Evaluating approved medications to treat allergic rhinitis in the United States: an evidence-based review of efficacy for nasal symptoms by class


CRD summary
This review concluded that intranasal steroids produced the greatest improvements in nasal symptoms in patients with seasonal allergic rhinitis. They were also effective for perennial allergic rhinitis, but data quality was variable and oral antihistamines may be equally effective for some patients. Lack of quality assessment and direct treatment comparisons and possible bias suggest the conclusions should be interpreted cautiously.

Authors' objectives
To evaluate the effectiveness of medications currently approved for allergic rhinitis in USA to treat nasal symptoms when examined according to Food and Drugs Administration (FDA)-indicated uses and dosages.

Searching
MEDLINE (1966 to September 2008), EMBASE (from 1974) and The Cochrane Library (2007) were searched for English-language studies. Search terms were reported. Reference lists of published articles were searched.

Study selection
Randomised, placebo controlled trials (with at least 20 patients) of patients with physician-documented allergic rhinitis who took medication that targeted multiple nasal symptoms in FDA-approved dosages and approved for treating allergic rhinitis in USA (oral antihistamines, nasal antihistamines, intranasal steroids, leukotriene receptor antagonists (LTRAs) and cromolyn sodium) were eligible for inclusion. Included studies had to report: end-of-treatment data (two-week data for seasonal allergic rhinitis; four- to six-week data for perennial allergic rhinitis) or data to calculate percentage change from baseline; primary efficacy variable of total nasal symptom score (TNSS) (defined in report); secondary efficacy variables of individual nasal symptom scores; and data using three- and four-point scales.

Most studies were of oral antihistamines; others were of nasal antihistamines, LTRAs and cromolyn sodium. Mean age of participants ranged from 4.4 to 40 years. Most studies were of adults and children with seasonal allergic rhinitis, others were in adults and children with perennial allergic rhinitis and one study was of children with perennial allergic rhinitis and seasonal allergic rhinitis. In two seasonal allergic rhinitis studies and one perennial allergic rhinitis study physician-documented history of allergic rhinitis was less than two years. Where reported in seasonal allergic rhinitis studies, mean duration of allergic rhinitis was 17.1 years (range 7.5 to 20.5 years). In perennial allergic rhinitis studies, mean duration was 8.3 years (range 5.9 to 10.3 years). Various measurement tools were used. Placebos were unclear.

The number of reviewers who selected studies for inclusion was not reported.

Assessment of study quality
The authors did not state that they assessed study quality.

Data extraction
Percentage changes from baseline and inter-quartile ranges (IQRs) were extracted for outcomes (TNSS and individual nasal symptom scores) and reviewed twice by the full panel.

The authors did not state how many reviewers extracted data.

Methods of synthesis
Box plots were presented and median percentage changes in symptom scores and maximum and minimum values were presented. Statistical significance was calculated using Kruskal-Wallis tests. Results were presented by type of allergic rhinitis. Where possible, box plots were presented.
Results of the review
Fifty-four RCTs were included (n=at least 14,000 adults and 1,580 children).

Seasonal allergic rhinitis (25 RCTs): The greatest median change in TNSS was reported for intranasal steroids compared with all other treatment classes over two weeks at -43.7% (range -24.5% to -50.0%, p<0.001; seven RCTs). Median changes for other treatment classes were -22.2% for nasal antihistamines (eight RCTs), -23.5% for oral antihistamines (11 RCTs) and -15.0% for placebo (14 RCTs) and all had wide and overlapping ranges. Data for LTRAs were not included in the statistical analysis. Trend analysis for individual nasal symptom scores at two weeks indicated that intranasal steroids were superior for all symptoms, with reductions of at least 40%.

Perennial allergic rhinitis (eight RCTs): The median reduction in TNSS over four to six weeks for oral antihistamines was -51.5% (range -23.7% to 62.0%; p<0.05; five RCTs). For intranasal steroids, median reduction in TNSS was -37.3% (range -32.3% to -42.4%; four RCTs) and for placebo median reduction was -24.8% (range -14.4% to -37.2%; six RCTs). There was wide variability and overlap in the ranges.

Some figures and numbers of studies were inconsistent between box plots and tables/text (number of studies indicated in box plots presented here).

Trend analysis for individual symptom scores was not available for perennial allergic rhinitis data.

Authors' conclusions
Limited data confirmed that intranasal steroids produced the greatest improvements in nasal symptoms in patients with seasonal allergic rhinitis. Intranasal steroids were also effective for perennial allergic rhinitis, but data were of variable quality and oral antihistamines may be equally effective for some patients.

CRD commentary
The review question was supported by clear inclusion criteria. Only English-language studies were included, so language bias could not be ruled out. Some attempts to locate unpublished data were reported. The review process was not well reported and it was unclear whether steps were taken to reduce reviewer error and bias. Study quality was not formally assessed, so the reliability of the results of the primary studies was unknown. The appropriateness of pooling was unclear due the differences between studies and unknown study quality. There was some inconsistency in reporting of results between box plots and tables/text. The findings of the studies were short-term and the comparisons were not head-to-head. The authors acknowledged variability among studies. Financial disclosures were reported.

Due to the lack of quality assessment, the possibility of bias and unclear appropriateness of pooling, the authors' conclusions should be interpreted with caution.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that standards of reporting were needed for allergic rhinitis studies (further details in the report). More data were needed for perennial allergic rhinitis, especially for comparison of oral antihistamines and intranasal steroids. Differences between individual oral antihistamines should be investigated. The authors suggested head-to-head comparisons with the various classes of medications.

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