Impact of topical nasal steroid therapy on symptoms of nasal polyposis: a meta-analysis

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CRD summary
This review claimed there was improvement of patient symptoms using steroids compared to placebo in chronic rhinosinusitis with polyposis. Given the lack of detail on included studies, uncertain methodological quality and potential variations in results, the presented evidence seems to suggest a positive effect of steroid treatment but the results are only moderately reliable.

Authors' objectives
To determine the impact of topical steroid therapy on nasal symptoms in patients with nasal polyposis.

Searching
MEDLINE was searched from 1947 to March 2011. Search terms were reported. Seven additional databases, including DARE, the HTA database and NHS EED were also searched. Dates of these searches and search terms were not reported. Reference lists of identified studies were examined for eligible studies.

Study selection
Only randomised controlled trials (RCTs) that compared topical steroid medication applied to the nasal cavity with a placebo control group were eligible for inclusion. Participants had to have visible nasal polyps. Studies that did not report any symptom-based outcomes were excluded. Also excluded were studies that investigated concomitant oral steroid use.

Included studies were published between 1993 and 2010. Most studies were conducted in Europe. One study was conducted in Europe and North America, another worldwide. Budesonide, fluticasone, and mometasone were investigated. Most studies investigated nasal sprays; drops and Turbuhalers were also examined. Steroid dose ranged from 128μg to 800μg. All studies investigated twice daily or four times daily treatment schedules. The most commonly reported outcomes were nasal blockage and nasal congestion. Scoring systems, including visual analogue scales, symptom severity ranking scales and treatment efficacy scales, were most frequently used to assess outcomes. Participant details were not reported.

It was not reported how many reviewers were involved in study selection.

Assessment of study quality
Participant and assessor blinding as well as use of intention-to-treat analyses were evaluated. Two reviewers independently conducted the assessment.

Data extraction
Data were extracted on study and participant details, information on prior polypectomy, treatment formulation, dose and delivery method, study duration, outcome measures and criteria for treatment success. Data on treatment success or failure were extracted to calculate risk ratios. When studies reported several separate symptoms, outcomes related to nasal congestion/obstruction or total/composite symptoms were used for analyses.

Two independent reviewers extracted data.

Methods of synthesis
Studies were synthesised using a random-effects meta-analysis to calculate risk ratios with corresponding 95% confidence intervals. The I² statistic was used to assess heterogeneity between studies. Sensitivity analyses were performed by removing individual studies one at a time and repeating the analysis. Meta-regression was used to explore sources of heterogeneity. Subgroup analyses were conducted by type of steroid used. Begg and Egger tests as well as a funnel plot were used to explore possible publication bias.

Studies that reported continuous outcomes were included in the review but not in the meta-analysis. These studies were
Results of the review

Nineteen RCTs (number of participants not reported) met the inclusion criteria; 12 were included in the meta-analysis. Trial duration ranged from four weeks to approximately five years. Patients and assessors were judged to have been blinded in all trials.

Compared to placebo, participants in the steroids group had significant improvement in their symptoms (RR 1.72, 95% CI 1.41 to 2.09; 12 RCTs). Heterogeneity levels for this analysis were not reported.

Sensitivity analyses revealed that no study changed the direction of the effect.

Subgroup analyses by steroid type showed that all steroids included in this review significantly improved participants' symptoms: budesonide (RR 1.90, 95% CI 1.53 to 2.35; four RCTs), mometasone (RR 1.39, 95% CI 1.07 to 1.81; four RCTs) and fluticasone (RR 2.26, 95% CI 1.23 to 4.16; four RCTs). Heterogeneity was observed in the mometasone (I²=79.8%) and fluticasone (I²=82.5%) analyses.

Meta-regression investigated heterogeneity and suggested that none of the pre-specified factors (study duration, gender, age and prior polypectomy status) influenced steroid efficacy (p>0.05 for all). A cumulative meta-analysis showed that effects of steroids have been stable from 1995 to 2009.

Visual inspection of the funnel plot as well as results from Begg and Egger tests suggested potential publication bias. This was explored further using the trim-and-fill method which estimated five theoretically missing studies. Inclusion of these studies in the meta-analysis did not change the direction of the result.

Seven studies that reported continuous outcomes were summarised narratively. All studies showed a significant reduction in symptoms in the treatment groups compared to the control groups.

Authors' conclusions

Topical nasal steroids improve patient symptoms in chronic rhinosinusitis with polyposis.

CRD commentary

The review question and inclusion criteria were clear. Relevant sources were searched but due to the inconsistent reporting of search terms, the scope of searches could not be evaluated. The potential for language bias was unclear. The authors do not seem to have made any attempts to identify unpublished studies and the potential for publication bias was confirmed in analyses. This was judged to be unlikely to affect the results. The use of duplicate, independent processes for data extraction and quality assessment reduced the risk of reviewer error and bias in these domains. It was unclear if similar processes were in place for study selection.

As no patient details and sample sizes were reported, important information about included studies was missing, which made it difficult to assess the generalisability of the results. The methods of synthesis were appropriate and suitable measures were used to assess and explore heterogeneity between studies. However, heterogeneity was reported inconsistently, hindering an assessment of the true extent of variation between studies. A basic quality assessment was conducted, which focused exclusively on blinding without taking other important domains into account.

This review claimed to show an improvement of patient symptoms in chronic rhinosinusitis with polyposis when comparing steroids to placebo. However, there were high levels of variation between the trials in some analyses. The poor reporting of participant details and results made it difficult to assess the reasons for variation between included studies.

Given the lack of detail on the included studies, uncertain methodological quality, and potential variations in the results, the presented evidence seems to suggest a positive effect of steroid treatment but the results are only moderately reliable.

The authors have been consultants for and have received grants from several medical companies producing products used in this area.
Implications of the review for practice and research

**Practice:** The authors recommended that topical steroids should be considered strongly in the comprehensive management of chronic rhinosinusitis with polyposis patients.

**Research:** The authors recommend further studies be conducted to evaluate long-term outcomes, preferably using validated outcome measures.

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