

# Efficacy of intranasal corticosteroids in improving nasal airway obstruction in children with symptomatic adenoidal hypertrophy: a meta-analysis and systematic review

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## Background

Adenoidal hypertrophy is considered one of the most common diseases in otolaryngology. It is usually associated with nasal obstruction symptoms like snoring and hyponasality. If not treated well, children will encounter many complications like otitis media with effusion and craniofacial abnormalities. Adenoidectomy is the main line of treatment for many otolaryngologists, but recently medical treatment by using intranasal corticosteroids (INCS) has shown beneficial effects in reducing the size of adenoids or improving the obstruction symptoms.

## Objectives

To assess the efficacy of nasal corticosteroids in improving nasal airway obstruction in children with symptomatic adenoidal hypertrophy.

## Patients and methods

A comprehensive search in MEDLINE and CENTRAL was undertaken (1985–2017). We identified all randomized controlled trials in children with adenoidal hypertrophy that compared the effects of nasal corticosteroids and normal saline nasal spray on different outcomes. The primary outcomes were improvement of nasal obstruction symptoms assessed by any symptoms score and reduction in adenoid size as demonstrated by fiberoptic nasopharyngoscopy or lateral nasopharynx radiograph.

## Results

Twenty-three relevant potential citations were identified and screened for retrieval; nine articles were suitable for these meta-analyses. The included randomized controlled trials were enrolled in five meta-analyses. Three meta-analyses showed significant improvement in adenoid size after the use of INCS with a risk ratio of 0.68, standardized mean difference (SMD)=-2.97, SMD=-0.67, respectively. Two meta-analyses showed insignificant improvement in nasal obstruction symptoms with SMD=-1.53 and SMD=0.67, respectively.

## Conclusion

INCS can be used in children with moderate to severe adenoid hypertrophy to reduce the adenoid size and improve the associated symptoms. Close monitoring of improving of the symptoms is a must to predict the need of nonmedical management.

## Keywords:

adenoids, corticosteroids, hypertrophy, intranasal

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## Introduction

Enlarged adenoids usually cause upper airway obstruction. The common associated symptoms are mouth breathing, speech hyponasality, and nocturnal snoring. In more severe cases, complications may occur like otitis media with effusion, obstructive sleep apnea, neurocognitive disturbance, growth failure, and cor pulmonale [1].

The lateral nasopharynx radiograph is a widely used investigation for diagnosis. The low cost, widespread availability, noninvasive nature, and good correlation with symptoms are the main advantages of this

diagnostic test [2]. Fiberoptic nasopharyngeal endoscopy is considered the gold standard for the diagnosis and evaluation of adenoidal hypertrophy. However, the requirements of costly equipment and the need for child cooperation limit this diagnostic approach [3].

The management of symptomatic adenoidal hypertrophy is dependent on the degree of nasal

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**Table 1 Results of the first meta-analysis**

Model	References	Risk ratio	95% LCL	95% UCL	Z value	P value
	Cengel and Akyol [11]	0.57	0.41	0.80	-3.33	<0.01
	Chan <i>et al.</i> [9]	0.87	0.26	2.85	-0.24	0.81
	Ciprandi <i>et al.</i> [10]	0.74	0.58	0.93	-2.53	0.01
FEM		0.68	0.56	0.82	-4.00	<0.01
Heterogeneity						
Q value	DF (Q)	P value	$I^2$			
1.60	2	0.45	0.00			

Tests of heterogeneity showed unimportant heterogeneity as (Cochran Q, 1.60;  $I^2$ , 0.00). 95% LCL, 95% lower confidence limit; 95% UCL, 95% upper confidence limit; DF (Q), degrees of freedom for Q test; FEM, fixed effects model. Risk ratio=0.68.

airway obstruction and any associated morbidity. When the patients are suffering from complications, adenoidectomy is generally indicated [4]. The risk-benefit ratio of surgical intervention for the individual patient needs to be carefully assessed in the light of potential anesthetic complications and postoperative complications. In less severe cases, intranasal corticosteroids (INCS) may be considered. Their effects in symptomatic adenoidal hypertrophy have been assessed by many randomized trials [5,6].

### Patients and methods

A comprehensive search in MEDLINE and CENTRAL was undertaken (1985–2017). This is a meta-analysis study depended on other studies which made their ethical approval from their ethical committees individually. We identified all the randomized controlled trials (RCTs) in children with adenoidal hypertrophy that compared the effects of INCS and intranasal saline (INS) on different outcomes. The measured outcomes were improvement of nasal obstruction symptoms and reduction in adenoid size. Statistical analysis was done using Comprehensive Meta-Analysis, version 2.2.064 (Biostat, New Jersey, USA). Risk ratio, standardized mean differences, and their 95% confidence intervals were calculated for binary and continuous data, respectively. Heterogeneity was measured by using the  $I^2$  statistics and Cochran  $Q\chi^2$  test. Publication bias was assessed by examination of the funnel plot.

### Results

Twenty-three articles were related to our search question. Nine articles met our inclusion criteria and the other 14 were excluded.

The nine included studies compared between the effect of INCS versus INS on the adenoid size and nasal obstruction symptoms. Two of our included studies are cross-over studies. The two stages were enrolled in the meta-analysis as two separate studies

[7,8]. The included studies were enrolled in five meta-analyses concerning the adenoid size and associated symptoms.

Results of the first meta-analysis (which includes three studies) and report the risk ratio for having adenoids with grade III or grade IV after the use of INCS and INS, showed a significant reduction of the adenoid size, assessed by fiberoptic nasopharyngoscopy, after the use of INCS with unimportant heterogeneity and with some evidence of publication bias [9–11] (Table 1 and Fig. 1).

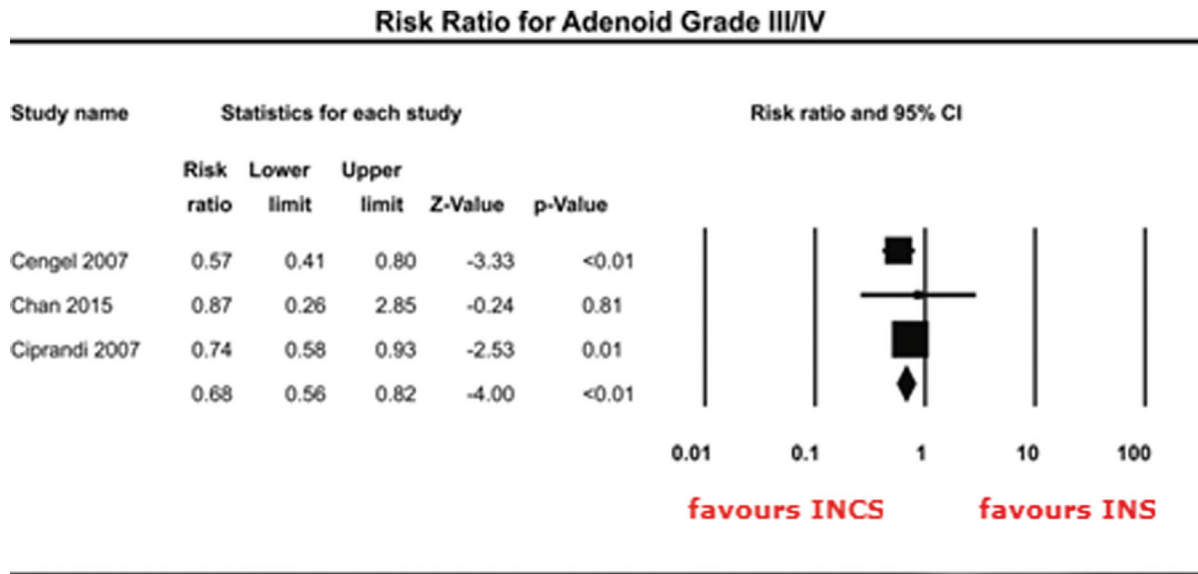
The results of the second meta-analysis (which includes five studies) and which is reporting the mean and SD of the adenoid size after the use of INCS and INS has shown significant reduction of the adenoid size, assessed by fiberoptic nasopharyngoscopy, after the use of INCS with considerable heterogeneity and no evidence of publication bias [7,8,12] (Table 2 and Fig. 2).

The results of the third meta-analysis (which includes three studies) and which reports the mean of the adenoid size and *P* value of the unpaired *t* test showed significant reduction of the adenoid size, assessed by fiberoptic nasopharyngoscopy, after the use of INCS with unimportant heterogeneity and no evidence of publication bias [13–15] (Table 3 and Fig. 3).

The results of the fourth meta-analysis (which includes three studies) and which reports the mean and SD of the symptom score after the use of INCS and INS showed nonsignificant improvement after the use of INCS with considerable heterogeneity and no evidence of publication bias [7,9] (Table 4 and Fig. 4).

The results of the fifth meta-analysis (which includes three studies) and which reports the mean and SD of the symptom score after the use of INCS and INS, showed the nonsignificance of INCS in improving the obstructive symptoms, with unimportant heterogeneity and no evidence of publication bias [13–15] (Table 5 and Fig. 5).

Figure 1



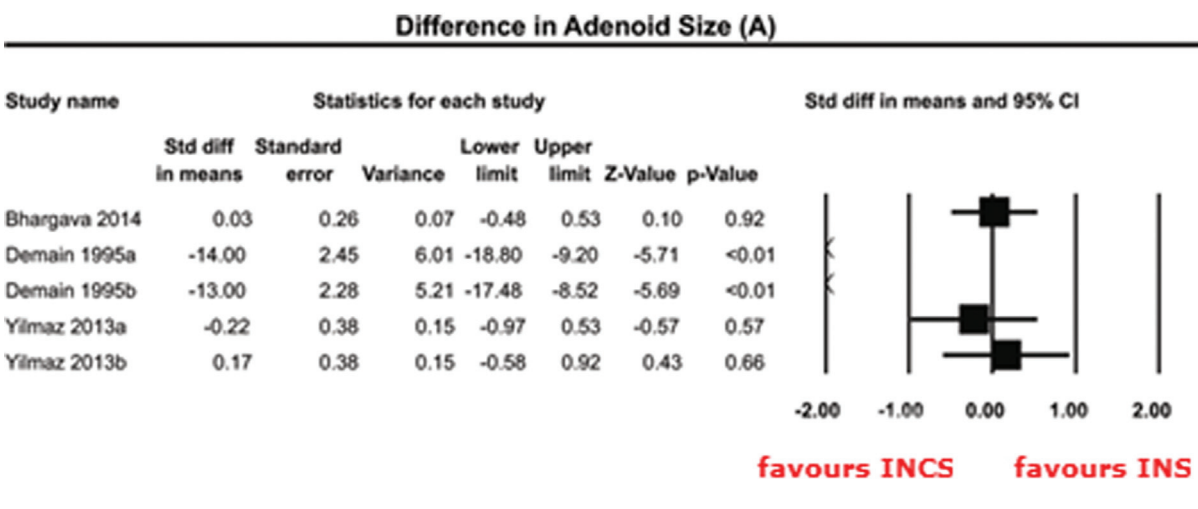
Forest plot of the first meta-analysis. Pooling of the studies showed a risk ratio of 0.68. This means that there is low risk of having adenoids with grade III or IV after using INCS, and this reflects the significance of INCS in reducing the adenoid size. INCS, intranasal corticosteroid; INS, intranasal saline.

Table 2 Results of the second meta-analysis

Models	Reference	SMD	SE	Var.	95% LCL	95% UCL	Z value	P value
	Bhargava and Chakravarti [12]	0.03	0.26	0.07	-0.48	0.53	0.10	0.92
	Demain and Goetz [8] (Study a)	-14.00	2.45	6.01	-18.80	-9.20	-5.71	<0.01
	Demain and Goetz [8] (Study b)	-13.00	2.28	5.21	-17.48	-8.52	-5.69	<0.01
	Yilmaz et al. [7] (Study a)	-0.22	0.38	0.15	-0.97	0.53	-0.57	0.57
	Yilmaz et al. [7] (Study b)	0.17	0.38	0.15	-0.58	0.92	0.43	0.66
REM		-2.79	0.96	0.92	-4.67	-0.90	-2.90	<0.01
Heterogeneity								
Q value	DF (Q)	P value	$I^2$					
64.77	4	<0.01	93.82					

Tests of heterogeneity showed considerable heterogeneity among the included studies (Cochran Q, 64.77;  $I^2$ , 93.82). 95% LCL, 95% lower confidence limit; 95% UCL, 95% upper confidence limit; DF (Q), degrees of freedom for Q test; REM, random effects model; SMD, standardized mean difference; Var., variance.

Figure 2

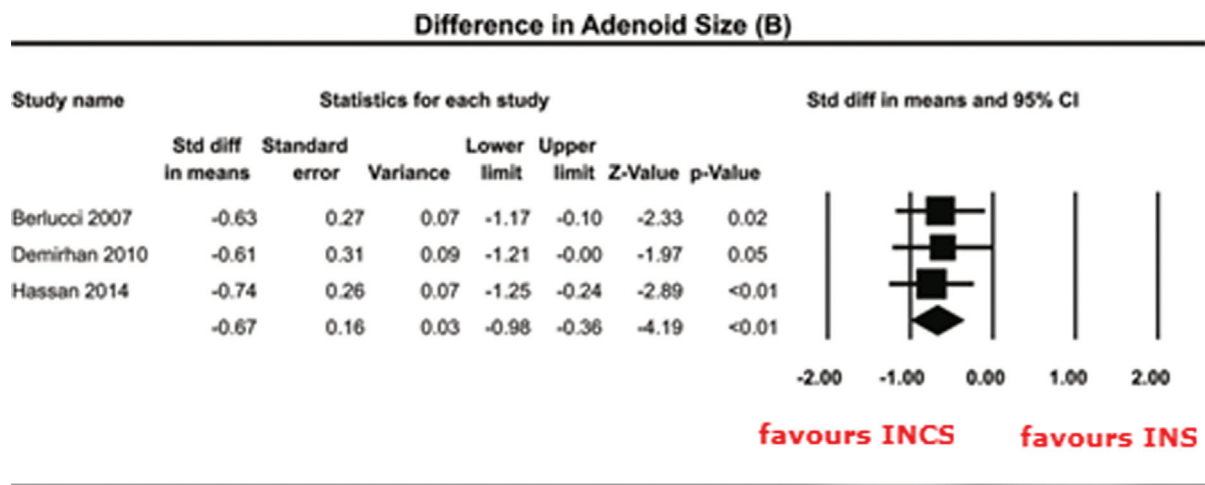


Forest plot of the second meta-analysis. Pooling of the studies showed a standardized mean difference (SMD) of -2.79 (negative value which favors the intervention). This means that the adenoid size decreased in children of the intervention groups that used INCS, reflecting the significance of using INCS in reducing the adenoid size. INCS, intranasal corticosteroid; INS, intranasal saline.

**Table 3 Results of the third meta-analysis**

Models	References	SMD	SE	Var.	95% LCL	95% UCL	Z value	P value
	Berlucchi <i>et al.</i> (2007)	-0.63	0.27	0.07	-1.17	-0.10	-2.33	0.02
	Demirhan <i>et al.</i> [14]	-0.61	0.31	0.09	-1.21	0.00	-1.97	0.05
	Hassan [13]	-0.74	0.26	0.07	-1.25	-0.24	-2.89	<0.01
FEM		-0.67	0.16	0.03	-0.98	-0.36	-4.19	<0.01
Heterogeneity								
Q value	DF (Q)	P value	$I^2$					
0.14	2	0.93	0.00					

Tests of heterogeneity showed unimportant heterogeneity among the included studies (Cochran Q, 0.14;  $I^2=0.00$ ). 95% LCL, 95% lower confidence limit; 95% UCL, 95% upper confidence limit; DF (Q), degrees of freedom for Q test; FEM, fixed effects model; SMD, standardized mean difference; Var., variance.

**Figure 3**

Forest plot of the third meta-analysis. Pooling of the studies showed a standardized mean difference (SMD) of -0.67 (negative value favors the intervention). This means that the adenoid size decreased in children of the intervention group that INCS, reflecting the significance of using INCS in reducing the adenoid size. INCS, intranasal corticosteroid; INS, intranasal saline.

**Table 4 Results of the fourth meta-analysis**

Models	References	SMD	SE	Var.	95% LCL	95% UCL	Z value	P value
	Chan <i>et al.</i> [9]	-3.77	0.47	0.22	-4.70	-2.85	-8.00	0.00
	Yilmaz (2013a)	-0.68	0.39	0.15	-1.45	0.09	-1.73	0.08
	Yilmaz (2013b)	-0.19	0.38	0.15	-0.94	0.56	-0.50	0.61
REM		-1.53	1.05	1.09	-3.58	0.52	-1.46	0.14
Heterogeneity								
Q value	DF (Q)	P value	$I^2$					
38.33	2	<0.01	94.78					

Tests of heterogeneity showed considerable heterogeneity among the included studies (Cochran Q, 38.33;  $I^2$ , 94.78). 95% LCL, 95% lower confidence limit; 95% UCL, 95% upper confidence limit; DF (Q), degrees of freedom for Q test; REM, random effects model; SMD, standardized mean difference; Var., variance.

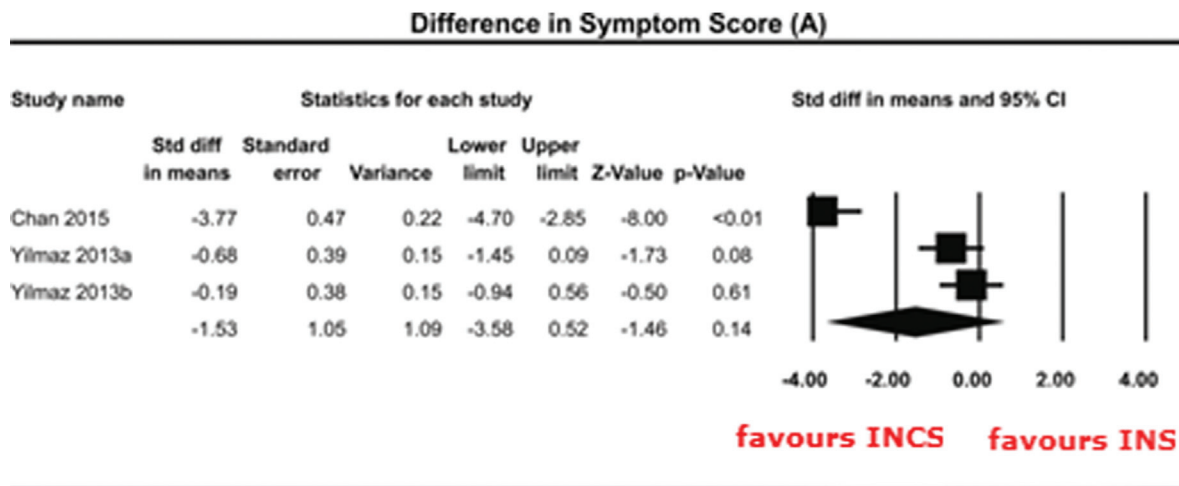
## Discussion

Nine studies were included in this meta-analysis. Two of them were cross-over studies and were conducted in two stages. The two stages were enrolled in the meta-analysis as two separate studies.

A total of 667 children were enrolled in the study: 280 children in the control arm and 387 children in the treatment arm.

The studies used different visual analog scales for the assessment of adenoid hypertrophy symptoms like nasal obstruction, rhinorrhea, cough, snoring, and mouth breathing. All included studies used fiberoptic nasopharyngeal endoscopy for the assessment of the adenoid size. Seven of them depended on Cassano classification which is classified into four grades (grade 1: adenoid/choanal ratio <25%, grade 2: adenoid/choanal ratio from 25 to

Figure 4



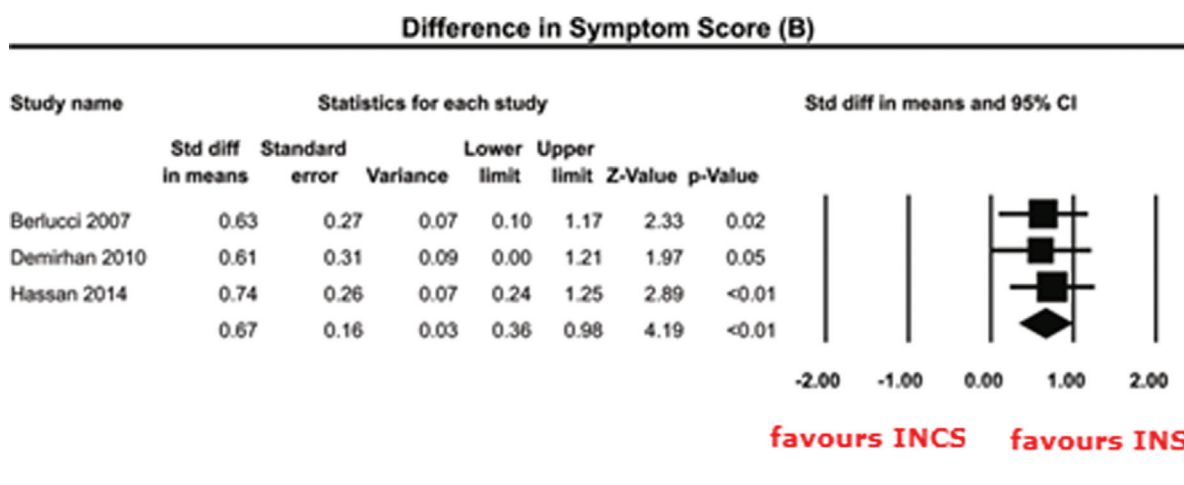
Forest plot of the fourth meta-analysis. Pooling of the studies showed a standardized mean difference (SMD) of -1.53. Although the value of SMD is negative which usually favors the intervention, the  $P$  value=0.14 reflects the nonsignificance of INCS in improving the associated obstructive symptoms. INCS, intranasal corticosteroid; INS, intranasal saline.

Table 5 Results of the fifth meta-analysis

Models	References	SMD	SE	Var.	95% LCL	95% UCL	Z value	P value
	Berlucchi <i>et al.</i> (2007)	0.63	0.27	0.07	0.10	1.17	2.33	0.02
	Demirhan <i>et al.</i> [14]	0.61	0.31	0.09	0.00	1.21	1.97	0.05
	Hassan [13]	0.74	0.26	0.07	0.24	1.25	2.89	<0.01
FEM		0.67	0.16	0.03	0.36	0.98	4.19	<0.01
Heterogeneity								
Q value	DF (Q)	P value	$I^2$					
0.14	2	0.93	0.00					

Tests of heterogeneity showed unimportant heterogeneity among the included studies (Cochran  $Q$ , 0.14;  $I^2$ , 0.00). 95% LCL, 95% lower confidence limit; 95% UCL, 95% upper confidence limit; DF (Q), degrees of freedom for Q test; FEM, fixed effects model; SMD, standardized mean difference; Var., variance.

Figure 5



Forest plot of the fifth meta-analysis. Pooling of the studies showed a standardized mean difference (SMD) of 0.67 with  $P$  value being less than 0.01. The value of SMD is positive, favoring the control, and denoting the nonsignificance of INCS in improving the symptoms. INCS, intranasal corticosteroid; INS, intranasal saline.

50%, grade 3: adenoid/choanal ratio < 75%, grade 4: adenoid/choanal ratio > 75%) [16].

Before being enrolled in the meta-analysis, the individual results of the included studies have shown that nasal obstruction symptoms were improved with INCS in all studies except in one study [10] in which there was not a clear comment about it, but they stated that there was an improvement in adenoid size in 46 children and therefore adenoidectomy was avoided. Also they revealed that there is a reduction in adenoid size with INCS in seven of the included studies [8,10–15] and there was no marked reduction in two studies [7,9].

By using appropriate statistical methods, we made five meta-analyses as regards the adenoid size and the associated symptoms in the treatment and control arms after the use of INCS and INS. Three of them have shown significant reduction in adenoid size. The fourth meta-analysis showed a nonsignificant improvement in nasal obstruction symptoms. The fifth meta-analysis showed significant improvement in symptoms score after the use of INS denoting the nonsignificance of intranasal steroids.

We think that the significant improvement in the adenoid size was due to the direct effect of INCS. Recently, it has been demonstrated that adenoid tissue from children with adenoid hypertrophy had abundant glucocorticoid receptors. This suggests that these children may respond favorably to therapy with INCS. Potential mechanisms for the efficacy of steroids on the reduction of nasal airway obstruction include lympholytic action through the glucocorticoid receptors that causes a direct reduction in adenoid size; a reduction of adenoid inflammation through the anti-inflammatory effect of steroids; or steroid modulation of recurrent infection within the adenoids.

The fourth and the fifth meta-analyses showed nonsignificant improvement in nasal obstruction symptoms after INCS. The included studies in these meta-analysis showed a slightly significant improvement in nasal obstruction [7,9,14,15].

The results of the five meta-analyses tilt the balance in favor of the use of INCS. Yet, the results of the fourth and fifth meta-analyses which revealed no benefit from the use of INCS may be explained, in our opinion, by the following points:

(1) The included studies used different measures to describe their results despite the prevalence of

adenoid hypertrophy. So, there is a need to establish a unified measure to assess the adenoid size and the associated obstruction symptoms to allow easy polling of all data in one meta-analysis, otherwise we would have to depend on the quality of each study.

- (2) The quality of the included studies was assessed by the Jadad score. Only one study got five points from five [9], one study got four points [8], and three studies got three points [7,8,15], while four studies got two points [10,11,13,14]. This would reflect the extent to which high-quality studies are needed.
- (3) Only one study used sample size calculation [9] by which a set of participants is selected from the population, and is less in number (size) but should adequately represent the intended population. So, the true inferences about the intended population could not be drawn from the results obtained.
- (4) Information about the minimum dose of intranasal steroids that would initiate significant improvement was not enough, which may affect the results.
- (5) The long duration of adenoidal obstruction may lead to secondary sites of collapse in the nose and oropharynx, and redundancy in pharyngeal tissues. These consequences may delay the improvement of nasal obstruction symptoms.
- (6) Visual analog scales were assessed by the parents not the children and the parents are usually more pessimistic as regards improving of the symptoms of their children.
- (7) Children mostly continue to be mouth breathers even after adenoidectomy for months and this may affect the interpretations of nasal obstruction symptoms.

Of importance to be pointed out here is the useful information that can be gained from the excluded studies which did not meet the inclusion criteria. Two RCTs showed significant reduction in adenoid size [17,18], while two RCTs showed insignificant improvement in nasal obstruction symptoms [18,19]. These results correspond with the results of our meta-analyses.

Other results from excluded RCTs showed insignificant reduction in adenoid size and other RCTs showed significant improvement in nasal obstruction symptoms [5,17,19,20]. These results contradict our results.

The use of nasal steroids in children is well established, particularly for allergic rhinitis, and its safety is widely

recognized [21]. Six hundred and sixty-seven children participated in all RCTs, less than 2% had epistaxis as a common local side effect which resolved spontaneously without treatment and less than 1% withdrew from the studies because of the local adverse events [9].

## Conclusion

We can use INCS in children with adenoid hypertrophy to reduce the adenoid size and improve the associated symptoms. These recommendations are not applicable to the patients who are already suffering from adenoid hypertrophy complications like significant obstructive sleep apnea or craniofacial malformations. Close monitoring of improving of the symptoms is a must to predict the need of nonmedical management.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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