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Intranasal corticosteroids for nasal airway obstruction in children with moderate to severe adenoidal hypertrophy (Review)

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[Intervention Review]

Intranasal corticosteroids for nasal airway obstruction in children with moderate to severe adenoidal hypertrophy

Linjie Zhang[1], Raúl A Mendoza-Sassi[2], Juraci A César[3], Neil K Chadha[4]

[1]Faculty of Medicine, Federal University of Rio Grande, Rio Grande, RS, Brazil. [2]Department of Internal Medicine, Federal University of Rio Grande, Rio Grande, RS, Brazil. [3]Department of Maternal and Child Health, Federal University of Rio Grande, Rio Grande, RS, Brazil. [4]Division of Pediatric Otolaryngology, BC Children's Hospital, Vancouver, Canada

Contact: Linjie Zhang, Faculty of Medicine, Federal University of Rio Grande, Rua Visconde Paranaguá 102, Centro, Rio Grande, RS, 96201-900, Brazil. zhanglinjie63@yahoo.com.br.

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ABSTRACT

Background

This is an update of a Cochrane Review first published in *The Cochrane Library* in Issue 3, 2008.

Adenoidal hypertrophy is generally considered a common condition of childhood. When obstructive sleep apnoea or cardio-respiratory syndrome occurs, adenoidectomy is generally indicated. In less severe cases, non-surgical interventions may be considered, however few medical alternatives are currently available. Intranasal steroids may be used to reduce nasal airway obstruction.

Objectives

To assess the efficacy of intranasal corticosteroids for improving nasal airway obstruction in children with moderate to severe adenoidal hypertrophy.

Search methods

We searched the Cochrane Ear, Nose and Throat Disorders Group Trials Register; the Cochrane Central Register of Controlled Trials (CENTRAL); MEDLINE; EMBASE; ISI Web of Science; Cambridge Scientific Abstracts; ISRCTN and additional sources for published and unpublished trials. The date of the most recent search was 4 May 2010.

Selection criteria

Randomised controlled trials comparing intranasal corticosteroids with placebo, no intervention or other treatment in children aged 0 to 12 years with moderate to severe adenoidal hypertrophy.

Data collection and analysis

Two authors independently extracted data from the included trials and assessed trial quality. Meta-analysis was not applicable and we summarised data in a narrative format.

Main results

Six randomised trials involving a total of 394 patients were included. Five of the six trials demonstrated a significant efficacy of intranasal corticosteroids in improving nasal obstruction symptoms and in reducing adenoid size.

The first eight-week cross-over study showed that treatment with beclomethasone (336 mcg/day) yielded a greater improvement in mean symptom scores than placebo (-18.5 versus -8.5, P < 0.05) and a larger reduction in mean adenoid/choana ratio than placebo (right, -14% versus +0.4%, P = 0.002; left, -15% versus -2.0%, P = 0.0006) between week 0 and week 4. The second four-week cross-over study showed that the Nasal Obstruction Index decreased by at least 50% from baseline in 38% of patients treated with beclomethasone (400 mcg/day) between week 0 and week 2, whereas none of the patients treated with placebo had such improvement (P < 0.01). The third parallel-group trial showed that 77.7% of patients treated with mometasone (100 mcg/day) for 40 days demonstrated an improvement in nasal obstruction symptoms and a decrease in adenoid size, such that adenoidectomy could be avoided, whereas no significant improvement was observed in the placebo group. The fourth parallel-group trial showed that eight weeks of treatment with flunisolide (500 mcg/day) was associated with a larger reduction in adenoid size than isotonic saline solution (P < 0.05). The fifth parallel-group trial demonstrated that eight weeks of treatment with fluticasone (400 mcg/day) significantly reduced nasal obstruction symptoms and adenoid size, and adenoidectomy was avoided in 76% of these patients compared with 20% of the patients treated with normal saline (P < 0.05).

In contrast, one parallel-group trial did not find a significant improvement in nasal obstruction symptoms nor adenoid size after eight weeks of treatment with beclomethasone (200 mcg/day).

Authors' conclusions

Current evidence suggests that intranasal corticosteroids may significantly improve nasal obstruction symptoms in children with moderate to severe adenoidal hypertrophy, and this improvement may be associated with a reduction in adenoid size. The long-term efficacy of intranasal corticosteroids in these patients remains to be defined.

PLAIN LANGUAGE SUMMARY

Topical steroids for nasal airway obstruction in children with moderately to severely enlarged adenoids

Adenoidal hypertrophy is generally considered a common condition of childhood and represents one of the most frequent indications for surgery in children. In less severe cases, non-surgical interventions may be considered, however few medical alternatives are currently available. This review was conducted to assess the effectiveness of intranasal corticosteroids for improving nasal airway obstruction in children aged 0 to 12 years with moderate to severe adenoidal hypertrophy. Evidence derived from five of the six randomised controlled trials included in this review suggests that intranasal steroids may significantly improve symptoms of nasal obstruction in children with adenoidal hypertrophy and that this improvement may be associated with the reduction of adenoid size. One study did not find a significant improvement in nasal obstruction symptoms. Further large and high-quality randomised controlled trials are warranted.

BACKGROUND

This is an update of a Cochrane Review first published in *The Cochrane Library* in Issue 3, 2008.

Description of the condition

The pharyngeal tonsils (adenoids) are a lobulated mass of lymphoid tissue located on the upper and posterior walls of the nasopharynx. This lymphoid structure is capable of considerable hypertrophy (enlargement) under adverse conditions such as chronic and recurrent infection of the upper respiratory tract or allergies (or both) (Brodsky 1993; Javadyan 2003; Raphael 1987). There are few prevalence or incidence data available, but adenoidal hypertrophy is generally considered a common condition of childhood and represents one of the most frequent indications for surgery in children (Rutkow 1986).

Enlarged adenoids can obstruct the nasopharyngeal airway, particularly at night when the patient is supine. Classically, the symptoms and physical signs considered indicative of adenoidal nasal airway obstruction in children are mouth breathing, hyponasal voice and nocturnal snoring (Kenna 2000; Paradise 1998). In more severe cases obstructive sleep apnoea may occur, potentially causing neurocognitive disturbance, growth failure and cor pulmonale (Brouillette 1982; Gozal 1998; Guilleminault 1981; Menashe 1965). Enlarged adenoids may also obstruct the Eustachian tube orifice resulting in a conductive hearing loss. The presence of fluid in the middle ear (otitis media with effusion) is frequently associated with adenoidal hypertrophy and suggests Eustachian tube dysfunction or chronic adenoidal infection (Grimmer 2005; Kenna 2000).

A diagnosis of adenoidal hypertrophy should be considered when a child presents with signs or symptoms of nasal airway obstruction. The validity of standardised clinical assessment of adenoidal obstruction of the nasopharynx has been confirmed by a well-designed prospective study (Paradise 1998). The degree of a patient's mouth breathing and speech hyponasality were rated by one of eight study-team nurse practitioners on a four-point scale (none = 1; mild = 2; moderate = 3; marked = 4). The two ratings were averaged to obtain a Nasal Obstruction Index (NOI) from 1 to 4. This study demonstrated a high inter-observer agreement for mouth breathing and speech hyponasality (weighted k = 0.84 to 0.91). The overall correlation between NOI and radiological assessment ratings was moderate, however a high correlation was found in children with NOI values at the lower and upper extremes (i.e. 1.0 and 3.5 respectively). Another instrument for the clinical measurement of nasal obstruction symptoms associated with adenoidal hypertrophy is a parent-administered symptom questionnaire (Demain 1995). This encompasses assessment of a child's nasal congestion, nasal voice, snoring, daytime drowsiness, sleep quality, nasal discharge, ear popping or pain, and bad breath. The degree of each symptom was scored from 0 (never) to 10 (constant) using a visual analogue scale.

As nasal obstruction may be caused by other conditions, such as rhinitis, nasal polyps or septal deviation, complementary examinations are needed for a definitive diagnosis of adenoidal hypertrophy. The lateral neck radiograph remains a widely employed investigation in some countries for children with suspected adenoidal hypertrophy. The low cost, widespread availability, non-invasive nature and good correlation with symptoms and fibreoptic nasopharyngeal endoscopic findings are the main advantages of this diagnostic test (Mary 2005; Modrzynski 2005). The following radiological assessment methods have been reported to measure the adenoidal size in children:

1. Cohen and Konak's method (Cohen 1985): the ratio between the soft plate thickness (1 cm below the hard palate or 1/2 cm in children under three years old) and the air column width between the palate and the highest point of convexity of the adenoidal shadow;
2. Fujioka's method (Fujioka 1979): the ratio between the maximal thickness of the adenoidal shadow and the distance measured along a line from the superior/posterior edge of the hard palate to spheno-occipital synchondrosis on the skull base;
3. Johanneson's method (Johanneson 1968): the distance between the perpendicular line from the pharyngeal tubercle on the skull base and the adenoidal shadow convexity.

Of these methods, Cohen and Konak's shows the best correlation with endoscopic findings and clinical symptoms (Modrzynski 2005; Wormald 1992). This method accounts for the relationship between nasopharyngeal and adenoidal size and it is known that it is not the absolute adenoidal size but its ratio to the dimensions of the whole nasopharyngeal cavity which seems crucial in the clinical manifestation of adenoidal hypertrophy (Wang 1994).

Another method for the assessment of adenoidal size is trans-oral mirror visualisation. A high correlation between mirror examination and fibreoptic nasopharyngeal endoscopy has been demonstrated by a recent prospective and blinded study, however the degree of choanal obstruction may be underestimated by this diagnostic test (Chisholm 2005). Fibreoptic nasopharyngeal endoscopy is considered the gold standard for the diagnosis and evaluation of adenoidal hypertrophy. This diagnostic method allows direct visualisation of the nasal cavity and the nasopharynx providing a dynamic evaluation of the magnitude of nasal airway obstruction (Wang 1992). The diagnostic accuracy of fibreoptic nasopharyngeal endoscopy may be of fundamental importance in establishing suitable indications for adenoidectomy (Neri 2004; Wang 1992), however the requirement of costly equipment and the need for child co-operation limit this diagnostic approach.

Description of the intervention

The management of adenoidal hypertrophy in children is dependent on the degree of nasal airway obstruction and any associated morbidity. When obstructive sleep apnoea (OSA) or cardio-respiratory syndrome occurs, adenoidal and tonsillar hypertrophy are usually implicated and adenoidectomy is generally indicated. However, the effects of surgical intervention in children with OSA attributable to adenoidal hypertrophy have not yet been sufficiently investigated by randomised controlled trials (Lim 2009). Other potential indications for adenoidectomy include chronic sinusitis and otitis media with effusion (Gates 1992; Paradise 1995). The risk-benefit ratio of surgical intervention for the individual child needs to be carefully assessed in the light of potential anaesthetic complications (cardiac arrhythmia, malignant hyperthermia, vocal cord trauma and aspiration) and postoperative complications (haemorrhage, airway obstruction secondary to oedema, prolonged muscular paralysis and palato-pharyngeal insufficiency). In less severe cases, non-surgical interventions may be considered, however few medical alternatives are currently available. Commonly medical

management is limited to the treatment of concurrent infections and the complications of adenoidal enlargement (Sclafani 1998). The effects of intranasal corticosteroids in children with adenoidal hypertrophy have been assessed by randomised trials (Criscuoli 2003; Demain 1995).

How the intervention might work

The mechanism by which intranasal corticosteroids reduce nasal airway obstructive symptoms is unclear, however the following mechanisms have been suggested (Demain 1995):

1. direct reduction of adenoidal size by lympholytic action of steroids on adenoidal tissues;
2. reduction in adenoidal and nasopharyngeal inflammation by anti-inflammatory effects of steroids; and
3. reduction in the significance of the adenoids as a reservoir for infection.

Why it is important to do this review

Despite the uncertainty of the precise mechanism, establishing a therapeutic role for intranasal corticosteroids in children with adenoidal hypertrophy may have significant clinical implications. This modality may provide an effective non-surgical alternative treatment for children with adenoidal hypertrophy. The use of intranasal corticosteroids has been generally considered safe in the paediatric population, despite uncommon reports of some local and systemic adverse events, including epistaxis, nasal mucosal irritation, septal perforation, moderate adrenal suppression and growth retardation (Adamopoulos 1995; Gazis 1999; LaForce 1985; Skoner 2000). There is a need for a comprehensive systematic review and meta-analysis of the evidence for the effects of intranasal corticosteroids on reducing nasal airway obstruction associated with adenoidal hypertrophy in children.

OBJECTIVES

To assess the effectiveness of intranasal corticosteroids for improving nasal airway obstruction in children with moderate to severe adenoidal hypertrophy.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials (RCTs).

Types of participants

Children aged 0 to 12 years with symptoms of nasal obstruction and moderate to severe adenoidal hypertrophy, as demonstrated by fibreoptic nasopharyngeal endoscopy and/or indirect examination (lateral neck X-ray or intra-oral mirror visualisation).

Types of interventions

Intranasal corticosteroids versus placebo, no intervention or other treatment.

Types of outcome measures

Primary outcomes

- Improvement in nasal obstruction assessed by the Nasal Obstruction Index or any other symptom score.

Secondary outcomes

- Reduction in adenoid size assessed by fibreoptic nasopharyngeal endoscopy and/or indirect examination (lateral neck X-ray or intra-oral mirror visualisation).
- Improvement in quality of life assessed by validated quality of life questionnaire.
- Adverse events.

Search methods for identification of studies

We conducted systematic searches for randomised controlled trials. There were no language, publication year or publication status restrictions. The date of the last search was 4 May 2010, following a previous search update in April 2008, and original searches in May 2007.

Electronic searches

We searched the following databases from their inception for published, unpublished and ongoing trials: the Cochrane Ear, Nose and Throat Disorders Group Trials Register; the Cochrane Central Register of Controlled Trials (CENTRAL Issue 2, *The Cochrane Library* 2010); MEDLINE; EMBASE; CINAHL; AMED; LILACS; KoreaMed; IndMED; SIGLE; Cambridge Scientific Abstracts; ISRCTN; the National Research Register; and ISI Web of Science.

We modelled subject strategies for databases on the search strategy designed for CENTRAL. Where appropriate, we combined subject strategies with adaptations of the highly sensitive search strategy designed by the Cochrane Collaboration for identifying randomised controlled trials and controlled clinical trials (as described in *The Cochrane Handbook for Systematic Reviews of Interventions* Version 5.0.2, Box 6.4.b. (Handbook 2009)). Search strategies for major databases including CENTRAL are provided in Appendix 1.

Searching other resources

We searched the reference lists of the retrieved articles from electronic searches. We contacted trial authors (Ciprandi 2007; Berlucchi 2007; Ciprandi 2007; Criscuoli 2003; Demain 1995; Lepcha 2002) by e-mail for information about possible unpublished or ongoing studies. Four authors (Ciprandi 2007; Ciprandi 2007; Criscuoli 2003; Demain 1995) responded, but no additional trials were identified. We also searched PubMed, TRIPdatabase, NHS Evidence - ENT & Audiology and Google to retrieve existing systematic reviews relevant to this systematic review, so that we could scan their reference lists for additional trials.

Data collection and analysis

Selection of studies

Two authors (ZL, MRA) independently assessed the titles and abstracts of all studies identified by the searches. The full articles were obtained when they appeared to meet the inclusion criteria or there were insufficient data in the title and abstract to make a clear decision about their inclusion. We excluded articles that did not meet the inclusion criteria. We noted the reasons for

their exclusion (see 'Characteristics of excluded studies' table). Any disagreement between the authors about study inclusion was resolved by discussion.

Data extraction and management

Two authors (ZL, MRA) independently extracted data from the included randomised controlled trials using a standardised data extraction form. Data extraction was checked by a third author (CJA). Any disagreement was resolved by discussion. The extracted data were entered into RevMan 5.0. We extracted the following data:

- study characteristics: publication status, year, country of study and setting;
- methods: method of allocation, masking of participants and assessment of outcome, exclusion of participants after randomisation, proportion of losses to follow up and intention-to-treat analysis;
- participants: sample size, age, gender, inclusion and exclusion criteria;
- intervention: type of intranasal steroids, dosage and treatment duration;
- control: placebo, nil, oral corticosteroids, or other treatment;
- outcomes: primary and secondary outcomes as described previously.

Assessment of risk of bias in included studies

Two authors independently assessed the methodological quality of all included trials using the five-point scoring instrument proposed by Jadad (Jadad 1996). This instrument evaluates the reported quality of randomisation, blinding and description of withdrawals and drop-outs. Any disagreement between the authors was resolved by discussion.

Quality of allocation concealment was also ranked independently by two authors (ZL, MRA) using the Cochrane approach:

Grade A: adequate concealment;
Grade B: uncertain;
Grade C: clearly inadequate concealment.

Assessment of reporting biases

We did not use funnel plots or other statistical approaches to deal with the potential publication bias, given the lack of reliable methods and the small number of studies included in this review.

Data synthesis

Given the significant heterogeneity of outcome measures across the included trials, we planned to convert the result of each individual study into a standard measure by calculating a standardised mean difference (SMD) which is the difference of the means of both treatment arms divided by the pooled standard deviation. For a cross-over study without a wash-out period, we planned to include in the analysis only the data from the first treatment period. Unfortunately, after contacting the corresponding authors, we were only able to obtain original data from the study by Lepcha et al (Lepcha 2002). This precluded performing a formal meta-analysis, and data were therefore summarised in a narrative format.

If in the future data become available that are suitable for meta-analysis, we will proceed as follows. Data analysis will be on an intention-to-treat basis. The Cochrane Ear, Nose and Throat Disorders Group statistical guidelines and plan for assessment of heterogeneity will be followed. We will perform pooling of data if the data extracted from the included trials are comparable and of sufficient quality. We will calculate risk ratios (RRs) and 95% confidence intervals (CI) for all dichotomous data. For continuous data, we will calculate the weighted mean differences (WMDs) or standard mean differences (SMDs) and 95% confidence intervals (CI). We will use a random-effects model for meta-analysis.

Sensitivity analysis

If in the future there are sufficient included trials, we will conduct sensitivity analyses to assess the impact on overall outcomes of the following potentially important factors:

1. study quality;
2. differences in medications used in intervention and comparison groups;
3. delivery forms of intranasal steroids (spray versus drops);
4. analysis using random-effects and fixed-effect models;
5. analysis by study design: parallel versus cross-over studies.

RESULTS

Description of studies

Results of the search

The original searches for this review identified 65 potential studies for inclusion. After reviewing the titles and abstracts, seven papers were retrieved and assessed independently by two authors (ZL, MRA) for possible inclusion. Five trials were included in the original review. The updated search in May 2010 yielded seven citations, from which one additional suitable trial was identified (Demirhan 2010). Six randomised trials are therefore included in the updated review (see 'Characteristics of included studies' table).

Included studies

Study design

Two studies (Criscuoli 2003; Demain 1995) were randomised cross-over trials. One of these (Demain 1995) was an eight-week, placebo-controlled, double-blind trial and the other (Criscuoli 2003) was a four-week, saline solution-controlled, single-blind trial. There were no wash-out periods between the two treatment periods in either of the cross-over trials. Sixteen-week (Demain 1995) and 24-week (Criscuoli 2003) open-label follow-on studies were continued after the completion of the cross-over trials. During the open-label studies all patients received intranasal steroids.

The other four studies (Berlucchi 2007; Ciprandi 2007; Demirhan 2010; Lepcha 2002) were randomised, placebo-controlled, parallel-group trials. The duration of the Lepcha 2002, Ciprandi 2007 and Demirhan 2010 trials was eight weeks. The Berlucchi 2007 trial was divided into two stages. The first stage was a 40-day, placebo-controlled, double-blind trial. In the second stage, the patients who were allocated to the steroid group in the first stage and showed subjective and objective clinical improvement were randomly divided into two subgroups to receive "maintenance therapy" for a further three months. One group received intranasal steroids on

alternate days for the first two weeks per month, whereas the other group received daily intranasal steroids for the first two weeks per month.

Participants

Moderate to severe adenoidal hypertrophy was diagnosed by lateral neck X-ray in two trials (Criscuoli 2003; Lepcha 2002) and by fibreoptic nasopharyngeal endoscopy in four trials (Berlucchi 2007; Ciprandi 2007; Demain 1995; Demirhan 2010). All six trials excluded children who had used intranasal or systemic steroids within the last year, who had an acute upper respiratory infection within two weeks of entering the study and who had a history of chronic epistaxis or immunodeficiency.

Interventions

During an eight-week cross-over study, Demain 1995 used aqueous nasal beclomethasone spray as the active intervention, two sprays in each nostril twice daily (336 mcg/day). In the subsequent 16-week, open-label, follow-on study all patients received beclomethasone: one spray in each nostril twice daily (168 mcg/day). Lepcha 2002 used intranasal beclomethasone spray as active intervention, one puff (50 mcg) in each nostril twice daily (200 mcg/day) for eight weeks. Criscuoli 2003 used intranasal aqueous beclomethasone as active treatment, two sprays (50 mcg/spray) in each nostril twice daily (400 mcg/day) during the four-week cross-over. In the subsequent 24-week, open-label, follow-on study all patients received beclomethasone, one spray in each nostril twice daily (200 mcg/day). Berlucchi 2007 used mometasone furoate aqueous spray as active intervention during the first-stage randomised, placebo-controlled trial, at a dosage of one spray (50 mcg) in each nostril once daily (100 mcg/day) for 40 days. In the three-month, second-stage "maintenance therapy" period, one group received mometasone on alternate days for the first two weeks of each month, and the other group received daily mometasone for the first two weeks of each month. Ciprandi 2007 used intranasal flunisolide drops as active intervention for eight weeks. The dosage of flunisolide was described in the article as "drop number=0.5xKg/bw, twice daily", but the corresponding author confirmed that the dosage was 500 mcg/day. Demirhan 2010 used fluticasone propionate nasal drops at a dose of six drops in each nostril once daily (400 mcg/day) for eight weeks.

Outcome measures

Improvement in symptoms of nasal obstruction was employed as an outcome measure in five trials (Berlucchi 2007; Criscuoli 2003; Demain 1995; Demirhan 2010; Lepcha 2002), however different symptom scores were used to assess the degree of nasal obstruction. A visual analogue scale ranging from 0 (never has the symptom) to 10 (constantly has the symptom) was used by Demain 1995 to measure patients' nasal obstruction symptoms (nasal congestion, nasal voice, snoring, daytime drowsiness, restless sleep, nasal discharge, ear popping/pain and bad breath). The total symptom score varied from 0 to 80. In the Criscuoli 2003 trial a Nasal Obstruction Index with a four-point scale was used to assess nasal obstruction symptoms (1 = absent, 2 = mild, 3 = moderate, 4 = marked). In the Lepcha 2002 trial nasal obstruction, snoring and nasal discharge were scored as follows: 0 = none at all, 1 = occasional during colds, 2 = frequent, 3 = constant. Berlucchi 2007 used a clinical scoring system ranging from 0 to 3 (0 = absent; 1 = occasional; 2 = frequent; 3 = daytime and night-time symptoms) to assess the degree of nasal obstruction, rhinorrhoea, cough, snoring and obstructive sleep apnoea. In the Demirhan 2010 trial nasal congestion, mouth breathing, snoring, nasal speech and apnoea were scored as: 0 = none, 1 = sometimes, 2 = often, 3 = day-long, whereas cough was scored as: 0 = none, 1 = mild, 2 = moderate and 3 = severe.

Adenoid size was an outcome measure in five trials (Berlucchi 2007; Ciprandi 2007; Demain 1995; Demirhan 2010; Lepcha 2002). In the Demain, Ciprandi, Berlucchi and Demirhan trials adenoid size was assessed using photographic images taken during fibreoptic nasopharyngeal endoscopic examination. The degree of adenoid obstruction was estimated as the ratio of the two-dimensional area of the adenoid relative to the area of the posterior choana (Berlucchi 2007; Demain 1995; Demirhan 2010). Ciprandi 2007 and Demirhan 2010 classified adenoid obstruction into four degrees: 1) first degree: the adenoid tissue occupied only the upper segment in the nasopharyngeal cavity (< 25%) and choanal openings were free, 2) second degree: the adenoid tissue was confined to the upper half (< 50%) of the nasopharyngeal cavity, 3) third degree: the adenoid tissue extended over the nasopharynx (< 75%) with obstruction of the choanal openings and partial closure of Eustachian tube orifice, 4) fourth degree: the obstruction was almost total and both the Eustachian tube orifice and the lower choanal border could not be observed. In the Lepcha 2002 trial adenoid size was measured by neck X-ray and by fibreoptic nasopharyngeal endoscopy. For radiological assessment the narrowest distance between the nasopharyngeal soft tissues and the soft palate was measured and scored as 1) > 6 mm, 2) 4 to 6 mm and 3) 0 to 3 mm. For endoscopic examination, the distance from the adenoid tissues to the vomer was measured and scored as 1) > 1 cm, 2) 0.5 to 1 cm and 3) < 0.5 cm.

None of the six trials used quality of life as an outcome measure.

Side effects associated with intranasal treatment were reported in five trials (Berlucchi 2007; Ciprandi 2007; Demain 1995; Demirhan 2010; Lepcha 2002).

Risk of bias in included studies

None of the six studies explicitly described the method of randomisation. Allocation concealment was adequate in one trial (Demain 1995) and unclear in the remaining five trials. The methods for double-blinding and the description of withdrawals and drop-outs were appropriate in three trials (Berlucchi 2007; Demain 1995; Lepcha 2002). The Jadad score was four in three trials (Berlucchi 2007; Demain 1995; Lepcha 2002), two in Ciprandi 2007 and one in Criscuoli 2003 and Demirhan 2010.

Compliance with drug administration was adequately assessed only in one trial (Demain 1995).

Effects of interventions

A total of 394 children were enrolled in the six included studies and 376 completed the trials. Five studies showed beneficial effects of intranasal corticosteroids in improving nasal obstruction symptoms (Berlucchi 2007; Criscuoli 2003; Demain 1995; Demirhan 2010) and a reduction in adenoid size (Berlucchi 2007; Ciprandi 2007; Demain 1995; Demirhan 2010). In contrast, one trial (Lepcha 2002) did not find a significant difference between the nasal steroid group and the placebo group in terms of nasal obstruction symptoms or adenoid size.

Primary outcome

Improvement in nasal obstruction symptoms

Although there were differences in the symptom scores used for measuring nasal obstruction, four trials (Berlucchi 2007; Criscuoli 2003; Demain 1995; Demirhan 2010) demonstrated an improvement in nasal obstruction symptoms with intranasal corticosteroids.

In the eight-week cross-over study with 17 patients (Demain 1995), improvement in mean symptom scores was significantly larger in the beclomethasone group than that in the placebo group during the first four-week period (-18.5 versus -8.5, P < 0.05). The improvement in the beclomethasone group represented approximately a 45% reduction in the initial mean symptom scores. Over the full eight-week cross-over study the mean (± SD) obstruction score after beclomethasone treatment (20.5 ± 3.0) was significantly improved compared to baseline (43.1 ± 2.9) and placebo scores (31.1 ± 4.2) (P < 0.05). Improvement in nasal obstruction was maintained during the subsequent 16-week treatment with beclomethasone at a lower dose.

In another four-week cross-over study (Criscuoli 2003), 38% (10/26) of patients treated with beclomethasone between week 0 and week 2 had at least a 50% reduction in the Nasal Obstruction Index compared with baseline, but none of the patients treated with placebo had such an improvement (P < 0.01). Among the patients who had responded to the initial two-week steroid therapy, an additional 24-week treatment with beclomethasone at a lower dosage was associated with a significant 51- and 100-week improvement in nasal obstruction symptoms and with a reduction in the need for adenoidectomy compared with patients who had not responded after the initial two-week steroid therapy (relative risk (RR) 0.65, 95% confidence interval (CI) 0.44 to 0.98).

In Demirhan 2010 eight weeks of treatment with fluticasone yielded a significantly greater reduction in each of the six measured symptom scores (nasal congestion, mouth breathing, nasal speech, snoring, apnoea and cough) compared with normal saline. At the end of eight weeks the average total symptom score decreased from 13.72 to 2.96 in the fluticasone group, while the normal saline group score changed from 14.85 to 14.65. Adenoidectomy was avoided in 76% of patients treated with fluticasone compared with 20% of those treated with normal saline (P < 0.05).

In Berlucchi 2007, after a 40-day treatment period, 77.7% (21/27) of patients in the mometasone group were classified as responders (defined as having an improvement in clinical findings and a decrease in adenoid size, such that adenoidectomy could be avoided), whereas no such improvement was observed in the placebo group (n = 30). The mean overall symptom score decreased from 11 to 3 in the mometasone group and from 10 to 9 in the placebo group. The decrease in individual symptom scores (nasal obstruction, rhinorrhoea, obstructive sleep apnoea, cough, snoring) was also significantly greater in the mometasone group than in the placebo group.

In contrast, the results of Lepcha 2002 did not show a significant reduction in symptom scores following an eight-week treatment period with beclomethasone (n = 13) compared with the placebo group (n = 13). The reduction in mean symptom scores (±SD) in the beclomethasone group and in the placebo group were as follows: nasal blockage (-1.54 ± 0.97 versus -1.7 ± 1.1, P = 0.71); snoring (-1.3 ± 1.2 versus -1.8 ± 1.0, P = 0.29); and nasal discharge (-1.1 ± 1.0 versus -1.5 ± 1.2, P = 0.39).

Secondary outcomes

Reduction in adenoid size

In Demain 1995 the reduction in mean adenoid/choana ratio was greater in the beclomethasone group than in the placebo group during the first four-week study period (right -14% versus +0.4%, P = 0.002; left -15% versus -2.0%, P = 0.0006). Reduction in adenoid size was maintained during the subsequent 16-week treatment with beclomethasone at a lower dose.

In Berlucchi 2007, after a 40-day treatment, the median reduction (interquartile range) in the adenoid:choana ratio was 20.0% (12.5% to 32.5%) in the mometasone group and 0.0% (0.0% to 0.0%) in the placebo group.

In Ciprandi 2007 an eight-week treatment with flunisolide yielded a greater mean reduction in adenoid size than normal saline solution (-0.89 versus -0.28, P < 0.05).

In Demirhan 2010 the mean adenoid/choana ratio decreased from 86.9% to 56.2% after eight weeks of treatment with fluticasone, while the mean ratio decreased from 87.2% to 85.2% after eight weeks of treatment with normal saline.

The Lepcha 2002 trial showed that a five-fold reduction in the mean endoscopy scores (±SD) was obtained by an eight-week treatment with beclomethasone over the placebo, however the difference did not reach statistical significance (-0.39 ± 0.51 versus -0.08 ± 0.28, P = 0.067).

Improvement in quality of life assessed by validated quality of life questionnaire

None of the six included trials used quality of life as an outcome measure.

Adverse events

In Demain 1995 side effects associated with the use of intranasal aqueous spray were similar for subjects when receiving beclomethasone or placebo. During an eight-week cross-over study (n = 17) stinging was reported by six patients while taking beclomethasone and one patient while receiving placebo (P = 0.06); epistaxis was recorded by two patients on beclomethasone and one in the placebo group (P = 1.00); and sneezing was reported by one subject while receiving beclomethasone compared to four receiving placebo (P = 0.25). The Lepcha 2002 study reported that there was no untoward effect of the nasal spray and parents did not complain of nasal bleeding, stinging or allergies in either beclomethasone (n = 13) or placebo group (n = 13). In Berlucchi 2007 only one patient in the steroid group (n = 30) reported episodic epistaxis. No clinically relevant adverse events were reported by Ciprandi 2007 in either the flunisolide (n = 139) or normal saline group (n = 39). No clinically relevant adverse events were reported by Ciprandi 2007 and Demirhan 2010.

DISCUSSION

Among the six trials included in this review, five showed significant benefits of intranasal corticosteroids in improving nasal obstruction symptoms and in reducing adenoid size (Berlucchi

2007; Ciprandi 2007; Criscuoli 2003; Demain 1995; Demirhan 2010). In contrast, another trial (Lepcha 2002) did not find significant efficacy of intranasal corticosteroids in improving nasal blockage, nasal discharge or snoring, although a five-fold reduction in adenoid size was observed in the nasal corticosteroid group compared with the placebo group. However, this difference did not reach statistical significance. Low statistical power due to a small sample size may have contributed to this negative result. Unfortunately meta-analysis was not applicable in this review, so we could not pool the data derived from these five trials to estimate the overall effect size.

The mechanism by which topical steroids would improve nasal airway obstructive symptoms remains unclear. Three trials demonstrated that intranasal corticosteroids could improve nasal obstruction symptoms as well as reduce adenoid size (Berlucchi 2007; Demain 1995; Demirhan 2010). Moreover, a good correlation between nasal symptom score and adenoid/choana ratio was found (Demain 1995). These data suggest that the improvement in nasal obstruction symptoms may be associated with the effect of intranasal corticosteroids of reducing adenoid size.

None of the six included trials specifically addressed the question of minimum adequate intranasal corticosteroid dosage in children with adenoidal hypertrophy. Among the three trials using intranasal beclomethasone, the two that showed significant benefits in improving nasal obstruction symptoms or in reducing adenoid size (or both) after the two-week treatment used initial daily doses of 336 and 400 mcg respectively (Criscuoli 2003; Demain 1995). These benefits were maintained during the subsequent maintenance treatment with beclomethasone at lower doses (168 to 200 mcg/day). In contrast, beclomethasone was administered at a lower dosage (200 mcg/day) in Lepcha 2002 and no significant benefits were observed during the eight-week treatment. These results suggest that a moderate initial dose of intranasal beclomethasone may be needed for treatment of children with adenoidal hypertrophy, although a low dose may be effective for maintenance therapy. However, there is still a need to establish the adequate dosage through further randomised controlled trials.

The duration of treatment with intranasal corticosteroids in the six trials varied from eight to 24 weeks. None of the trials investigated the relationship between the effect size of intranasal corticosteroids and the duration of treatment. More studies are needed to establish the optimal duration of treatment with intranasal corticosteroids in children with adenoidal hypertrophy. The benefits may be expected shortly after initiation of treatment as one trial (Criscuoli 2003) showed that 45% of patients treated with beclomethasone had a significant improvement in nasal obstruction after a two-week treatment. In spite of the short-term effect of intranasal corticosteroids demonstrated by four trials, the long-term outcome in patients who respond to the therapy remains unclear. Only one study (Criscuoli 2003) had a relatively long-term follow-up period (100 weeks). Among 24 patients who had responded to the initial two-week therapy with beclomethasone and received an additional 24-week treatment at a lower steroid dosage, 13 (54%) patients still needed adenotonsillectomy at the 100-week follow-up. This means that nasal obstruction symptoms reappeared or worsened in more than half of patients two years after the clinical improvement obtained by a 26-week treatment with intranasal corticosteroids. These results suggest that, in a considerable proportion of patients with adenoidal hypertrophy, the effect of intranasal corticosteroids may only be maintained for a relatively short period of time. Further studies are needed to define the long-term outcome in patients who initially respond to the steroid therapy.

Intranasal corticosteroids have been generally well-tolerated and cause only mild side effects, even in the paediatric population (Al Sayyad 2007; Taramarcaz 2003). In this review, adverse events associated with intranasal corticosteroids were observed in three of the included trials. Epistaxis was reported in two trials (Berlucchi 2007; Demain 1995) and stinging and sneezing in one trial (Demain 1995). The occurrence of these events was infrequent and none of the withdrawals were associated with adverse events. However, a relatively small number of patients included in this review does not permit any conclusion regarding a side effect profile of intranasal corticosteroids, especially potential adverse systemic effects such as adrenal suppression and growth retardation. The safety of long-term use of intranasal corticosteroids in the paediatric population still needs to be addressed by further prospective studies.

Numerous methodological flaws could be observed in the included studies and they may weaken the strength of evidence provided in this review. In none of the six studies was the method of randomisation explicitly described, sample size calculated or analysis based on the intention-to-treat principle. Allocation concealment was clear in only one trial (Demain 1995). Moreover, the reporting of the results was generally not standardised and this made it impossible to extract sufficient data from the individual trials regarding the effect size of the interventions and their precision, so as to enable meta-analysis.

AUTHORS' CONCLUSIONS

Implications for practice

Current evidence suggests that intranasal corticosteroids may significantly improve nasal obstruction symptoms in children with moderate to severe adenoidal hypertrophy and that this improvement may be associated with a reduction in adenoid size. Given the potential clinically relevant benefits and relatively good tolerability of intranasal corticosteroids, these drugs may be indicated as an alternative treatment for children with moderate to severe adenoidal hypertrophy when adenoidectomy is not urgently required or not available. However, more robust evidence is needed to make a formal recommendation to use intranasal corticosteroids as an effective treatment in children with adenoidal hypertrophy.

Implications for research

Further large, high-quality randomised controlled trials are still needed to confirm the results of the six randomised trials included in this review. The reporting of future trials should follow the recommendations of the Consolidated Standards of Reporting Trials (CONSORT) statement, which would facilitate any future meta-analyses. For a cross-over design, an appropriate wash-out period between intervention and placebo is needed. The optimal duration of treatment, minimum adequate intranasal corticosteroid dosage and risk of adverse events, including adrenal suppression and growth retardation, also need to be explored in future studies. The follow-up period should be sufficient to assess the long-term outcome of patients who respond to treatment with intranasal corticosteroids.

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CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Berlucchi 2007

Methods	Study design: 2-stage, randomised controlled trial First stage: a 40-day, placebo-controlled, double-blind trial Second stage: a 3-month "maintenance therapy". Patients who were allocated to the steroid group in the first stage and showed subjective and objective clinical improvement were randomly divided into 2 subgroups: one group received intranasal corticosteroid on alternate days for the first 2 weeks per month, whereas the other group received daily intranasal corticosteroids for the first 2 weeks per month. Study setting: Department of Paediatric Otorhinolaryngology, Spedali Civili of Brescia, Italy The method of randomisation was not explicitly described. The method of double-blinding and the description of withdrawals/drop-outs were appropriate.
Participants	60 children (31 male, 29 female) with adenoidal hypertrophy and referred for exclusive adenoidectomy Inclusion criteria: 1) Adenoid pad occluding >= 75% of the nasopharynx, as determined with fibreoptic nasopharyngeal endoscopy 2) Aged between 3 and 7 years 3) Symptoms consistent with adenoidal hypertrophy lasting >= 12 months 4) No previous adenoidectomy Exclusion criteria: Children with concomitant tonsillar hypertrophy; positive history of allergy or atopy; upper respiratory infection within the past 2 weeks; nasal anatomic anomalies (e.g. nasal septum deviation) or sinonasal diseases such as hypertrophy of inferior turbinates and/or nasal polyposis; craniofacial malformations including labiopalatal clefts; genetic diseases (e.g. Down syndrome); neurologic disorders; cardiovascular diseases; immunodeficiency; history of epistaxis; hypersensitivity to steroids; or intranasal, topical or systemic steroid or antibiotic treatment within the past 4 weeks
Interventions	First stage: mometasone furoate aqueous spray (50 mcg) or placebo; 1 spray in each nostril once daily for 40 days 3-month second stage: "maintenance therapy"; one group received intranasal mometasone on alternate days for the first 2 weeks per month and another group received daily intranasal mometasone for the first 2 weeks per month
Outcomes	Clinical scoring system ranging from 0 to 3 (0 = absent; 1 = occasional; 2 = frequent; 3 = daytime and night-time symptoms) used to assess the degree of nasal obstruction, rhinorrhoea, cough, snoring and obstructive sleep apnoea Clinical information was obtained from the parents with a questionnaire at recruitment and at each subsequent visit. Adverse effects (e.g. nasal bleeding) were also reported by parents. Adenoid size was assessed using photographic images taken during fibreoptic nasopharyngeal endoscopy. The ratio of the 2-dimensional area of the adenoid relative to the area of the posterior choana was measured to assess the degree of adenoidal obstruction.
Notes	Compliance with drug administration was assessed bi-weekly in telephone interviews with parents

Berlucchi 2007 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Ciprandi 2007

Methods	Study design: 8-week, randomised, normal saline solution-controlled, single-blind parallel trial Study setting: 4 hospitals in Naples, Italy The method of randomisation was not explicitly described The method of single-blinding and the description of withdrawals/drop-outs were appropriate
Participants	178 children (97 males and 81 females), aged 3 to 6 years (mean age 4.5 years) with the complaint of chronic nasal obstruction and on the waiting list for adenoidectomy. 178 patients completed the study. Inclusion criteria: Patient had a third or fourth degree of adenoid obstruction on the initial fibreoptic nasopharyngeal endoscopy Exclusion criteria: Children had used intranasal, topical or systemic steroids within the last year; had used any intranasal medication within 2 weeks of entering the study; had an active upper respiratory infection within 2 weeks of entering the study; or had a history of chronic epistaxis, immunodeficiency or hypersensitivity to flunisolide.
Interventions	Intranasal flunisolide drop (drop number = 0.5 x kg/bw) or normal saline solution, twice daily
Outcomes	Adenoid size was assessed using photographic images taken during fibreoptic nasopharyngeal endoscopic examination Adenoid obstruction was classified into 4 degrees: 1) first degree: the adenoid tissue occupied only the upper segment in the rhinopharyngeal cavity (< 25%) and choanal openings were free; 2) second degree: the adenoid tissue was confined to the upper half (< 50%) of the rhinopharyngeal cavity; 3) third degree: the adenoid tissue extended over the rhinopharynx (< 75%) with obstruction of choanal openings and partial closure of tube ostium; 4) fourth degree: the obstruction was almost total and both the tube ostium and the lower choanal border could not be observed
Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Criscuoli 2003

Methods	Study design: 4-week , randomised, single-blind, saline solution-controlled cross-over trial. At the completion of the 4-week cross-over study, a 24-week, open-label, follow-on study was continued Study setting: outpatient department of Santobono Pediatric Hospital in Naples, Italy

Criscuoli 2003 *(Continued)*

	The method of randomisation was not explicitly described The method of blinding and the description of withdrawals/drop-outs were not appropriate
Participants	60 children (mean age 3.8 years) with adenotonsillar hypertrophy. 53 patients (25 male, 28 female) completed the study. Inclusion criteria: 1) Had symptoms of nasal obstruction for at least 6 months 2) Adenoidal hypertrophy assessed on radiography as an adenoidal/nasopharyngeal ratio > 0.5 or 2+ or 3+ tonsillar hypertrophy assessed on clinical evaluation 3) Subject was booked for adenotonsillectomy after the initial assessment Exclusion criteria: Children had used intranasal, topical or systemic steroids within the last year; had a history of chronic epistaxis or immunodeficiency; or had an active upper respiratory infection within 2 weeks of entering the study
Interventions	During the 4-week, cross-over study, intranasal aqueous beclomethasone (50 mcg/spray) or saline solution, 2 sprays in each nostril twice daily In a subsequent 24-week, open-label, follow-on study, all patients received beclomethasone 1 spray (50 mcg) in each nostril twice daily
Outcomes	Nasal Obstruction Index with a 4-point scale was used to assess nasal obstruction symptoms (1 = absent, 2 = mild, 3 = moderate, 4 = marked). After the 4-week cross-over trial, children who showed a reduction in nasal obstruction index of at least 50% compared with baseline were considered as "responders" compared with those whose index did not change at all or decreased by < 50% ("nonresponders").
Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Demain 1995

Methods	Study design: 8-week, randomised, double-blind, placebo-controlled, cross-over trial. A 16-week, open-label, follow-on study was continued after the completion of the cross-over trial. Study setting: the Wilford Hall Medical Center Allergy and Immunology Clinic, Lackland, TX, USA The method of randomisation was not explicitly described The method of double-blinding and the description of withdrawals/drop-outs were appropriate
Participants	20 children, aged 5 to 11 years, presenting with the complaint of chronic nasal obstruction. 17 patients completed the study. Inclusion criteria: Patients had an estimated 90% or greater adenoidal obstruction of the nasal airway on initial fibreoptic nasopharyngeal endoscopic examination Exclusion criteria: Children had used intranasal, topical or systemic steroids within the last year; had used any intranasal medication within 2 weeks of entering the study; had an active upper respiratory infection within 2

Demain 1995 *(Continued)*

	weeks of entering the study; had history of chronic epistaxis, immunodeficiency or hypersensitivity to beclomethasone
Interventions	During 8-week, cross-over study, aqueous nasal beclomethasone (42 mcg/spray) or placebo, 2 sprays in each nostril twice daily In a subsequent 16-week, open-label, follow-on study, all patients received beclomethasone 1 spray in each nostril twice daily
Outcomes	A visual analogue scale ranging from 0 (never has the symptom) to 10 (constantly has the symptom) were used to measure each nasal obstruction symptom (nasal congestion, nasal voice, snoring, daytime drowsiness, restless sleep, nasal discharge, ear popping/pain and bad breath). The total symptom score varied from 0 to 80. Adenoid size was assessed using photographic images taken during fibreoptic nasopharyngeal endoscopic examination. The ratio of the 2-dimensional area of the adenoid relative to the area of the posterior choana was measured to assess the degree of adenoidal obstruction. Middle ear pressures were measured by tympanometry and speech thresholds and pure-tone thresholds were measured by audiometry Bed wetting score (range 0.0 to 10) was used to measure this symptom in the subgroup of patients who had enuresis
Notes	Compliance with drug administration was assessed by parental report and total weight of drug dispensed

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - Adequate

Demirhan 2010

Methods	Study design: 8-week, randomised, normal saline solution-controlled, parallel trial Study setting: otorhinolaryngology clinic, Istanbul, Turkey The method of randomisation was not explicitly described It is unclear whether participants and investigators were blinded to treatment assignment. Withdrawals/drop-outs were not described.
Participants	45 children (20 males and 25 females), aged 4 to 16 years (mean age 9.7 years) Inclusion criteria: Adenotonsillectomy-indicated patients with recurrent tonsillitis, presenting with normal sized rather than hypertrophic tonsils were included if they had been having symptoms associated with adenoid hypertrophy for at least 6 months Exclusion criteria: Patients who had undergone adenoidectomy previously or patients with upper respiratory tract infection or allergic rhinitis or turbinate hypertrophy, who had taken intranasal topical or systemic steroid in the last 1 year; who had taken any intranasal medical treatment; who had a history of chronic nosebleeding, immunodeficiency or a history of hypersensitivity, positive allergy or atopy against fluticasone; who had tonsillar hypertrophy; who had chronic otitis media with effusion and type B tympanogram; who had anatomic deformity of the nose or sinonasal disease such as nasal polyposis or in-

Demirhan 2010 *(Continued)*

	ferior turbinate hypertrophy; or who had craniofacial abnormalities such as cleft lip/cleft palate, genetic diseases such as Down Syndrome, neurological diseases or cardiovascular diseases
Interventions	Fluticasone propionate nasal drops (400 mcg/day, 6 drops each nostril, once daily) or normal saline solution
Outcomes	Nasal congestion, mouth breathing, snoring, nasal speech and apnoea were scored as follows: 0 = none, 1 = sometimes, 2 = often, 3 = day-long and night-long. Cough was scored as: 0 = none, 1 = mild, 2 = moderate, 3 = severe. Adenoid size was assessed according to fibre-endoscopic images or rigid nasal endoscopic images; using the nasal passage, choanal openings from top to bottom were graded (grade 1 to 4) and determined as: 1st grade: only top segment of the choana is obstructed < 25%, 2nd grade: upper half of the choana is obstructed < 50%, 3rd grade: adenoid extending to the nasopharynx and Eustachian tube opening is partially obstructed < 75%, 4th grade: the choana is almost completely obstructed
Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Lepcha 2002

Methods	Study design: 8-week, randomised, placebo-controlled, double-blind parallel trial Study setting: ENT/paediatric outpatient department of Christian Medical College and Hospital in Vellore, India The method of randomisation was not explicitly described The method of double-blinding and the description of withdrawals/drop-outs were appropriate
Participants	31 children aged 3 to 12 years, diagnosed as having adenoid hypertrophy Inclusion criteria: Children had a diagnosis of adenoid hypertrophy based on the symptoms (nasal obstruction, snoring and/or nasal discharge) and lateral cephalometric radiographs (enlarged soft tissue convex bulge in the roof of nasopharynx compressing the nasopharyngeal airways); resided in/near Vellore and could come for monthly follow up; and were accompanied by either parent or guardian who resided with the child and could supervise the usage of drug Exclusion criteria: Children had used intranasal or systemic steroids within the last year; had used any intranasal medication such as decongestants or anti-allergens within 2 weeks of entering the study; had an acute upper respiratory infection within 2 weeks of entering the study; had history of chronic epistaxis, immunodeficiency disorders or hypersensitivity to beclomethasone
Interventions	Intranasal beclomethasone spray (50 mcg) or placebo 1 puff in each nostril twice daily
Outcomes	Nasal obstruction, snoring and nasal discharge were scored as follows: 0 = none at all, 1 = occasional during colds, 2 = frequent, 3 = constant Adenoid size was measured by neck X-ray and by fibreoptic nasopharyngeal endoscopy. For radiological assessment, the narrowest distance between the nasopharyngeal soft tissues and the soft palate was measured and scored as 1) > 6 mm, 2) 4 to 6 mm and 3) 0 to 3 mm. For endoscopic examination,

Lepcha 2002 *(Continued)*

	the distance of the adenoid tissues from the vomer was measured and scores as 1) > 1 cm, 2) 0.5 to 1 cm and 3) < 0.5 cm.
Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Berlucchi 2008	This was a follow-up study of a previous trial (Berlucchi 2007)
Brouillette 1982	Participants were patients with obstructive sleep apnoea and primary outcome was the frequency of obstructive apnoea and hypopnoea
Cengel 2006	This trial included children older than 12 years
Varricchio 2009	The study was stated to be a placebo-controlled, but the data from the placebo group were not reported

APPENDICES

Appendix 1. Search strategies

CENTRAL	MEDLINE	EMBASE
#1 ADENOIDS single term (MeSH) #2 ADENOID* OR ADENOTONSIL* OR ADENO NEXT TONSIL* OR PHARYN* NEAR TONSIL* #3 #1 OR #2 #4 HYPERTROPHY single term (MeSH) #5 HYPERTROPH* OR ENLARGE* OR SWOLLEN OR OVERGROW* OR OVER NEXT GROW* #6 #4 OR #5 #7 #3 AND #6 #8 STEROIDS explode all trees (MeSH) #9 ANTI-INFLAMMATORY-AGENTS explode all trees (MeSH) #10 ANTI-INFLAMMATORY-AGENTS-NON-STEROIDAL explode all trees (MeSH) #11 #9 NOT #10 #12 GLUCOCORTICOIDS explode all trees (MeSH)	1. ADENOIDS.DE. 2. (ADENOID$2 OR ADENOTONSIL$3 OR ADENO ADJ TONSIL$3 OR PHARYN$4 NEAR TONSIL $3).TI,AB. 3. 1 OR 2 4. HYPERTROPHY.DE. 5. (HYPERTROPH$3 OR ENLARGE$4 OR SWOLLEN OR OVERGROW$3 OR OVER ADJ GROW$3).TI,AB. 6. 4 OR 5 7. 3 AND 6 8. STEROIDS#.W..DE. 9. ANTI-INFLAMMATORY-AGENTS#.W..DE. 10. ANTI-INFLAMMATORY-AGENTS-NON-STEROIDAL#.W..DE. 11. 10 NOT 11 12. GLUCOCORTICOIDS#.W..DE. 13. STEROID$2 OR CORTICOSTEROID$2 14. GLUCOCORTICOID$2	1. ADENOID.W..DE. 2. (ADENOID$2 OR ADENOTONSIL$3 OR ADENO ADJ TONSIL$3 OR PHARYN$4 NEAR TONSIL$3).TI,AB. 3. 1 OR 2 4. HYPERTROPHY.W..DE. 5. (HYPERTROPH$3 OR ENLARGE$4 OR SWOLLEN OR OVERGROW$3 OR OVER ADJ GROW$3).TI,AB. 6. 4 OR 5 7. 3 AND 6 8. CORTICOSTEROID#.DE. 9. STEROID$2 OR CORTICOSTEROID$2 10. GLUCOCORTICOID$2 11. BECLOMETHASONE OR 4419-39-0.RN. 12. BETAMETHASONE OR 378-44-9.RN.

(Continued)

#13 STEROID* OR CORTICOSTEROID*
#14 GLUCOCORTICOID*
#15 BECLOMETHASONE OR BECLAMET OR BECLOCORT OR BECOLMETASONE OR BECOTIDE OR BETAMETHASONE OR CLENIL OR BECLOSOL
#16 BUDESONIDE OR HORACORT OR PULMICORT OR RHINOCORT OR BUDECORT
#17 CORTISONE OR DEXAMETHASONE OR HEXADECADROL OR DECADRON OR DEXASONE
#18 HEXADROL OR METHYLFLUOR-PREDNISOLONE OR MILLICORTEN OR ORADEXON OR FLUNISOLIDE OR FLUTI-CASONE OR HYDROCORTISONE OR CORTISOL OR FLIXONASE OR FLIXOTIDE OR PLURAIR
#19 METHYLPREDNISOLONE OR MOMETASONE OR PREDNISOLONE OR PREDNISONE OR NASONEX
#20 TRIAMCINOLONE OR NASACORT OR AIRCLIN
#21 #8 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20
#22 #7 AND #21

15. BECLOMETHASONE OR 4419-39-0.RN. OR BECLAMET OR BECLOCORT OR BECOLMETASONE OR BECOTIDE
16. BETAMETHASONE OR 378-44-9.RN.
17. BUDESONIDE OR 51333-22-3.RN. OR HORA-CORT OR PULMICORT OR RHINOCORT
18. CORTISONE OR 53-06-5.RN.
19. DEXAMETHASONE OR 50-02-2.RN. OR HEXA-DECADROL OR DECADRON OR DEXASONE
20. HEXADROL OR METHYLFLUORPREDNISOLONE OR MILLICORTEN OR ORADEXON
21. FLUNISOLIDE OR 3385-03-3.RN.
22. FLUTICASONE OR 90566-53-3.RN.
23. (FLUTICASONE ADJ PROPIONATE) OR 80474-14-2.RN.
24. HYDROCORTISONE OR CORTISOL OR 50-23-7.RN.
25. METHYLPREDNISOLONE OR 83-43-2.RN.
26. MOMETASONE OR 105102-22-5.RN.
27. PREDNISOLONE OR 50-24-8.RN.
28. PREDNISONE OR 53-03-2.RN.
29. TRIAMCINOLONE OR 124-94-7.RN.
30. FLIXONASE OR FLIXOTIDE OR PLURAIR OR BUDECORT OR NASONEX OR CLENIL OR BE-CLOSOL OR NASACORT OR AIRCLIN
31. 8 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30
32. 7 AND 31

13. BUDESONIDE OR 51333-22-3.RN.
14. CORTISONE OR 53-06-5.RN.
15. DEXAMETHASONE OR 50-02-2.RN.
16. FLUNISOLIDE OR 3385-03-3.RN.
17. FLUTICASONE OR 90566-53-3.RN.
18. (FLUTICASONE ADJ PROPIONATE) OR 80474-14-2.RN.
19. HYDROCORTISONE OR CORTISOL OR 50-23-7.RN.
20. METHYLPREDNISOLONE OR 83-43-2.RN.
21. MOMETASONE OR 105102-22-5.RN.
22. PREDNISOLONE OR 50-24-8.RN.
23. PREDNISONE OR 53-03-2.RN.
24. TRIAMCINOLONE OR 124-94-7.RN.\
25. FLIXONASE OR FLIXOTIDE OR PLURAIR OR BUDECORT OR NASONEX OR CLENIL OR BECLOSOL OR NASACORT OR AIRCLIN
26. 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25
27. 7 AND 26

WHAT'S NEW

Date	Event	Description
18 July 2010	New search has been performed	New full searches were run on 4 May 2010. One new study has been included (Demirhan 2010), however the conclusions of the review are unchanged.

HISTORY

Protocol first published: Issue 4, 2006
Review first published: Issue 3, 2008

Date	Event	Description
10 April 2008	Amended	Converted to new review format.

CONTRIBUTIONS OF AUTHORS

ZL conceived the idea and wrote the draft of the protocol. MRA, CJA and NKC provided input for writing the protocol.

ZL, MRA and CJA were responsible for study selection, quality assessment, data collection and data analysis.

MRA wrote the following parts of the review: 'Description of studies' and 'Risk of bias in included studies'. ZL wrote the remaining parts of the review. NKC provided expert advice on the review. The final draft of the review was approved by all authors.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- Department of Maternal and Child Health, Federal University of Rio Grande, Brazil.

External sources

- No sources of support supplied

INDEX TERMS

Medical Subject Headings (MeSH)

Adenoids [*pathology]; Administration, Intranasal; Adrenal Cortex Hormones [administration & dosage] [*therapeutic use]; Hypertrophy [complications] [drug therapy]; Nasal Obstruction [*drug therapy] [etiology]; Randomized Controlled Trials as Topic

MeSH check words

Child; Humans