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Correlation between erythromycin and azithromycin resistance in *Streptococcus pneumoniae*

To the Editor: Erythromycin has long been used as an alternative to penicillin for the treatment of upper and lower respiratory tract infections in children. Modifications of the original chemical structure of erythromycin have produced macrolides such as azithromycin that have improved therapeutic properties. Azithromycin given as a single daily dose for 3 days is used for the treatment of acute group A streptococcal pharyngitis[1] and a meta-analysis of randomised controlled trials found 30 mg / kg of azithromycin, given over 3 - 5 days, to be as effective as longer courses of other antibiotics for the treatment of upper respiratory tract infections.[2] There have, however, been recent reports of macrolide resistance resulting in azithromycin failure for the treatment of group A streptococcal pharyngitis.[3]

In South Africa, azithromycin is frequently prescribed for the treatment of acute otitis media in children; however, the increasing prevalence of erythromycin resistance in *Streptococcus pneumoniae* isolates may adversely affect the efficacy of this therapy. A survey of pneumococci isolated from blood and cerebrospinal fluid (CSF) of children in the public sector of South Africa between 1991 and 1998 found a small but statistically significant increase in resistance to erythromycin, from 1.8% of pneumococci isolated between 1991 and 1994 to 4.2% of pneumococci isolated from 1995 to 1998.[4] In contrast, 39% of pneumococci carried in the nasopharynx of children aged 1 month - 5 years who were sampled prospectively while attending private paediatricians in Johannesburg were resistant to erythromycin.[5]

To evaluate the correlation between resistance to erythromycin and azithromycin, 100 erythromycin-resistant *S. pneumoniae* isolates (minimum inhibitory concentrations MICs) ranged from 1µg / ml to > 256 µg / ml were tested for concomitant resistance to azithromycin. The isolates had been obtained from middle-ear fluid of children with acute otitis media (N = 34), cases of invasive pneumococcal disease (N = 19), and from the nasopharynx of asymptomatic children (N = 47). MICs were determined by agar dilution (100 isolates) and E-test (98 isolates) using standardised methods and criteria for determination of resistance.[6] The azithromycin powder and methods for susceptibility testing were obtained from the manufacturer. For the pneumococci tested, the MICs for azithromycin correlated with the MICs for erythromycin for 100% of the isolates using both the agar dilution and E-test methods. Therefore, resistance to erythromycin can be used as a surrogate for resistance to azithromycin. Similar results were found in a study of 120 isolates from the USA.[7]

In addition, a study of the impact of azithromycin on carriage of antibiotic-resistant pneumococci found that 5 days of azithromycin treatment resulted in a four-fold increase in the prevalence of erythromycin-resistant pneumococci.[8] These results suggest that in South Africa, where erythromycin-resistant pneumococci are common, macrolide treatment for otitis media infections in children under 4 years of age may have reduced efficacy.

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