Topical antimicrobials in the management of chronic rhinosinusitis: a systematic review

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CRD summary
This review assessed the evidence for the use of topical antimicrobials for patients with chronic rhinosinusitis. The reviewers concluded that the treatment was effective in the management of chronic rhinosinusitis. Methodological weaknesses, limited reporting of the review process and the poor quality of the extracted data precluded a thorough evaluation of the reliability of the reviewer's conclusions.

Authors' objectives
To identify evidence for the use of topical antibiotics in the treatment of chronic rhinosinusitis (CRS) and exacerbations of CRS.

Searching
The databases MEDLINE, EMBASE, CINAHL, Cochrane Central Register of Controlled Trials and Cochrane Database of Systematic Reviews were searched for the period December 1949 to September 2007. There were no language restrictions. Search terms were reported.

Study selection
All articles published in peer-reviewed journals were eligible for inclusion. Exclusion criteria were: concomitant use by all subjects of nasal steroids; and/or the study compared the use of topical antimicrobial with a combination treatment of topical antimicrobials and nasal steroids.

Seven of the fourteen included studies were controlled trials. Five of the controlled trials were randomised controlled trials (RCTs) that used double-blinding. The topical antimicrobials in the included studies were doxycycline, aminoglycoside, neomycin, tramazoline, tobramycin, ceftazidime, amphotericin, N-chlorotaurine mupirocin, trimethoprim-sulfamethoxazole, and fosfomycin (given at a range of doses and regimens). The patient populations were heterogeneous and included patients with stable CRS and patients with exacerbations of CRS, patients who had previous surgery and (in one paper) patients who had cystic fibrosis. The outcome measures used in each of the studies varied and included patient symptom reports, clinical and/or endoscopic findings, necessity of repeat surgery and quality of life measurements. The authors stated neither how the papers were selected for the review nor how many reviewers performed the selection.

Assessment of study quality
Study validity was not formally assessed, although the reviewers classified each study according to the levels of evidence hierarchical grading system. The authors did not state how the validity assessment was performed.

Data extraction
Data were collected on the success rates of each intervention for the outcomes assessed in each study. In addition, data on side effects of the treatments under study were also extracted if they were presented in each study. No particular outcome of interest was pre-determined by the review authors before data extraction commenced. The authors stated neither how the data were extracted for the review nor how many reviewers performed the data extraction.

Methods of synthesis
The data from the trials was combined in tables grouped by treatment delivery type for CRS. A brief narrative summary was provided on the studies grouped by treatment delivery type and on post-functional endoscopic sinus surgery patients, empiric (nonculture-directed therapy) and patients with acute exacerbations of CRS. There was no attempt to combine the results statistically in any way.

Results of the review
Topical antimicrobials delivered by nasal spray. There was no evidence in two double blind RCTs (n=128) for the delivery of antimicrobials by nasal spray in patients with stable CRS.
Topical antimicrobials delivered by nasal irrigation: one small (n=30) RCT found statistically significant improvements in mucosal thickening and intranasal inflammatory markers in patients who received Amphotericin compared to those who received placebo. The patients in this trial had stable CRS with previous surgery. Another RCT found no differences in any outcome measure between the treatment and placebo groups. An additional five studies (four single-arm cohort studies and one clinical experience report) showed positive outcomes with treatment by nasal irrigation. Most of the patients had stable CRS, although some had previous surgery and some experienced acute exacerbations in their condition.

Nebulised antimicrobials: one small double-blind RCT (n=20) showed statistically significant improvements from baseline for both treatment (with Tobramycin) and control groups (saline only) in endoscopic findings, quality of life and symptom severity. There were no differences in outcomes at follow-up observed between the Tobramycin and saline groups. In the remaining cohort studies and one multiple-arm controlled study, benefits were observed from treatment with nasal microbials in endoscopy findings, symptoms and quality of life scores for the groups receiving antimicrobials.

Post-functional endoscopic sinus surgery patients: eight studies (n=330). Two RCTs (n=71) showed no benefit of treatment. In the smaller RCT (n=20) there was no significant difference between treatment and control groups, although both groups showed statistically significant improvements on all outcomes examined. The remaining six studies on this subset of patients were cohort studies. All of these studies showed a beneficial effect for both irrigated and nebulised antimicrobials.

Empiric therapy: 10 studies presented empiric (nonculture-directed) therapy. Of the six studies that showed efficacy with antimicrobial treatment, only one was a small RCT (n=30).

Acute exacerbations of CRS: one multiple-arm controlled study (n=42) showed some benefit in the outcome of longer infection-free periods. A small cohort study found some benefit of nasal irrigation with antimicrobials in symptomatic improvement clinical and endoscopic findings.

Authors’ conclusions
Topical antibiotics appeared to be effective in the management of CRS. Given the combination of low-level evidence and the level Iib evidence being limited to patients with cystic fibrosis, topical antibiotics should not be first-line management, but may be attempted in patients who do not respond to topical steroids and oral antibiotics.

CRD commentary
This review was broad in scope. Inclusion criteria relating to study designs, patients and outcomes were not clearly specified a priori, although studies in which antimicrobials were compared to steroids or where patients were using steroid concomitantly were excluded. The authors searched relevant databases for published articles and non-English language articles were eligible for inclusion. There was no apparent attempt to locate unpublished material and no evidence that the bibliographies of relevant articles were checked for further reports. This may mean that relevant studies were missed. Study validity was not formally assessed. There was potential for bias and error throughout the review process, particularly given that little detail was supplied on how each stage was conducted. Lack of reporting of some aspects of the review process made it difficult to judge if studies may have been missed or errors made in data extraction. Little data was reported in the review and there were no statistical test results included in the review. There was little evidence of benefit of antimicrobial treatment observed in the few small RCTs included in the review. The authors’ conclusions seemed reliable only on the basis of the beneficial effects of treatment observed in a number of cohort studies and non-randomised studies, which are vulnerable to bias and confounding. There was very limited evidence from the few small RCTs included from which to assess the accuracy and reliability of the authors’ conclusions. Limited evidence, together with potential methodological flaws in the review process, means that the reliability of the conclusions was unclear.

Implications of the review for practice and research
Implications for practice: given the combination of low-level evidence and the level Iib evidence being limited to patients with cystic fibrosis, topical antibiotics should not be first-line management, but may be attempted in patients who do not respond to topical steroids and oral antibiotics.
Implications for research: larger and well-designed RCTs were required to further evaluate the use of topical antimicrobials for patients with CRS. The control group treatment should be an equivalent sinonasal placebo rather than alternate methods of therapy. Additional useful comparisons could involve the use of different antimicrobial delivery methods, antibacterials compared to antifungal medication, surgical versus non-surgical patients and culture-directed compared to empiric treatment.

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