Effectiveness and safety of short-course vs long-course antibiotic therapy for group a beta-hemolytic streptococcal tonsillopharyngitis: a meta-analysis of randomized trials

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CRD summary
The authors concluded that short-course antibiotic treatment for group A beta-haemolytic streptococcal tonsillopharyngitis, particularly with penicillin V, was associated with inferior bacteriological eradication rates. The evidence appeared to support the authors’ conclusions, but the generally poor quality of included trials and the restricted search may limit the reliability of the review.

Authors’ objectives
To evaluate the safety and effectiveness of short versus long course antibiotic treatment of group A beta-haemolytic streptococcal tonsillopharyngitis.

Searching
PubMed and the Cochrane Central Register of Controlled Trials (CENTRAL) were searched up to November 2007; no lower date limit for searches was applied. Search terms were reported. Reference lists of relevant articles were screened. Studies had to be published in English, Spanish, French, German, Italian or Greek. Conference abstracts were excluded.

Study selection
Randomised controlled trials (RCTs) that compared short-course antibiotics (up to seven days) with long-course antibiotics (at least two days longer than the short course) in patients (of any age) diagnosed with group A beta-haemolytic streptococcal tonsillopharyngitis were eligible for inclusion. Eligible trials had to use the same antibiotic in the same daily dose in each treatment arm, enrol at least 25 patients in each treatment arm, and report safety or effectiveness data.

The primary review outcome was microbiological eradication of group A beta-haemolytic streptococcus (GAS) from the throat at the end of treatment. Secondary outcomes were clinical success (complete or substantial resolution of symptoms and signs), bacteriological relapse (growth in throat culture of same type of GAS as the initial isolate after its initial eradication), bacteriological recurrence (growth in throat culture of a different GAS), total adverse events, withdrawal due to adverse events and immunological complications of tonsillopharyngitis. Acceptable definitions of secondary efficacy outcomes were reported.

Included trials were published between 1972 and 2003. Most trials evaluated either oral penicillin or oral second/third-generation cephalosporins. The duration of short courses ranged from one to seven days; long course duration ranged from three to ten days. Most trials included children or adolescents (where reported); other trials enrolled a mix of adults and children or adolescents. Diagnostic inclusion criteria were based on different combinations of clinical characteristics, symptoms and signs; most trials required verification of diagnosis using throat culture plus other objective tests.

Two reviewers independently conducted searches and selected studies.

Assessment of study quality
Validity was assessed using the Jadad criteria (randomisation, blinding, and withdrawals). Trials scoring more than 2 out of the maximum possible 5 points were considered to be of adequate quality.

The authors did not state how many reviewers assessed validity.

Data extraction
Two reviewers independently extracted the numbers of patients with outcomes of interest in each treatment arm to allow calculation of odds ratios (OR) and 95% confidence intervals (CIs).

**Methods of synthesis**

Pooled odds ratios and 95% confidence intervals were calculated using the DerSimonian and Laird random-effects model. Heterogeneity was assessed using the $\chi^2$ test.

The primary analysis compared short courses of five to seven days versus long courses of 10 days. Secondary analysis compared short-course with long-course regimens of any duration.

Subgroup analyses were used to explore the influence of age, class of antibiotics, and single or double-blinding.

**Results of the review**

Eleven RCTs were included in the review (n=2,389 patients in intention-to-treat population; sample size ranged from 60 to 520). Four trials were double-blinded and one was single-blinded. Three trials scored more than 2 out of 5 on the Jadad scale; the other trials scored 2.

**Primary outcome** (eight RCTs, n=1,607 patients): Short-course antibiotic regimens were associated with a statistically significant reduction in microbiological eradication of group A beta-haemolytic streptococcus (GAS) from the throat at the end of treatment compared with long-course regimens (OR 0.49, 95% CI 0.32 to 0.74). No significant heterogeneity was found. Short courses (lasting five to seven days) of penicillin V were associated with lower rates of microbiological eradication than long courses (OR 0.36, 95% CI 0.13 to 0.99; three RCTs, n=500 patients). There was no statistically significant difference for short versus long courses of cephalosporins (four RCTs, n=1,018 patients). Short-course regimens were associated with significantly lower rates of microbiological eradication than long courses in trials of predominantly children or adolescents (OR 0.63, 95% CI 0.40 to 0.98; six RCTs, n=1,258 patients) and in blinded RCTs (OR 0.31 (95% CI 0.16 to 0.58; three RCTs, n=469 patients).

**Secondary outcomes**: Short-course regimens were associated with lower rates of clinical success (OR 0.49, 95% CI 0.25 to 0.96; five RCTs, n=1,217 patients) and higher rates of bacteriological recurrence (OR 3.02, 95% CI 1.06 to 8.56; three RCTs, n=698 patients) than long-course regimens, but there was no significant difference in bacteriological relapse (five RCTs, n=981 patients) or adverse events (three RCTs, n=879 patients).

No significant heterogeneity was found for the above analyses.

Results for other analyses were reported in the paper.

**Authors’ conclusions**

Short-course (five to seven days) antibiotic treatment for group A beta-haemolytic streptococcal tonsillopharyngitis, particularly with penicillin V, was associated with inferior bacteriological eradication rates than long-course (10 days) antibiotic treatment.

**CRD commentary**

The review question was clearly stated and inclusion criteria were appropriately defined. Limiting the search to studies listed in two databases plus references, but excluding abstracts, may have resulted in the omission of other relevant studies and raised the possibility of publication bias. Some attempts were made to minimise language bias. Methods were used to minimise reviewer errors and bias in the selection of studies and extraction of data, but it was not clear whether similar steps were taken during the validity assessment.

Trial quality was assessed but, apart from blinding, only aggregate scores were reported. Most trials appeared to be of limited quality. Appropriate methods were used for the meta-analyses. Heterogeneity was assessed. Various pre-defined subgroup and sensitivity analyses were conducted.

The evidence appeared to support the authors’ conclusions, but the generally poor quality of included trials and limited search may limit the reliability of the review.
Implications of the review for practice and research

Practice: The authors stated that, although the clinical relevance of review findings may not be clear, the findings do support the idea that penicillin V should be given for a full 10 days for group A beta-haemolytic streptococcal tonsillopharyngitis.

Research: The authors did not state any implications for research.

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