

# Can We Shorten the Duration of Treatment for Acute Streptococcal Pharyngitis?

DHEERAJ SHAH

*Department of Pediatrics, University College of Medical Sciences, Delhi, India. E-mail: shahdheeraj@hotmail.com*

*Altamimi S, Khalil A, Khalaiwi KA, Milner R, Pusic MV, Al Othman MA. Short versus standard duration antibiotic therapy for acute streptococcal pharyngitis in children. Cochrane Database of Systematic Reviews 2009; 1: CD004872. This version first published online: 21 January, 2009.*

**T**reatment of acute streptococcal sore throat is advocated to hasten clinical resolution, prevent suppurative sequelae and decrease the incidence of rheumatic fever and glomerulonephritis. A 10-day course of penicillin is the standard treatment recommended for Group A beta hemolytic streptococci (GABHS) infection. Many antibiotics, including other beta lactams, macrolides, and clindamycin are also effective against streptococci and have the potential to shorten the duration of therapy. The present review was conducted with the objective of evaluating the efficacy of short course (2 to 6 days) of oral antibiotics in treating children with acute streptococcal pharyngitis, compared with a 10-day course of oral penicillin, on duration of symptoms (fever and sore throat), eradication of the organism, and, recurrence and complication rates (acute rheumatic fever and acute poststreptococcal glomerulonephritis).

## SUMMARY

Twenty randomized controlled studies (24 trial arms because of more than two arms in some studies) enrolling 13,102 children (aged between 1 to 18 years) with acute GABHS pharyngitis (diagnosis based on a positive rapid antigen testing or positive throat swab culture) were included in this review. The intervention antibiotics were macrolides (azithromycin in 6, clarithromycin in 3, and erythromycin in 2 trials), cephalosporins

(cefuroxime in 3; cefixime, cefprozil, cefpodoxime, cefdinir, ceftibuten and loracarbef in one each), other penicillins (amoxicillin+clavulanate in 2 and amoxicillin in 1), and josamycin ( $n=1$ ).

Compared to standard duration treatment, the trial short duration treatment had shorter periods of fever [mean difference (MD)  $-0.30$  days, 95% CI  $-0.45$  to  $-0.14$ ; 348 participants, 2 trials] and throat soreness (MD  $-0.50$  days, 95% CI  $-0.78$  to  $-0.22$ ; 188 participants, 1 trial); lower risk of early clinical treatment failure (OR 0.80, 95% CI 0.67 to 0.94; 11,713 participants, 23 trial arms); no significant difference in early bacteriological treatment failure (OR 1.08, 95% CI 0.97 to 1.20; 11,555 participants, 23 trial arms), or late clinical recurrence (OR 0.95, 95% CI 0.83 to 1.08; 8,068 participants, 17 trials). However, the overall risk of late bacteriological recurrence was more in the short duration treatment (OR 1.31, 95% CI 1.16 to 1.48; 10,249 participants, 24 trial arms). Only three studies reported long duration complications with no statistically significant difference (OR 0.53, 95% CI 0.17 to 1.64). The compliance was better (OR 0.21, 95% CI 0.16 to 0.29) with short duration therapy whereas the side effects were more.

The authors concluded that three to six days of oral antibiotics had comparable efficacy compared to the standard duration 10 day oral penicillin in treating children with acute GABHS pharyngitis.

**COCHRANE CONCLUSION**

- A short course (2 to 6 day) of oral antibiotics has comparable efficacy compared to the standard duration 10 day oral penicillin in treating children with acute GABHS pharyngitis.

**OUR CONCLUSIONS**

- The efficacy of short duration therapy in prevention of rheumatic fever and glomerulonephritis is doubtful.
- Short course treatment with azithromycin in the dose of 10 mg/kg is associated with a markedly inferior microbiological eradication.
- Risk of bacteriological recurrence is high with short course therapy.

**COMMENTARY***Are the results valid?*

The problem addressed in this review is specific and relevant. The search of literature was extensive but only studies up to November 2007 were searched. At least one more eligible trial(1) and one meta-analysis(2) has been published since the data were searched last by authors. Most included trials had methodological concerns; randomization was not described or inappropriate in majority; none used intention-to-treat analysis and only 3 of the 20 studies were blinded. The heterogeneity issues in this review were related to comparison of antibiotics with different half-lives rendering the issue of duration of treatment less important. The strength of the review lies in its sample size involving 24 study arms enrolling more than 13,000 children with microbiologically proven GABHS.

The primary outcomes such as duration of fever and sore throat are functionally important but the more important issue is the prevention of sequelae such as rheumatic fever and glomerulonephritis. This review was, however, not powered enough to comment validly on this outcome as only 3 of the 20 included studies addressed this issue with a total of only 14 events (3 acute rheumatic fever and 11 glomerulonephritis/proteinuria). Lack of bacteriological cure can also serve as a surrogate marker for the same.

*Clinical Importance and Precision of the Results*

Shortening of the duration of fever and sore throat by one-third to half day with the use of short course antibiotics, though statistically significant, does not

appear to be clinically important in this otherwise self limiting condition. Also, these outcomes have been evaluated in only two and one trial, respectively. More important is the issue of prevention of systemic sequelae by complete eradication of the organism.

Late bacteriological recurrence was significantly more common in the children treated with short course antibiotics whereas early treatment failure was comparable. Azithromycin, the most common short-course drug evaluated in this review, was associated with a markedly increased risk of early treatment failure (OR 3.25, 95% CI 2.47 to 4.27) and late recurrence (OR 3.62, 95% CI 2.66 to 4.92) when used in the standard dose of 10 mg/kg. When converted to absolute risk reduction, short course therapy with 10 mg/kg of azithromycin had 20% increase in risk of early treatment failure and 22% increase in risk of late bacteriological recurrence in comparison to 10 day course of penicillin (33% vs. 13% and, 38% vs. 22%, respectively). This means for every 5 children treated with short course azithromycin (10 mg/kg), one additional child would have early treatment failure and one additionally would have late bacteriological recurrence [Number needed to harm (NNH)=5 and 4.5, respectively]. This difference in the outcome between azithromycin and penicillin was largely overcome when the former was used in the daily dose of 20 mg/kg. Incomplete eradication of the organism by use of short course therapy might turn out to be a risk factor for long term sequelae like rheumatic fever or glomerulonephritis. It is also to be noted that all three events of rheumatic fever occurred in children treated with short course antibiotics.

*Implications for Practice and Policy*

Evidence provided in this review suggests that a short course (2 to 6 days) of alternative antibiotics achieves satisfactory clinical improvement with better compliance in comparison to a 10 day course of oral penicillin. However, short course treatment especially with azithromycin (10mg/kg) is associated with a higher risk of bacteriological treatment failure and recurrence. Since the primary purpose of 10 day antibiotic therapy for streptococcal pharyngitis is prevention of long-term systemic sequelae and not just clinical improvement, short course treatment can not be recommended based on the findings from this review. In another recent meta-analysis comparing the same antibiotic given for shorter duration or 10 days, it was reported that clinical success and microbiological eradication was inferior in patients who received short-course treatment(2). Thus, a 10 day course of oral penicillin or any other effective antibiotic still remains the treatment of choice for acute streptococcal sore throat.

*Funding:* None.

*Competing interests:* None stated.

**REFERENCES**

1. Pichichero ME, Casey JR, Block SL, Guttendorf R, Flanner H, Markowitz D, *et al.* Pharmacodynamic analysis and clinical trial of amoxicillin sprinkle administered once daily for 7 days compared to penicillin V potassium administered four times daily for 10 days in the treatment of tonsillopharyngitis due to *Streptococcus pyogenes* in children. *Antimicrob Agents Chemother* 2008; 52: 2512-2520.
2. Falagas ME, Vouloumanou EK, Matthaiou DK, Kapaskelis AM, Karageorgopoulos DE. Effectiveness and safety of short-course vs. long-course antibiotic therapy for group A beta hemolytic streptococcal tonsillopharyngitis: a meta-analysis of randomized trials. *Mayo Clin Proc* 2008; 83: 880-889.