichever is longer)
	-If carditis present, for 10 years after last attack, or at least until 25 years (whichever is longer), -If more severe valvular disease or after valve surgery, life long

Table 1: WHO Guidelines for the secondary prophylaxis of rheumatic fever.

Dora Nginza hospital is in the Eastern Cape Province in South Africa which is known to have high levels of poverty and prone into developing rheumatic fever and rheumatic heart disease. The purpose of the study was to analyze the impact of penicillin in prevention of recurrent rheumatic fever and its sequel in the high risk population of the Eastern Cape Province in South Africa.

Results

A total of 60 patients were seen with ARF and RHD over the period of 8 years were reviewed. Ninety five per cent (n=57) of patients presented with RHD for the first time.

The average age at presentation was 10 years. The majority of patients presented with mitral valve regurgitation (Table 2). Ninety five per cent of patients were between the ages of 5-15 years. There were 3 patients who were under the age of 5 years. Only 3 patients presented with acute rheumatic fever according to the new world health federation diagnostic criteria for acute rheumatic fever.

Extent of the disease	Number (%)	Average age at diagnosis
Isolated MV regurgitation	35 (58)	10 years
MV regurgitation with MV stenosis	7 (12,5)	11 years
MV regurgitation with AV regurgitation	14 (25)	10 years
AV regurgitation	3 (5,3)	10 years
AV regurgitation with AV stenosis	1 (1,8)	11 years
(MV= mitral valve; AV=aortic valve)		

Table 2: Extent of the valve disease and average age at diagnosis.

Twenty four patients were operated for rheumatic valvular heart disease. Twelve patients had had mitral valve repair, five mitral valve replacements, three double valve replacements, and three aortic valve repairs. The average age at surgery was 10 years (Figure 1).

The three patients that had acute rheumatic fever were treated with non-steroidal anti-inflammatory drugs and heart failure therapy. They were also started on primary prevention with benzathine penicillin G according to the world health organisation guidelines.

Ninety five per cent (n=57) of patients were started on secondary prophylaxis with either benzathine penicillin G IM, 600,000 IU for patients who were <30 kg and 1, 2 million IU for patients who weighed >30 kg every 4 weeks or Phenoxymethylpenicillin 250 mg orally twice daily.

None of the patients developed recurrent rheumatic fever whilst on secondary prophylaxis. Patients were followed up clinically for more than 5 years.
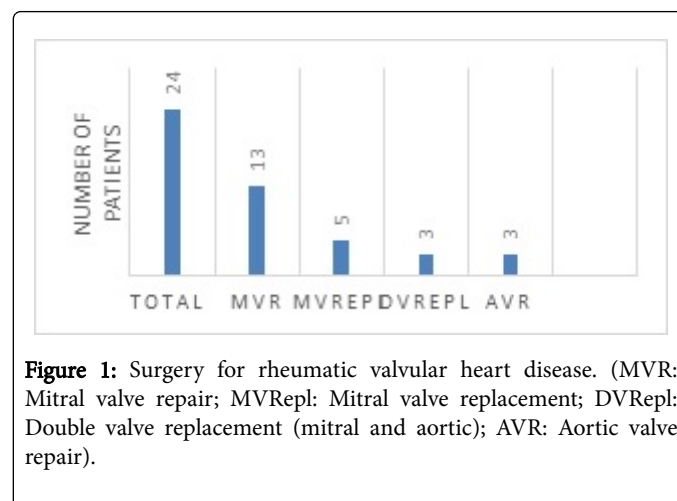

Figure 1: Surgery for rheumatic valvular heart disease. (MVR: Mitral valve repair; MVRepl: Mitral valve replacement; DVRepl: Double valve replacement (mitral and aortic); AVR: Aortic valve repair).

Discussion

Primary prevention is defined as the adequate antibiotic therapy for group a streptococcal upper respiratory tract infection [5]. Primary prevention is administered only when there is group a streptococcal upper respiratory tract infection.

Secondary prevention of rheumatic fever is defined as the continuous administration of specific antibiotics to patients with a previous attack of rheumatic fever, or well-documented rheumatic heart disease. The purpose is to prevent colonisation or infection of the upper respiratory tract with group a beta-haemolytic streptococci and the development of recurrent attacks of rheumatic fever [4].

The mainstay antibiotic is IM benzathine benzyl penicillin. Oral Phenoxymethylpenicillin and erythromycin are also used alternatives to IM penicillin. However, debate still remains regarding frequency of administration of IM benzathine penicillin. It is suggested that IM benzathine penicillin injections be given every 4 weeks as routine. Two or three weekly regimens should be reserved for those at high risk or

who are still having recurrences of RF, despite full adherence to the four week regimen [5]. It has been recommended that serum penicillin concentrations should be maintained above 0.02 mg/ml to prevent such recurrences.

In our cohort all the patients who were on IM benzathine penicillin were receiving the routine 4 weekly injections for the prevention of recurrent RF. None of the patients developed recurrent rheumatic fever. Studies in other countries have shown a recurrence rate of 3-8% over 5-6 years in patients on this regimen [5].

There was no patient who was hypersensitive to penicillin. Our patients were either on IM penicillin or oral penicillin.

Penicillin prophylaxis is effective in prevention of recurrent rheumatic fever and its sequel of severe rheumatic valvular heart diseases that require surgery. This is particularly of impact for third world countries where surgery for this patient is not readily available.

Conclusion

Routine IM benzathine penicillin once every 4 weeks is effective for prevention of recurrent rheumatic fever in patients from a high risk population with rheumatic heart disease. Two or three weekly regimens should be reserved for those at high risk or who are still having recurrences of RF despite full adherence to the four week regimen.

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