

## Amoxicillin for the secondary prevention of rheumatic fever in children not allergic to penicillin

**To the Editor:** In October 2014, a communication from the Department of Health substituted azithromycin for erythromycin for penicillin-allergic patients. This was for certain conditions including acute rheumatic fever and prophylaxis of rheumatic fever.

It has recently been suggested that owing to the challenges with the availability of oral penicillin, azithromycin should be used as a penicillin substitute for patients who are not allergic to penicillin.

In our opinion it is inappropriate to substitute a macrolide for another form of penicillin (amoxicillin) in this situation. The primary reason is that despite many decades of use, there is no significant group A beta-haemolytic streptococcal (GABHS) resistance to penicillin. There are, however, increasing reports of GABHS resistance to macrolides, and azithromycin in particular.<sup>[1-4]</sup>

A previously reported randomised trial<sup>[5]</sup> of 125 mg phenoxymethylpenicillin (pen VK) or amoxicillin given three times a day for 10 days to children with GABHS pharyngitis demonstrated that the recurrence of the original GABHS within 21 days after the end of therapy was higher with pen VK (20%) than with amoxicillin (13%). The geometric mean minimum inhibitory concentrations for amoxicillin and pen VK against 88 isolates of GABHS were 0.008 and 0.009 µg/mL, respectively. The mean concentrations of amoxicillin and pen VK in sera after 125 mg doses were 3.86 µg/mL and 1.74 µg/mL, respectively. In this study, therefore, amoxicillin was active against Gram-positive organisms at an inhibitory level similar to that of pen VK, but had higher blood levels. This study suggests that amoxicillin is probably at least as good as pen VK for the treatment of GABHS pharyngitis.

We therefore recommend, as per the South African Essential Drugs List, benzathine penicillin 600 000 units for children <30 kg and 1.2 million units for children ≥30 kg by intramuscular injection every 28 days for the secondary prevention of rheumatic fever. If it is not advisable to use an intramuscular form of penicillin (for example with a patient on warfarin), then in the absence of pen VK and in the absence of penicillin allergy, children weighing <20 kg should be given amoxicillin 125 mg twice daily, and children weighing ≥20 kg given 250 mg twice daily.

There is no defined azithromycin paediatric dosage for the secondary prevention of rheumatic fever in penicillin allergy. Azithromycin has however been dosed long term in clinical trials in children with cystic fibrosis.<sup>[6-8]</sup> There is no consensus on the dosage, but there is some support<sup>[6-9]</sup> for 250 mg once daily (<40 kg) or 500 mg once daily (≥40 kg) three times a week (Monday, Wednesday and Friday).

We recommend that azithromycin is used for the secondary prevention of rheumatic fever only in children who are allergic to penicillin and is dosed 250 mg (<40 kg) or 500 mg (≥40 kg), once a day three times a week (Monday, Wednesday and Friday).

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*S Afr Med J* 2016;106(4):317. DOI:10.7196/SAMJ.2016v106i4.10711