Efficacy of fluticasone furoate nasal spray vs. placebo for the treatment of ocular and nasal symptoms of allergic rhinitis: a systematic review

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CRD summary
The authors concluded that intranasal fluticasone furoate at a dose of 110mcg once daily was effective in improving ocular and nasal symptoms in adolescents and adults with allergic rhinitis. The authors' conclusions reflect the evidence presented, but it should be noted that not all outcomes appeared to demonstrate clinical significance.

Authors' objectives
To evaluate the effectiveness of fluticasone furoate nasal spray versus placebo for the treatment of ocular and nasal symptoms in patients with allergic rhinitis.

Searching
MEDLINE and EMBASE databases were searched to October 2010. The Cochrane Controlled Trials Register was searched to the third quarter 2010. Search terms were reported. The manufacturer's database was also searched. Only full publications were included. No language restrictions were applied.

Study selection
Randomised controlled trials that compared intranasal fluticasone furoate with placebo for the treatment of ocular and nasal symptoms in patients with clinically diagnosed seasonal or perennial allergic rhinitis were eligible for inclusion. Studies with co-interventions or that used a crossover design were excluded. Primary outcomes of interest were mean change in reflective total ocular symptom score (rTOSS), instantaneous total ocular symptom score (iTOSS), reflective total nasal symptom score (rTNSS) and instantaneous total nasal symptom score (iTNSS). Secondary outcomes included response to therapy, quality of life (assessed using the Rhino conjunctivitis Quality of Life Questionnaire) and adverse effects.

Over half the studies included patients with perennial allergic rhinitis and the remainder included patients with seasonal allergic rhinitis. Intranasal fluticasone furoate was administered to seasonal allergic rhinitis patients for two weeks and for perennial allergic rhinitis patients for between two and 54 weeks (median six weeks). The daily dosage of fluticasone furoate was 110mcg in all studies. Most studies included adolescents and adults (aged 12 years and over), while three studies included paediatric patients (under 12 years old).

Two reviewers independently selected studies for inclusion. Disagreements were resolved by consensus.

Assessment of study quality
Study quality was assessed using the Cochrane risk of bias tool covering adequacy of randomisation, concealment of allocation, blinding of patients, incomplete outcome data and selective outcome reporting.

Two reviewers independently assessed study quality. Disagreements were resolved by consensus.

Data extraction
Data were extracted to calculate mean change in rTOSS, iTOSS, rTNSS and iTNSS scores and 95% confidence intervals. Data for binary outcomes were used to calculate relative risks and corresponding 95% confidence intervals.

Data were extracted independently by two reviewers. Disagreements were resolved by consensus.

Methods of synthesis
Pooled weighted mean differences, relative risks and corresponding 95% confidence intervals were calculated using a random-effects model. The number-needed-to-treat for benefit or number-needed-to-harm were calculated where pooled estimates were significantly different between groups. Statistical heterogeneity was assessed using I² (high 60% to 100%; moderate 40% to 60%; low less than 40%). Publication bias was assessed by visual inspection of funnel plots.
and the Egger test. A sensitivity analysis was conducted using different statistical models. Planned subgroup analyses were conducted to explore the influence of age and seasonal versus perennial symptoms.

**Results of the review**

Sixteen trials (5,348 participants) were included. Only one trial met all five quality criteria, sequence generation and allocation concealment were unclear in the remaining studies. All studies were reported to be double blind.

**Ocular symptoms:** Compared to placebo, intranasal fluticasone furoate nasal spray significantly improved rTOSS for seasonal rhinitis patients (WMD -0.54, 95% CI -0.70 to -0.37; six trials) and for perennial rhinitis patients (WMD -0.33, 95% CI -0.61 to -0.05; three trials). Significant improvements were also found for iTTOSS for seasonal rhinitis patients (WMD -0.59, 95% CI -0.76 to -0.43; six trials) and for perennial rhinitis patients (WMD -0.38, 95% CI -0.69 to -0.07; two trials). There was no evidence of statistical heterogeneity ($I^2=0\%$ for all comparisons). Significant improvements were reported for eye itching, burning, tearing, watering and redness for both perennial and seasonal rhinitis groups compared to placebo.

**Nasal symptoms:** Compared to placebo, intranasal fluticasone furoate nasal spray also significantly improved rTNSS for seasonal rhinitis patients (WMD -1.14, 95% CI -1.57 to -0.72; six trials, ($I^2=80\%$) and for perennial rhinitis patients (WMD -0.83, 95% CI -1.08 to -0.59; seven trials, $I^2=32\%$). Significant improvements were also found for iTNSS for seasonal rhinitis patients (WMD -1.32, 95% CI -1.64 to -1.01; six trials; $I^2=62\%$) and for perennial rhinitis patients (WMD -0.90, 95% CI -1.33 to -0.48; four trials; $I^2=52\%$). There were also significant improvements reported for rhinorrhoea, nasal congestion, nasal itching and sneezing for both seasonal and perennial rhinitis patients compared to placebo.

There were no significant differences between intranasal fluticasone furoate and placebo for early withdrawals, adverse effects and serious adverse effects except for incidence of epistaxis for perennial allergic rhinitis patients (number-needed-to-harm was 15, 95% CI 11 to 21). Other results of secondary outcomes were also reported.

There was no evidence of significant publication bias. Results were similar regardless of statistical model, or type of rhinitis.

**Authors' conclusions**

Intranasal fluticasone furoate at a dose of 110mcg once daily was effective in improving ocular and nasal symptoms in adolescents and adults with allergic rhinitis. Significant benefits in quality of life and patient-perceived benefit were also demonstrated. These improvements were clinically significant and associated with a safe therapeutic profile.

**CRD commentary**

The review question was clear with defined inclusion criteria. Several relevant sources were searched and efforts were made to reduce publication and language bias. Appropriate methods were used to reduce reviewer error and bias in the review process. Study quality was assessed and the results reported. The method of synthesis appears appropriate and subgroup analyses were conducted. In their conclusion the authors report that improvements were clinically significant, but this was not demonstrated for all outcomes.

The authors’ conclusions reflect the evidence presented, but it should be noted that not all outcomes appeared to demonstrate clinical significance.

**Implications of the review for practice and research**

**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated that further studies were needed to assess the efficacy and safety of intranasal fluticasone furoate in children.

**Funding**

Funding was provided by the salary of one of the authors.

**Bibliographic details**

Rodrigo GJ, Neffen H. Efficacy of fluticasone furoate nasal spray vs. placebo for the treatment of ocular and nasal
symptoms of allergic rhinitis: a systematic review. Clinical and Experimental Allergy 2011; 41(2): 160-170

PubMedID
21121980

DOI
10.1111/j.1365-2222.2010.03654.x

Original Paper URL

Indexing Status
Subject indexing assigned by NLM

MeSH
Administration, Intranasal; Androstadienes /administration & dosage /therapeutic use; Anti-Allergic Agents /administration & dosage /therapeutic use; Humans; Nasal Sprays; Placebos; Rhinitis, Allergic, Seasonal /drug therapy

AccessionNumber
12011006913

Date bibliographic record published
14/07/2012

Date abstract record published
27/03/2013

Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.