Macrolide therapy for chronic rhinosinusitis: a meta-analysis
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CRD summary
This review found no evidence of clinically significant improvements associated with macrolide antibiotic therapy for adults with chronic rhinosinusitis. This conclusion reflected evidence presented. However, limitations of the review and evidence suggest that the conclusions should be regarded as provisional.

Authors' objectives
To systematically review patient-reported outcomes of long-term macrolide therapy in adults with chronic rhinosinusitis.

Searching
EMBASE and PubMed were searched to October 2011. Search terms were reported. Only studies published in English were eligible for the review. The authors referred to lack of resources to translate Japanese publications as a limitation of the review.

Study selection
Prospective studies that compared an oral macrolide antibiotic (with or without additional therapy) to any non-macrolide comparator in adults with chronic rhinosinusitis were eligible for inclusion. Participants had to meet specified diagnostic criteria (details in the review). Studies had to report disease-specific or symptom-based outcomes.

The included studies compared clarithromycin plus additional therapy with an active comparator; and azithromycin and roxithromycin with placebo. Treatment duration was three weeks for clarithromycin and 12 weeks for the other macrolides.

Final study selection was done by two reviewers. Disagreements were resolved by discussion to reach consensus.

Assessment of study quality
Risk of bias (residual confounding, lack of blinding, reporting bias, attrition bias and absence of a priori treatment and analysis protocols) was assessed as part of data extraction. Results were not reported in the paper.

Data extraction
For continuous outcome scales (Sinonasal Outcome Test and patient response scale), data were extracted to derive mean differences in change from baseline between groups at various time points. Data on changes in symptoms were also extracted.

It appeared that two reviewers extracted data and disagreements were resolved by consensus.

Methods of synthesis
Pooled mean differences and associated 95% confidence intervals were calculated using a fixed-effect inverse variance model. Statistical heterogeneity was assessed using Cochran's Q statistic and $I^2$.

Results of the review
Three randomised controlled trials with 183 participants were included. Two trials compared macrolides with placebo and one compared a macrolide with another antibiotic (both with additional therapy). In the placebo-controlled trials there was a statistically significant difference favouring macrolide for change in Sinonasal Outcome Test score at 24 weeks (mean difference -0.43, 95% CI -0.82 to -0.05), but was not considered clinically significant. Differences between groups were not significant at six or 12 weeks. Heterogeneity was moderate at 12 and 24 weeks ($I^2=45-50\%$).

One trial reported significant differences favouring macrolide in Sinonasal Outcome Test scores at all three time points for a subgroup of patients with low immunoglobulin E (IgE). There was a statistically significant difference favouring the macrolide group for change in patient response at 12 weeks (mean difference -0.95, 95% CI -1.41 to -0.49) but with high heterogeneity ($I^2=98\%$).
The trial that compared two antibiotic regimens found no statistically significant differences for any of seven symptoms assessed at the end of the study.

Authors' conclusions
Current evidence suggested no clinically significant improvement in patient-oriented quality of life measures with macrolide therapy.

CRD commentary
The review question was clear and supported by relevant inclusion criteria. Inclusion criteria for study design were broad, but all included studies were randomised trials. The search covered two databases and the review was limited to studies in English. The authors mentioned the existence of Japanese publications that were not translated, so language bias could not be ruled out. Study selection and data extraction were done in duplicate, which minimised the risk of errors or bias. Study quality was apparently assessed but was of little value because the results were not reported. The two placebo-controlled trials were pooled using standard methods of meta-analysis; statistical heterogeneity was assessed.

The authors’ conclusions reflect the evidence presented but the limitations of the review and of the evidence (few small trials of uncertain quality) suggest that the conclusions should be regarded as provisional.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.
Research: The authors stated that future studies should be designed and powered investigate the possibility of a subgroup effect based on levels of IgE and other inflammatory markers.

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