Intranasal corticosteroids versus oral H1 receptor antagonists in allergic rhinitis: systematic review of randomised controlled trials

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Authors' objectives
To determine whether intranasal corticosteroids are superior to oral H1 receptor antagonists (antihistamines) in the treatment of allergic rhinitis.

Searching
MEDLINE and EMBASE were searched for randomised controlled trials published between 1966 and 1997. The search terms were not given. Review articles identified were surveyed for additional and earlier citations. HealthGate and Winspirs software were used to search MEDLINE for more recently published studies. Where relevant abstracts were identified in conference proceedings, MEDLINE searches were conducted and enquiries made of the authors or sponsoring companies to identify any subsequent full publications. Publications in languages other than English were considered.

Study selection

Study designs of evaluations included in the review
Only double-blinded randomised controlled trials (RCTs) were included.

The treatment duration of included studies was 6 to 8 weeks, although this was not a criteria for inclusion.

Specific interventions included in the review
Intranasal corticosteroids: beclomethasone dipropionate, budesonide, flunisolide, flucortin, fluticasone propionate, mometasone, and triamcinolone acetonide. Comparison groups were any form of oral antihistamine, but studies that used topical antihistamines or topical mast cell stabilisers were excluded. All types of delivery vehicle (aqueous and non-aqueous) were considered.

Corticosteroids actually used in studies included in the review were: budesonide (200ug, 400ug), beclomethasone (336ug, 400ug), fluticasone (200ug) and triacinolone (220 ug).

Anti-histamines actually used in studies included in the review were: dextrorphan (12mg), terfenadine (120mg), astemizole (10mg), loratadine (10mg) and cetirizine (10mg).

Participants included in the review
Participants had allergic rhinitis. Studies investigating the treatment of nasal polyps were excluded. The mean age of participants was 32 (range 12 to 75 years), and 55% of these were men.

Outcomes assessed in the review
Nasal blockage, nasal discharge, sneezing, nasal itch, postnasal drip, nasal discomfort, total nasal symptom score, nasal function (including nasal resistance), eye symptoms, global symptoms, and quality of life.

The mean daily cost of intranasal corticosteroids and of non-sedating oral antihistamines available in Australia was also calculated.

How were decisions on the relevance of primary studies made?
Inclusion of studies was decided by a majority decision of all three reviewers, who independently read the methods sections of papers identified by the search strategy, and applied the stated criteria.

Assessment of study quality
The concealment of allocation was assessed following the guidelines of the Cochrane Collaboration (see Other Publications of Related Interest). Independent assessment by two reviewers.

**Data extraction**
The authors do not state how the data were extracted for the review, or how many of the authors performed the data extraction.

Categorical outcomes were analysed as odds ratios and 95% confidence intervals calculated by Peto's method. Continuous outcomes were analysed as standardised mean differences, which allow the scores from different assessment scales to be combined.

**Methods of synthesis**
How were the studies combined?
Fixed-effect models were used to obtain statistics for the overall efficacy of intranasal corticosteroids on both categorical and continuous outcomes.

How were differences between studies investigated?
Chi-squared tests were used to assess heterogeneity between studies. Subgroup analyses were conducted to identify sources of heterogeneity.

**Results of the review**
Sixteen studies, comprising 2267 participants were included in the review.

None of the studies included in the review separately reported drug scores or quality of life.

The effects on sneezing, total nasal symptoms, and eye symptoms were significantly heterogeneous between studies. Other combined outcomes were homogeneous between studies.

Intranasal corticosteroids produced significantly greater relief than oral antihistamines of nasal blockage (14 studies; standard mean difference (SMD) = -0.63, 95% CI: -0.73, -0.53), nasal discharge (14 studies; SMD = -0.50, 95% CI: -0.60, -0.40), sneezing (14 studies; SMD = -0.49, 95% CI: -0.59, -0.39), nasal itch (11 studies; SMD = -0.38, 95% CI: -0.49, -0.27), postnasal drip (2 studies; SMD = -0.24, 95% CI: -0.42, -0.06), and total nasal symptoms (9 studies; SMD = -0.42, 95% CI: -0.53, -0.32). Global ratings gave an odds ratio for deterioration of symptoms (2 studies; OR = 0.26, 95% CI: 0.08, 0.8). There were no significant differences between treatments for nasal discomfort (1 study) or nasal resistance (1 study).

There was no significant difference between intranasal corticosteroids and oral antihistamines on eye symptoms (11 studies).

There was significant heterogeneity in studies reporting eye symptoms (chi-squared = 32.4, p<0.0005). Stratification by intranasal corticosteroids showed that most of the heterogeneity occurred in trials with beclomethasone. Trials that used intranasal fluticasone, triamcinolone, or budesonide all showed no difference from antihistamines. Stratification by antihistamine showed significant heterogeneity in trials that used terfenadine or astemizole. Stratification by the period of data extraction showed a small homogeneous benefit from intranasal corticosteroids (SMD = -0.17, 95% CI: -0.35, -0.05) in those trials reporting eye symptoms as a single end point. However, there was significant heterogeneity (chi-squared = 20.2, p<0.0005) when eye symptoms had been averaged over the duration of the trial.

**Cost information**
The cost-effectiveness of intranasal corticosteroids versus oral antihistamines was assessed in 3 RCTs on the treatment of allergic rhinitis. An American study showed that if a patient used terfenadine for more than 11 to 22 days, then fluticasone was a more cost effective choice. Two cost-effectiveness analyses performed in Canada produced cost-effectiveness ratios of 1: 2.5 and 1: 5.7 in favour of fluticasone versus terfenadine and loratadine respectively.
The review authors compared the mean daily cost of oral antihistamines in Australia with the mean daily cost of intranasal corticosteroids. The mean daily cost of oral antihistamines was 4.5 times that of intranasal corticosteroids.

**Authors' conclusions**
The results of this systematic review, together with data on safety and cost effectiveness, support the use of intranasal corticosteroids over oral antihistamines for allergic rhinitis.

**CRD commentary**
The review addresses a clear review question. Inclusion and exclusion criteria are appropriate. Sufficient details of the individual studies were presented.

Although the search is reasonably thorough, it could have been extended to include handsearching and an attempt to identify Grey literature and unpublished material. The authors restricted study inclusion to double-blind RCTs, and thus in terms of validity assessment, they only assessed concealment of allocation. In addition, they could have assessed whether the outcomes of people who withdrew from studies were described and included in the analysis, and whether the treatment groups being compared were comparable at entry.

The studies were combined according to outcome, and different drugs of a similar type were combined. This can create problems, for example, beclomethasone was clearly worse for eyes than other drugs that it was combined with. Instead of addressing this issue, the authors saw it as a source of heterogeneity to be removed.

This is a fairly thorough review, involving only high quality studies. Clear implications for practice are provided.

**Implications of the review for practice and research**
Practice: The authors recommend intranasal corticosteroids as first line treatment of allergic rhinitis. However, they suggest that there may be a role for oral antihistamines as ancillary treatment, particularly if eye symptoms or nasal itch are not controlled by intranasal corticosteroids.

Research: The authors did not make any suggestions for future research.

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