Antibiotic prophylaxis for preventing recurrent cellulitis: a systematic review and meta-analysis

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CRD summary
The authors concluded that antibiotics could prevent recurrence of cellulitis, without increasing the risk of major adverse events. The conclusions may be overstated given the small samples in the included trials, most of which were published over 20 years ago, and the differences in antibiotic regimens between trials.

Authors’ objectives
To evaluate the efficacy and adverse effects of antibiotics to prevent recurrence of cellulitis or erysipelas (more superficial infection).

Searching
The Cochrane Library, MEDLINE, EMBASE, and CINAHL were searched in August 2012. Guideline websites, Trip, and ongoing trial databases were searched; some search terms were reported. Experts on the topic were contacted. No language restrictions were applied.

Study selection
Randomised controlled trials (RCTs) of antibiotics, for recurrent cellulitis (one episode or more) in patients aged over 16 years, were eligible for inclusion. The primary outcome was the number of people with a recurrence of cellulitis. Eligible trials had to have a comparison group of patients who did not receive prophylactic antibiotics; they could receive other standard care, such as local skin care. Trials of patients with cellulitis that was secondary to filarial lymphoedema were excluded.

The included trials were of participants with more than one or two previous episodes of cellulitis. The average age of participants ranged from 45 to 67.5 years. The antibiotics were oral erythromycin (250mg, twice daily), oral penicillin (250mg, twice daily), intramuscular penicillin (~720mg, every 15 days), and oral phenoxymethylpenicillin (1g or 2g, twice daily), for six, 12 or 18 months, where reported. Comparators were placebo or no antibiotic treatment. The trials were conducted in the UK, France, Sweden or Israel, and were published between 1991 and 2012.

Two reviewers independently selected trials for inclusion, with any disagreements resolved through discussion and referral to a third reviewer.

Assessment of study quality
The Cochrane risk of bias tool was used to assess trial quality on six domains, including random sequence generation and allocation concealment.

Two reviewers independently assessed trial quality.

Data extraction
The data were extracted to calculate risk ratios, with 95% confidence intervals, for the total number of recurrences. The time to the next occurrence, quality of life measures, and adverse events were extracted. Primary authors were contacted for further information, where necessary.

The authors did not state how many reviewers extracted the data.

Methods of synthesis
A random-effects model was used to pool the number of recurrences of cellulitis. Statistical heterogeneity was assessed with I² and X². An I² of over 50% indicated moderate heterogeneity, and over 75% indicated substantial heterogeneity. Several subgroup analyses were planned, and sensitivity analysis was performed for study quality.
Results of the review
Five RCTs (535 participants; range 40 to 274) were included. Two trials were good quality, with the remainder being of unclear or low quality. Follow-up, where reported, ranged from 11.6 to 36 months.

Antibiotics were beneficial in preventing the recurrence of cellulitis (RR 0.46, 95% CI 0.26 to 0.79; five RCTs; I²=39%). Both the sensitivity analyses of high-quality and of lower or unclear-quality trials agreed that antibiotic prophylaxis was effective.

One trial reported that the median time to the next episode was 626 days with the antibiotic and 532 days without it.

The most commonly reported adverse events were nausea and diarrhoea; figures were similar for treatment and comparison groups (data not reported).

The results of subgroup analyses were reported, but each analysis was based on few patients.

Authors’ conclusions
Antibiotics could prevent recurrence of cellulitis and were generally well tolerated, without an increased risk of major adverse events.

CRD commentary
The review question and inclusion criteria were clearly stated. Various databases were searched, with no language restrictions. Steps were taken to prevent error and bias in some stages of the review, but there was potential for error and bias in data extraction. Suitable criteria were used to assess trial quality, and the results were used to inform the sensitivity analysis. While there was no significant statistical heterogeneity, the authors appropriately noted that the analysis was based on a few relatively varied trials, some of which had been published over 20 years before the review.

The conclusions may be overstated given the small samples in the included trials, and differences in antibiotic regimens between them.

Implications of the review for practice and research
Practice: The authors stated that their analyses supported the use of antibiotics to prevent recurrence of cellulitis or erysipelas.

Research: The authors stated that larger, randomised, controlled trials were needed to determine the best course of treatment (duration, dose, and when it should start), which patients might benefit most, and the best choice of antibiotic for those allergic to penicillin.

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