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Commentary

Commentary on 'Different antibiotic treatments for group A streptococcal pharyngitis (Review)'

This is a commentary of Cochrane review, published in this issue of EBCH, first published as: van Driel ML, De Sutter AIM, Keber N, Habraken H, Christiaens T. Different antibiotic treatments for group A streptococcal pharyngitis (Review). *Cochrane Database of Systematic Reviews* 2010, Issue 10. Art. No.:CD004406. DOI: 10.1002/14651858.CD004406.pub2.

Further information for this Cochrane review is available in this issue of EBCH in the accompanying Summary article.

Commentary by Robert S. Baltimore

Streptococcal pharyngitis is a classic infectious disease of childhood. It is one of the most common and best studied of childhood illnesses. Other than recommendations for pain relief, the major aspect of management of sore throat is determination of whether the patient should be treated for pharyngeal infection caused by group A beta-haemolytic streptococcus (GABHS). Determination of whether pharyngitis is caused by GABHS can be done by culturing the pharyngeal exudate on a blood agar plate or by rapid identification of GABHS antigen using a commercial kit. While some practitioners may try to diagnose streptococcal pharyngitis by clinical clues, these lack adequate specificity. In fact, acute pharyngitis is caused considerably more often by viruses than by bacteria. Viruses that commonly cause pharyngitis include influenza virus, parainfluenza virus, rhinovirus, coronavirus, adenovirus, respiratory syncytial virus, Epstein-Barr virus, enteroviruses and herpesviruses. Other causes of acute pharyngitis include groups C and G streptococci, *Mycoplasma pneumoniae*, and less commonly *Neisseria gonorrhoeae, Chlamydia pneumoniae* and *Arcanobacterium hemolyticum* (1).

Critical to evaluation and determination of the clinical relevance of van Driel *et al*. is a discussion of why we make the diagnosis of pharyngitis due to GABHS and why when we make the diagnosis do we treat the patient with an antibiotic? As noted by van Driel *et al*. (2), a previous Cochrane review found that there is only a modest symptomatic benefit of treating pharyngitis even if it is due to GABHS. In fact, for decades conventional wisdom was that antibiotic treatment had no benefit in altering the symptoms associated with GABHS pharyngitis and the reason to treat was only to prevent rheumatic fever. It was only in the 1980s when Nelson (3), Krober *et al*. (4) and Randolph *et al*. (5) published their controlled studies that there was sufficient proof of clinical efficacy that investigators took seriously the question of which antibiotic worked best for reducing symptoms.

The dilemma facing investigators studying the impact of antibiotics on prevention of acute rheumatic fever has been the rarity of acute rheumatic fever in technologically advanced countries where such studies can be performed and the difficulty to follow patients forward in those developing countries where acute rheumatic fever is still relatively common. Penicillin in its various forms has been the only antibiotic shown to prevent rheumatic fever (6–8). Therefore, newer studies comparing the effects of different antibiotics on GABHS pharyngitis have relied on surrogate endpoints: clinical response, eradication of GABHS from the throat and relapse (microbiological and clinical). Data correlating these surrogate endpoints with prevention of acute rheumatic fever are lacking. Nevertheless, authors have questioned the wisdom of our continuing to recommend penicillin as the first choice in treating GABHS pharyngitis, because in some published studies it did not perform best using these surrogate endpoints. Authors of some of these studies point out that these endpoints, rather than being surrogates for prevention of acute rheumatic fever, are important in themselves as even a short relief from acute pharyngitis and eradication of GABHS, when throat cultures are performed after 10 days of therapy, are clinically important. Such an argument based primarily on relapse rate but also symptomatic endpoints has been promoted by Casey *et al*. ((9–11)). These authors have questioned the wisdom of the American Heart Association, the American Academy of Pediatrics and the Infectious Diseases Society of America, all of whom recommend penicillin as the first-choice antibiotic for GABHS pharyngitis. Responses to opinions based on surrogate endpoints have been published by some GABHS researchers (12–15). They point out that data do not support increasing resistance of GABHS pharyngitis to penicillins, that the apparent superiority of some of the newer antibiotics is owing

to better eradication of GABHS from the throats of carriers which is not clinically relevant and that some of the studies referred to by Casey *et al*. have significant methodological flaws. In the newest version of the recommendations from the American Heart Association, once-daily amoxicillin is recommended as an equal favourite to oral penicillin G because once-daily administration is associated with better patient compliance (1,16).

Given the above context, the importance of van Driel *et al*. is that it looks at studies that compare different antibiotics as to their efficacy against GABHS, not at their ability to prevent acute rheumatic fever, but at other endpoints: resolution of symptoms, relapse, side effects of antibiotics and eradication for GABHS from the throat. The strength of this review is that they only chose studies meeting a high standard of study design. They address the issue of having carriers in the study populations only to mention that they would not contribute to clinical endpoints. I disagree as carriers may be entered into studies in the mistaken belief that they have acute pharyngitis due to GABHS and their lack of clinical response may be a result of their pharyngitis being due to an agent (probably a virus) that is not responsive to antibiotics. However, this analysis does support the use of penicillin as the first choice for GABHS in comparison with *antibiotics of other antibiotic classes*, as it is as effective clinically as these other agents and its price, safety and lack of antibiotic resistance make it the preferred treatment agent. Findings in favour of cephalosporins being more effective in prevention of relapse do not change this conclusion as it applies only to adults, for whom GABHS pharyngitis is an uncommon problem and with a number needed to treat to show benefit being too high for this finding to be considered meaningful.

Declaration of interest

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