



Canadian Agency for
Drugs and Technologies
in Health

RAPID RESPONSE REPORT: SUMMARY WITH CRITICAL APPRAISAL



TITLE: Intranasal Triamcinolone versus Intranasal Beclomethasone for Acute and Chronic Sinus Inflammation: A Review of Comparative Clinical Effectiveness and Safety

DATE: 29 January 2013

CONTEXT AND POLICY ISSUES

Acute and chronic sinusitis, rhinitis or rhinosinusitis are symptomatic inflammations of the nasal cavity and paranasal sinuses that happen frequently, even though the prevalence of the condition is not easily determined because many patients do not report to a doctor's office and elect to treat the symptoms themselves.^{1,2} Management of these conditions varies depending on whether the source is allergic, bacterial or viral infection, but usually includes intranasal glucocorticoids for symptomatic treatment of sneezing, nasal congestion and rhinorrhea.^{1,3} Currently, seven types of intranasal corticosteroids are being used in Canada, namely beclomethasone, budesonide, ciclesonide, flunisolide, fluticasone, mometasone and triamcinolone.⁴ Despite the proven effectiveness of intranasal corticosteroids, the systemic absorption rates (and therefore the bioavailability) are different among different types of corticosteroids,^{5,6} leading to concerns about their effects on the hypothalamic-pituitary-adrenal (HPA) axis and impact on children growth retardation. Epistaxis and ocular effects such as glaucoma are also potential side effects of intranasal corticosteroids.^{3,7,8}

This report will provide a review on the comparative clinical effectiveness and safety between intranasal triamcinolone and beclomethasone.

RESEARCH QUESTIONS

1. What is the comparative clinical effectiveness of using intranasal triamcinolone versus intranasal beclomethasone in adult patients with acute or chronic sinus inflammation?
2. What is the comparative safety of using intranasal triamcinolone versus intranasal beclomethasone in adult patients with acute or chronic sinus inflammation?

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KEY FINDINGS

Findings from the included meta-analysis on the comparative clinical efficacy and safety of intranasal triamcinolone and beclomethasone dipropionate in the treatment of allergic rhinitis showed that both drugs had similar efficacy in reducing nasal and ocular symptoms, but intranasal triamcinolone is safer than beclomethasone in terms of risk of epistaxis, long-term effects on growth, and systemic ocular effects.

METHODS

Literature Search Strategy

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2012, Issue 12), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2007 and December 19, 2012.

Selection Criteria and Methods

One reviewer screened the titles and abstracts of the retrieved publications and examined the full-text publications for the final article selection. Selection criteria are outlined in Table 1.

Table 1: Selection Criteria	
Population	Adult patients with acute or chronic nasal or sinus inflammation
Intervention	Intranasal triamcinolone
Comparator	Intranasal beclomethasone
Outcomes	Benefit: decreased inflammation Harm: interested in any adverse events, with particular emphasis on those due to HPA axis suppression (i.e., Addison's disease; adrenal insufficiency and adrenal crisis)
Study design	Health technology assessments, systematic reviews, and meta-analyses. If no systematic reviews were identified, randomized controlled trials (RCTs), and non-RCTs were selected for inclusion.

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria in Table 1, if they were published prior to January 2007, if they were duplicate publications of the same study, or if they were referenced in a selected systematic review.

Critical Appraisal of Individual Studies

The quality of the included systematic review was assessed using the AMSTAR checklist.⁹ Numerical scores were not calculated. Instead, the strengths and limitations of the systematic review are summarized and presented.

SUMMARY OF EVIDENCE

Quantity of Available Evidence

The literature search yielded 53 citations. Three additional studies were identified by searching the grey literature. After screening of abstracts, 12 potentially relevant studies were selected for full-text review. One study was included in the review.

The PRISMA flowchart in Appendix 1 details the process of the study selection.

Summary of Study Characteristics

A detailed summary of the included study is provided in Appendix 2.

Study design

One systematic review with meta-analysis,¹⁰ published in 2011, was identified for inclusion. A Medline search was carried out from 1966 to 2009. The review included placebo-controlled randomized trials, and observational reports for safety outcomes.

Population

Studies on patients with allergic rhinitis were included in the systematic review. Patient characteristics in the included studies were not reported.¹⁰

Interventions and comparators

The systematic review¹⁰ included studies examining dexamethasone, budesonide, fluticasone (propionate and furate), flunisolide, mometasone, triamcinolone, and beclomethasone. Ten included studies focused on beclomethasone, and eight included studies used triamcinolone as the intervention.

Outcomes

Efficacy outcomes (nasal symptoms, ocular symptoms, global assessment), safety outcomes (epistaxis, growth, systemic ocular effects), and therapeutic index (summation scores for efficacy and safety outcomes) were the main clinical outcomes reported in the systematic review.¹⁰

Summary of Critical Appraisal

The included systematic review performed meta-analysis based on a comprehensive literature search and a priori design but did not have reporting rigour; it did not provide a list of excluded studies, did not document the characteristics and quality of the included studies and did not assess the likelihood of publication bias.

Details of the strengths and limitations of the included systematic review are summarized in Appendix 3.

Summary of Findings

Main findings of included studies are summarized in detail in Appendix 4.

A systematic review performed meta-analysis on the comparative clinical efficacy and safety of six intranasal corticosteroids, including triamcinolone and beclomethasone dipropionate, in the treatment of allergic rhinitis.¹⁰ The systematic review included 10 placebo-controlled randomized trials for beclomethasone and eight placebo-controlled randomized trials for triamcinolone. Studied outcomes were efficacy (nasal symptoms, ocular symptoms and global assessment) and safety (epistaxis, long-term effect on growth) and systemic ocular effects (glaucoma, increased ocular pressure). The authors created a therapeutic index score (TI) for each outcome, with a high score in efficacy indicating a high efficacy, and a high score in adverse event indicating a high risk in safety. A final TI was also calculated as the ratio between the efficacy score and the safety (adverse events) score (the higher the final TI, the better the drug).

In terms of efficacy outcomes, triamcinolone and beclomethasone had similar nasal and ocular symptom scores, and similar patients' global assessment scores. On the other hand, triamcinolone scored much better than beclomethasone in terms of safety outcomes (risk of epistaxis, long-term effects on growth and systemic ocular effects). According to the meta-analysis calculations, beclomethasone had an overall efficacy score of 4 and an overall safety score of 7, resulting in a final TI of 0.57. Triamcinolone had an overall efficacy score of 5 and an overall safety score of 1, resulting in a final TI of 5. This finding showed that the two drugs are similar in terms of efficacy (score 5 vs 4), but triamcinolone is much safer than beclomethasone (score 1 vs 7), resulting in a final TI more than 8 times better (5/0.57) favoring triamcinolone.

Limitations

The literature search found evidence on allergic rhinitis alone. As such, the findings cannot be generalizable to other forms of nasal and sinus inflammations. The outcomes in the included systematic review can be subjective; more objective outcomes such as measurements of nasal inspiratory airflow could be meaningful in determining the efficacy of the drugs. More head-to-head comparisons between different intranasal corticosteroids are needed to maintain homogeneity of population characteristics and corticosteroids dosage, and render comparisons more precise.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING

Intranasal triamcinolone has a similar efficacy profile compared with intranasal beclomethasone in the treatment of allergic rhinitis, but triamcinolone has a better safety profile than the latter. According to the findings from the included systematic review, the therapeutic index of the six types of intranasal spray showed fluticasone furoate spray has the worst balance between efficacy and adverse events (TI = 0.33), followed by beclomethasone propionate (TI = 0.57), fluticasone propionate and budesonide (both have TI = 2), with triamcinole being the second best (TI = 5), then momethasone furoate being the best (TI = 7).

Considering the fact that a TI < 1 indicates that potential side effects outweigh efficacy, evidence from this review reminds caution in the use of beclomethasone spray in the treatment of allergic rhinitis.

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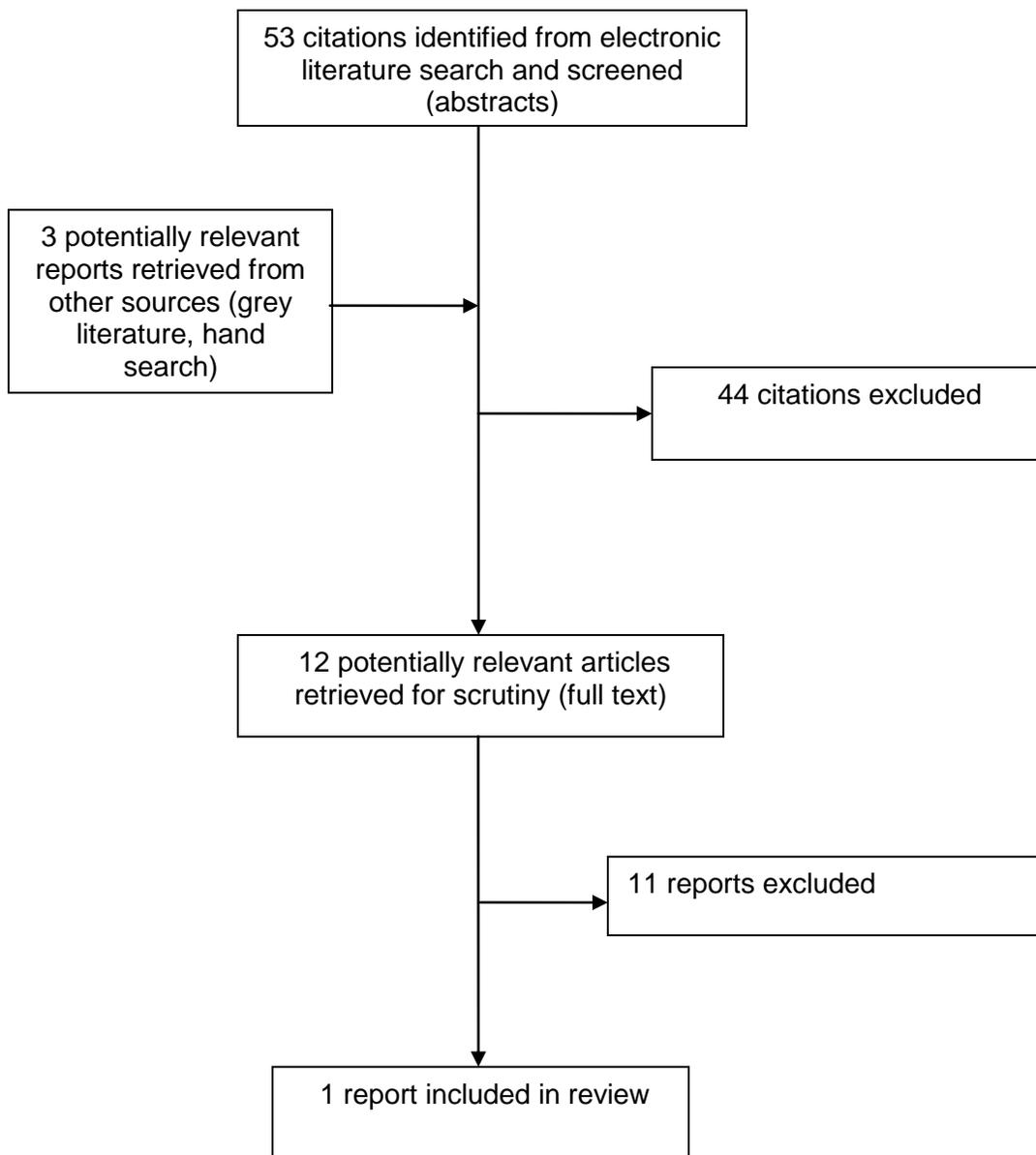
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Appendix 1: Selection of Publications



Appendix 2: Characteristics of Included Studies

Table A1: Characteristics of Included systematic review				
First Author, Year, Country,	Study objectives	Intervention Comparator(s)	Included patients and study types	Main comparative clinical outcomes reported
Schafer, ¹⁰ 2011 Germany, Belgium	<i>“For clinical decision-making, it would be helpful to have a systematic and summarizing overview on the efficacy and safety of these substances in a combined assessment. We therefore aimed to develop a therapeutic index (TIX) reflecting both efficacy and safety”</i> (p 273)	Dexamethasone, budesonide, fluticasone (propionate and furoate), flunisolide, mometasone, triamcinolone, beclomethasone	Patients with allergic rhinitis Placebo-controlled randomized trials and observational reports for safety outcomes (including 10 studies on beclomethasone and eight studies on triamcinolone).	Efficacy outcomes (nasal symptoms, ocular symptoms, global assessment) Safety outcomes (epistaxis, growth, systemic ocular effects) Therapeutic index (summation scores for efficacy and safety outcomes)

Appendix 3: Summary of Critical Appraisal of Included Studies

Table A2: Summary of Critical Appraisal of Included Studies		
First Author, Publication Year	Strengths	Limitations
Schafer, ¹⁰ 2011	<ul style="list-style-type: none"> • a meta-analysis was done • a priori design was provided • comprehensive literature search • status of publication was used as an inclusion criterion • methods to combine findings were appropriate • conflict of interest was stated 	<ul style="list-style-type: none"> • characteristics of included studies not provided • unsure if there were independent data extractors • quality of the included studies not documented • list of excluded studies not provided • likelihood of publication bias was not assessed

Appendix 4: Main Study Findings and Authors' Conclusions

Table A3: Main Study Findings and Authors' Conclusions		
First Author, Publication Year	Main Study Findings	Authors' Conclusions
Research question 1 (clinical efficacy of intranasal triamcinolone vs intranasal beclomethasone)		
Schafer, ¹⁰ 2011	<p>Total nasal symptom scores (SMD) Beclomethasone dipropionate: -0.68, 95% CI -0.90 to -0.46 Triamcinilone: -0.59, 95% CI -0.83 to -0.36 TI score Beclomethasone dipropionate: 2 Triamcinolone: 1</p> <p>Total ocular symptom scores (SMD) Beclomethasone dipropionate: -0.29, 95% CI -0.57 to -0.01 Triamcinilone: -0.39, 95% CI -0.76 to -0.02 TI score Beclomethasone dipropionate: 1 Triamcinolone: 2</p> <p>Patients' global assessment (OR) Beclomethasone dipropionate: 2.35, 95% CI 1.41 to 3.90 Triamcinilone: 3.02, 95% CI 2.06 to 4.43 TI score Beclomethasone dipropionate: 1 Triamcinolone: 2</p> <p>Sum efficacy (ES) score Beclomethasone dipropionate: 4 Triamcinolone: 5</p>	<p><i>"These findings resulted in TIX scores of 7 and 5 for MF and TRIAM, respectively, indicating a high efficacy and low potential of adverse events. Medium scores were reached by BUD and FP and lower scores by BDP and FF" (p. 276)</i></p>
Research question 2 (safety of intranasal triamcinolone vs intranasal beclomethasone)		
Schafer, ¹⁰ 2011	<p>Epistaxis (OR) Beclomethasone dipropionate: 1.51, 95% CI 0.98 to 2.32 Triamcinilone: 0.64, 95% CI 0.15 to 2.64</p> <p>TI score Beclomethasone dipropionate: 2 Triamcinolone: 0</p> <p>Long term side effects on growth TI score Beclomethasone dipropionate: 3 Triamcinolone: 0</p> <p>Systemic ocular side effects (glaucoma or increased ocular pressure) TI score Beclomethasone dipropionate: 2 Triamcinolone: 1</p> <p>Sum side effects (AES) score Beclomethasone dipropionate: 7 Triamcinolone: 1</p> <p>TI (ES/AES) Beclomethasone dipropionate: 0.57 Triamcinolone: 5</p>	

AES: sum of adverse events score; BDP: beclomethasone dipropionate; BUD: budesonide; ES: sum of efficacy score; FF: fluticasone fuorate; FP: fluticasone propionate; OR: odds ratio; STD: standardized mean difference; TI (or TIX): therapeutic index; TRIAM: triamcinilone