

## Effectiveness of azelastine nasal spray in the treatment of adenoidal hypertrophy in children

Berkiten G, Kumral TL, Çakır O, Yıldırım G, Salturk Z, Uyar Y, Atar Y

Department of Otorhinolaryngology-Head and Neck Surgery, Okmeydanı Training and Research Hospital, Istanbul, Turkey

### Abstract

**Aim:** To evaluate the effects of topical azelastine treatment on symptoms related to adenoid hypertrophy and the size of adenoid tissue in children.

**Material and Methods:** In total, 60 children who were found to have adenoid hypertrophy were included. A questionnaire on nasal symptoms, nasal endoscopy and skin prick tests was administered to all patients. All patients had complaints of chronic nasal obstruction symptoms and nasal endoscopy showed > 75% choanal obstruction, attributable to adenoid pads. The adenoid/nasopharyngeal areas were calculated. All of the patients underwent azelastine nasal spray therapy (1 spray per nostril, twice daily; 0.28 mg/dose) for 30 days. After 1 month, all children were reassessed. The efficacy of therapy, symptoms, adenoid / nasopharynx ratio, and obstruction ratio, obtained by endoscopy, were compared.

**Results:** Azelastine treatment was well tolerated by all patients. After the first treatment period, the severity of symptoms, endoscopic grade, and adenoid size decreased in all of the 60 patients. There were significant improvements in total subjective symptoms (nasal obstruction, rhinorrhea, cough, snoring, and obstructive sleep apnea) post-treatment.

**Conclusions:** Azelastine nasal spray may be useful in decreasing adenoid pad size and the severity of symptoms related to adenoidal hypertrophy. Hippokratia 2014; 18 (4): 340-345.

**Keywords:** Azelastine, topical administration, adenoid, pediatrics

**Corresponding author:** Güler Berkiten, Department of Otorhinolaryngology-Head and Neck Surgery, Okmeydanı Training and Research Hospital, Darülacez cad. Şişli/İstanbul, Turkey, tel: +905057278724, e-mail: gulerberkiten@gmail.com

### Introduction

Nasal obstruction is a common symptom in children. Adenoidal hypertrophy (AH) is the major causes, and may be related<sup>1</sup>. The etiology of AH is unknown, but inflammatory mechanisms may play an important role. Local and systemic inflammatory markers and pro-inflammatory cytokines are increased in these children; these promote lymphoid tissue proliferation. Proper treatment of this condition is essential for controlling nasal obstructive symptoms. Thus, systemic or topical anti-inflammatory agents have been suggested to have a role in the treatment of AH<sup>2-4</sup>.

Azelastine nasal spray (Allergodil, Lastin, Aflunon; Meda AB, Stockholm, Sweden) is a fast-acting, efficacious and well tolerated H1 receptor antagonist for the treatment of rhinitis<sup>5</sup>. It has mast cell stabilizing and anti-inflammatory properties, reducing the concentration of leukotrienes, kinins, and platelet-activating factor *in vitro* and *in vivo*, as well as reducing inflammatory cell migration in rhinitis patients<sup>6,7</sup>. Well controlled studies in patients with seasonal allergic rhinitis, perennial rhinitis or vasomotor rhinitis have confirmed that azelastine nasal spray has a rapid onset of action and improves the nasal symptoms associated with rhinitis such as nasal congestion

and postnasal drip<sup>8</sup>.

Enlarged adenoids and tonsils, consisting of hypertrophied lymphoid tissue, may lead to obstructive sleep apnea (OSA). In recent years, however, a new understanding of the inflammatory components of OSA has resulted in the idea that anti-inflammatory agents may be a useful non-invasive treatment option in children with OSA<sup>4,9</sup>. Thus, in this study, we sought to assess the efficacy of topical azelastine, which has anti-inflammatory properties, on symptoms and the size of adenoid tissue in children complaining of nasal obstruction.

### Material and Methods

This research was approved by the Ethics Committee of Okmeydanı Training and Research Hospital (protocol number: 0181/08). Sixty children that had been examined in our clinic with a prediagnosis of AH between July 2012 and April 2013 were included in the study. All the children were assessed clinically, endoscopically, and radiologically. Those who had a previous adenoidectomy history and positive history of allergy or atopy, craniofacial malformations including labiopalatal clefts and genetic diseases (eg, Down syndrome), neurologic

disorders, cardiovascular diseases, acute infections in the nose, palate or nasopharynx and history of chronic epistaxis, immunodeficiency disorders or hypersensitivity to azelastine, were excluded from the study. Inclusion criteria were: a history of habitual snoring for at least the previous 3 months and adenoidal hypertrophy confirmed by simple X-ray findings or an endoscopic examination by an otolaryngologist. Allergic rhinitis was diagnosed when a child had typical allergic symptoms and showed positive result in skin prick test.

At baseline, each child underwent a routine ear nose throat examination and nasal endoscopy; a clinical history was obtained from parents using a questionnaire. Patient history included age, gender, personal and family history of atopy, and use of drugs. Diagnosis of AH was confirmed by nasal endoscopy and lateral radiograph. Each cephalometric graph was evaluated by a blinded author. Effectiveness of the therapy was assessed by the change in symptoms and adenoid tissue, evaluated by nasal endoscopic examination and the adenoid/nasopharynx ratio on a lateral radiographic image before and at the end of therapy. After a 4-week course of therapy, all patients were reassessed to evaluate the efficacy of treatment.

Nasal obstruction, rhinorrhea, cough, snoring, and obstructive sleep apnea were the symptoms evaluated. These symptoms were graded according to severity, ranging from 0 to 3 (0: absent, 1: occasional, 2: frequent, 3: constant) developed by Berlucchi et al<sup>10</sup>. Unfortunately Turkish version of this questionnaire had not been validated.

Nasal endoscopy was performed to estimate adenoid size. After application of topical anesthesia in both nostrils (lidocaine 2%) and without decongestion, an endoscopic examination was conducted using a rigid (2.7 mm diameter) endoscope. All nasal endoscopies, conducted as the patient was performing quiet nasal breathing, were recorded using a Karl Storz camera (Karl Storz, Tuttlingen, Germany). The size of the adenoid was determined and the distance of the adenoid tissue from the vomer was assessed<sup>11</sup> and graded as: Grade 1: distance > 1 cm, Grade 2: distance 0.5-1.0 cm, Grade 3: distance < 0.5 cm.

A lateral nasopharyngeal X-ray was performed in all patients in the supine position during nasal inspiration with the necks slightly extended and the mouth closed at a distance of 1 m from the radiation tube. Using the reference points and lines on lateral radiographs of the nasopharynx, adenoid size and nasopharyngeal depth were calculated from all X-rays.

Adenoidal measurement (A) used the line beginning from the most convex point of adenoid tissue and extending to the anterior line of the basioccipital part of the oc-

cipital bone. The nasopharyngeal space (N) was the line extending from the posterior edge of the hard palate and anteroinferior side of the sphenobasioccipital synchondrosis or from the posteroinferior side lateral pterygoid plate to the bony part of the nasopharynx<sup>12</sup>. It was graded as Grade 1 if it was >6 mm, Grade 2 if it was 4-6mm, and Grade 3 if it was 0-3 mm. As adenoidal-nasopharyngeal ratio (A/N ratio) was defined the ratio of adenoid size/nasopharyngeal depth (Fujioka's method)<sup>13</sup>. A/N ratio pre-treatment and post-treatment were compared.

Statistical analyses were conducted using the NCSS (Number Cruncher Statistical System) 2007 and PASS (Power Analysis and Sample Size) 2008 Statistical Software (Utah, USA). Descriptive statistics (mean, standard deviation and frequency), as well as Kruskal Wallis test for the non-parametric data and Mann Whitney U test for post-hoc comparison were used to compare qualitative data for analysis. Spearman's correlation test was also used for the evaluation of the relationship between the parameters. P values <0.05 and p<0.01 were considered to indicate statistical significance.

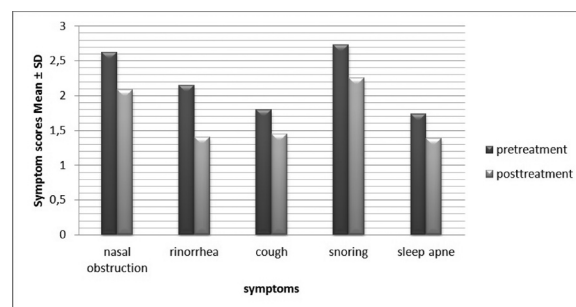
## Results

No patient had a personal or family history of allergy or atopy, had undergone previous surgery, had received any drugs in the past 4 weeks, or had immunodeficiencies.

In total, 60 children (32 males, 28 females), aged 6-14 years, with nasopharyngeal obstruction due to adenoid hypertrophy were included in the study. The mean age was  $8.52 \pm 2.48$  years (Table 1).

There were significant differences in nasal obstruction, rhinorrhea, cough, snoring, and obstructive sleep apnea between pre- and post-treatment ( $p = 0.001$ ) (Table 2, Figure 1).

There was statistically significant decrease of an av-



**Figure 1:** Pre-treatment and post-treatment symptom scores of the 60 children with adenoidal hypertrophy that were included in the study.

**Table 1:** Age and gender distribution of the 60 children with adenoidal hypertrophy that were included in the study.

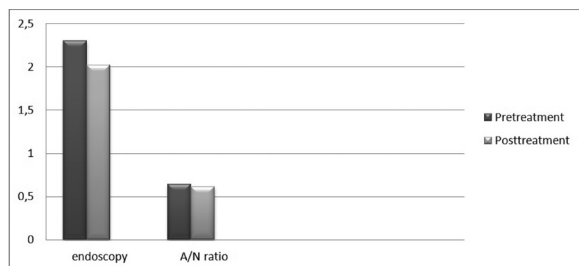
Age (years)	Total	Min-Max	Mean ± SD
		6-14	$8.52 \pm 2.48$
	Female 28 (46.7%)	6-14	$8.61 \pm 2.41$
	Male 32 (53.3%)	6-14	$8.44 \pm 2.58$

SD: standard deviation

**Table 2:** Evaluation of the pre-treatment and post-treatment symptom scores of the 60 childrens with adenoidal hypertrophy that were included in the study.

		Pre-treatment			Post-treatment			p <sup>a</sup>
		Score-1	Score-2	Score-3	Score-1	Score-2	Score-3	
Obstruction	n	0	23	37	11	33	16	0.001**
	%	0.0	38.3	61.7	18.3	55.0	26.7	
	Mean±SD	2.62 ± 0.49			2.08 ± 0.67			
	Median	3.00			3.00			
Rhinorrhea	n	5	41	14	36	24	0	0.001**
	%	8.3	68.3	23.3	60.0	40.0	0.0	
	Mean±SD	2.15 ± 0.55			1.40 ± 0.49			
	Median	2.00			1.00			
Cough	n	20	32	8	33	27	0	0.001**
	%	33.3	53.4	13.3	55.0	45.0	0.0	
	Mean±SD	1.80 ± 0.66			1.45 ± 0.50			
	Median	2.00			1.00			
Snoring	n	0	16	44	0	45	15	0.001**
	%	0.0	26.7	73.3	0.0	75.0	25.0	
	Mean±SD	2.73 ± 0.45			2.25 ± 0.44			
	Median	3.00			2.00			
Sleep Apnea	n	22	32	6	37	23	0	0.001**
	%	36.7	53.3	10.0	61.7	38.3	0.0	
	Mean±SD	1.73 ± 0.63			1.38 ± 0.49			
	Median	2.00			1.00			

n: number, SD: standard deviation, <sup>a</sup>: Wilcoxon Signed Ranks Test, \*\*: p<0.01.

**Figure 2:** The distribution of the pre-treatment and post-treatment endoscopy and adenoidal-nasopharyngeal ratio (A/N ratio).

average  $0.53 \pm 0.79$  units in the post-treatment nasal obstruction symptom scores, compared with pre-treatment scores ( $p < 0.01$ ). In the participating children, 61.7% ( $n=37$ ) showed no improvement while 38.3% ( $n=23$ ) had improvement (Table 2, Figure 1).

There was statistically significant decrease of an average  $0.75 \pm 0.57$  units in the post-treatment rhinorrhea symptom scores compared with pre-treatment scores ( $p < 0.01$ ). In the participating patients, 31.7% ( $n=19$ ) showed no improvement while 68.3% ( $n=41$ ) had improvement (Table 2, Figure 1).

There was statistically significant decrease of an average  $0.35 \pm 0.66$  units in the post-treatment cough symptom scores compared with pre-treatment scores ( $p < 0.01$ ). In the participating patients, 61.7% ( $n=37$ ) showed no improvement while 38.3% ( $n=23$ ) had improvement (Table 2, Figure 1).

There was statistically significant decrease of an average  $0.48 \pm 0.57$  units in the post-treatment snoring symptom

scores compared with pre-treatment scores ( $p < 0.01$ ). In the participating patients, 48.3% ( $n=29$ ) showed no improvement while 51.7% ( $n=31$ ) had improvement (Table 2, Figure 1).

There was statistically significant decrease of an average  $0.35 \pm 0.61$  units in the post-treatment sleep apnea symptom scores compared with pre-treatment scores ( $p < 0.01$ ). In the participating patients, 61.7% ( $n=37$ ) showed no improvement while 37.3% ( $n=23$ ) had improvement (Table 2, Figure 1).

There was a significant decrease in adenoid size endoscopically at the end of the therapy (Table 3;  $p=0.001$ ). The  $0.28 \pm 0.49$  units of mean decrease was statistically significant in the post-treatment endoscopy grades compared with pre-treatment endoscopy grades ( $p < 0.01$ ). In the participating patients, 73.3% ( $n=44$ ) showed no improvement while 26.7% ( $n=16$ ) had improvement (Table 3).

The mean A/N ratio was  $0.64 \pm 0.10$  before treatment and  $0.61 \pm 0.10$  after treatment. The decrease in the post-treatment A/N ratio compared with pre-treatment A/N ratio was statistically significant in patients participating in this study ( $p < 0.01$ ). Twenty three children (38.3% of this group) showed no improvement while 61.7% ( $n=37$ ) had improvement (Table 4, Figure 2).

The positive relationship at the level 68.8% between pre-treatment endoscopy scores and A/N ratio measurement was statistically significant ( $r=0.688$ ;  $p < 0.01$ ).

There was also statistically significant positive directional relationship at the level of 56.9% between post-treatment endoscopy scores and A/N ratio measurements ( $r=0.569$ ;  $p < 0.01$ ) (Tables 5 and 6). As the pre-treatment endoscopic grade increased, A/N ratio levels also showed

**Table 3:** The evaluation of the pre-treatment and post-treatment endoscopic grades of the 60 childrens with adenoidal hypertrophy that were included in the study.

	Pretreatment			Posttreatment			P <sup>a</sup>	
	Grade 1	Grade 2	Grade 3	Grade 1	Grade 2	Grade 3		
Endoscopy	n	11	20	29	18	23	19	
	%	18.3	33.3	48.3	30.0	38.3	31.7	
	Mean ± SD	2.30 ± 0.77			2.02 ± 0.79			0.001**
	Median	2.00			2.00			

n: number, SD: standard deviation, <sup>a</sup>: Wilcoxon Signed Ranks Test, \*\*: p<0.01.

**Table 4:** Pre-treatment and post-treatment A/N ratio measurements.

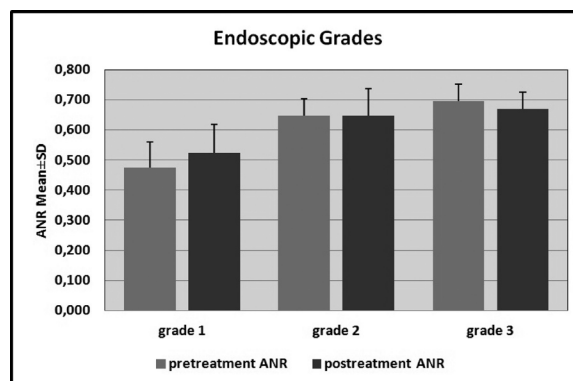
	Mean	Standart Deviation	p <sup>a</sup>
Pre-treatment A/N ratio	0.64	0.10	0.001**
Post-treatment A/N ratio	0.61	0.10	

<sup>a</sup>: Wilcoxon Signed Ranks Test, \*\*: p<0.01.

an increase (Figure 3). As the post-treatment endoscopic grade increased, A/N ratio levels also increased (Figure 3).

**Discussion**

AH is one of the most frequent pathological conditions in the pediatric age group, the clinical manifestations of which differ according to adenoid size. Bilateral nasal obstruction is a primary complaint that can be associated with



**Figure 3:** Pre-treatment and post-treatment endoscopy grades according to the adenoidal-nasopharyngeal ratio (A/N ratio).

**Table 5:** The relationship between endoscopy grades and A/N ratio measurements.

	Endoscopy Score - A/N ratio	
	r	p
Pre-treatment	0.688	0.001**
Post-treatment	0.569	0.001**

r: Spearman correlation coefficient, \*\*: p<0.01.

**Table 6:** The distribution of endoscopic grades according to A/N ratio measurements.

Endoscopic grade		Pre-treatment A/N ratio	Post-treatment A/N ratio
Grade 1	n	11	18
	Mean	0.475	0.523
	SD	0.085	0.097
	Median	0.48	0.53
	Minimum	0.33	0.33
	Maximum	0.6	0.75
GRADE 2	n	20	23
	Mean	0.648	0.647
	SD	0.057	0.090
	Median	0.64	0.63
	Minimum	0.57	0.51
	Maximum	0.77	0.81
GRADE 3	n	29	19
	Mean	0.697	0.669
	SD	0.056	0.056
	Median	0.68	0.67
	Minimum	0.6	0.57
	Maximum	0.79	0.76
p		0.001**	0.001**

Kruskal Wallis test was used, n: number, SD: standard deviation, \*\*p<0.01.

various sleep disorders, ranging from snoring to OSA<sup>14</sup>.

AH is also one of the most frequent indications for surgery in childhood and adenoidectomy is generally considered the definitive treatment for nasopharyngeal obstruction. As adjunctive treatments, few non-surgical alternatives that reduce adenoid size are available. Several authors have proposed the use of topical nasal steroids to decrease AH, with the intention of preserving immunologically active tissue and avoiding the risks of anesthesia and surgery inherent in adenoidectomy<sup>3,10,15-18</sup>. It is believed to be several mechanisms, such as direct lymphocytic action, inhibition of inflammation, and alterations in adenoid bacterial flora<sup>15</sup>. In this study, we aimed to assess the effects of azelastine therapy in children with adenoid hypertrophy. To our knowledge, no study of the use of topical azelastine for the treatment of AH has been published, so we evaluated the use of intranasal azelastine nasal spray for the treatment of AH. The use of a topical azelastine treatment has many advantages over a systemic treatment<sup>8</sup>. First, with a nasal spray, medication can be delivered directly to the site of the allergic inflammation. Second, higher concentrations of antihistamines can be achieved in the nasal mucosa by topical versus oral administration<sup>8</sup>. In controlled studies, azelastine nasal spray was well-tolerated for treatment durations up to 4 weeks in adults and children ( $\geq 12$  years)<sup>19,20</sup>. In this study, Azelastine treatment was well-tolerated by all patients (age range: 6-14 years).

There have been various studies of finger palpation, transoral mirror adenoid examination, baseline lateral soft-tissue radiographs of the nasopharynx, and nasal endoscopy; these are commonly used to assess adenoid size<sup>14,21-25</sup>. In recent decades, technological advances have resulted in the development of flexible and rigid endoscopes with small diameters (2.7mm), which enable accurate nasal endoscopic examination with fewer complications. Nasofiberoendoscopy is currently considered as the 'gold standard' examination for the evaluation of adenoid hypertrophy<sup>23</sup>. Fiberoptic and rigid endoscopic examinations is more effective in identifying AH<sup>26</sup>. However, fiberoptic and rigid endoscopic examinations of a child's nasopharynx can be challenging and might not be appropriate for all patients. In some children, it is impossible to examine the nasopharynx due to patient non-cooperation<sup>27</sup>. Fujioka et al<sup>13</sup> described the A/N ratio as an indicator of adenoidal size in 1979, and this method has since been adopted in many studies<sup>28</sup>. Thus, lateral nasopharyngeal radiography can be used to assess adenoidal size in children who will not cooperate with an endoscopic examination. Mlynarek et al<sup>29</sup> reported that direct video rhinoscopy was better correlated with the severity of symptoms than values obtained by lateral neck radiography. Office nasal endoscopy offers several advantages over the lateral skull radiograph in the evaluation of adenoid hypertrophy. Eustachian tube and airway obstruction can be readily identified through nasal endoscopy in all 3 planes. The relationship of the adenoid to the adjacent torus tubaris, vomer, and soft palate can

be easily evaluated in a dynamic fashion that allows for complete evaluation of the nasopharynx. In this study, we used lateral nasopharyngeal X-rays, nasal endoscopy, and symptom scores to assess adenoid hypertrophy. We examined the correlation between lateral nasopharyngeal X-ray, nasal endoscopy and subjective symptoms. The results of lateral neck X-ray and nasal endoscopy showed good correlation with actual adenoid size. Caylaklı<sup>30</sup> revealed significant correlation between A/N ratio and nasal endoscopic examination findings. The changes in A/N ratio and improvement of endoscopic findings showed a significant correlation in our study. As a result, this study suggests the use of endoscopic examination in assessing adenoid size in suitable patients because it avoids radiation exposure.

Our data indicate significant improvements in symptom scores, endoscopy, and A/N ratio in children with AH and allergic rhinitis after a 4-week trial of intranasal azelastine. Nasal obstruction, rhinorrhea, cough, snoring, and obstructive sleep apnea improved significantly. In our study, 37 of 60 children decreased A/N ratio after 4 weeks course of treatment ( $p=0.001$ ). Additionally, the rates of improvement of symptom scores, A/N ratio, and endoscopic examination were correlated, consistent with previous reports<sup>30</sup>. We think that this type of inflammation might exist in covering mucosa of adenoid which locates at narrowest area of upper airway. For this reason, application of topical azelastine for 4 weeks might reduce the inflammation of covering mucosa of adenoid.

In our study, 37 of 60 children (61.7%) who had been evaluated with lateral nasopharyngeal radiography showed a decreased A/N ratio after a 4-week course of treatment ( $p=0.001$ ). There were significant differences in symptom scores, X-ray findings (A/N ratio), and nasal endoscopic grade in children with AH. These findings suggest that azelastine is a suitable treatment choice in selected patients.

The main limitation of the present study is that we could not establish a control group due to lack of consent. At the early period of this study parents and caregivers refused to participate in our study because they wanted early solution. Another important limitation is the lack of long term follow up. Patients were followed up for 3 months after they completed therapy. None of them complained from the severe symptoms as at the beginning of the study. Therefore we can claim that azelastine can be used to delay operation date in necessary situations at least for 3 months.

### Conclusion

This study reported the efficacy of Azelastine nasal spray for the treatment of AH in children. Intranasal azelastine therapy appears to be useful in the treatment of AH in the general pediatric population with AR.

### Conflict of interest

There is no conflict of interest among authors.

### References

1. Ameli F, Brocchetti F, Tosca MA, Signori A, Ciprandi G. Adenoidal hypertrophy and allergic rhinitis: is there an inverse relationship? *Am J Rhinol Allergy*. 2013; 27: e5-e10.
2. Goldbart AD, Goldman JL, Veling MC, Gozal D. Leukotriene modifier therapy for mild sleep-disordered breathing in children. *Am J Respir Crit Care Med*. 2005; 172: 364-370.
3. Alexopoulos EI, Kaditis AG, Kalampouka E, Kostadima E, Angelopoulos NV, Mikraki V, et al. Nasal corticosteroids for children with snoring. *Pediatr Pulmonol*. 2004; 38: 161-167.
4. Friedman BC, Goldman RD. Anti-inflammatory therapy for obstructive sleep apnea in children. *Can Fam Physician*. 2011; 57: 891-893.
5. Zechel HJ, Brock N, Lenke D, Achterrath-Tuckermann U. Pharmacological and toxicological properties of azelastine, a novel antiallergic agent. *Arzneimittelforschung*. 1981; 31: 1184-1193.
6. Bernstein JA. Azelastine hydrochloride: a review of pharmacology, pharmacokinetics, clinical efficacy and tolerability. *Curr Med Res Opin*. 2007; 23: 2441-2452.
7. Lee TA, Pickard AS. Meta-analysis of azelastine nasal spray for the treatment of allergic rhinitis. *Pharmacotherapy*. 2007; 27: 852-859.
8. Horak F. Effectiveness of twice daily azelastine nasal spray in patients with seasonal allergic rhinitis. *Ther Clin Risk Manag*. 2008; 4: 1009-1022.
9. Kuhle S, Urschitz MS. Anti-inflammatory medications for obstructive sleep apnea in children. *Cochrane Database Syst Rev*. 2011; 19: CD007074.
10. Berlucchi M, Salsi D, Valetti L, Parrinello G, Nicolai P. The role of mometasone furoate aqueous nasal spray in the treatment of adenoidal hypertrophy in the pediatric age group: preliminary results of a prospective, randomized study. *Pediatrics*. 2007; 119: e1392-e1397.
11. Wang DY, Bernheim N, Kaufman L, Clement P. Assessment of adenoid size in children by fiberoptic examination. *Clin Otolaryngol Allied Sci*. 1997; 22: 172-177.
12. Cohen J. A coefficient of agreement for nominal scales. *Educ Psychol Measure*. 1960; 20: 37-46.
13. Fujioka M, Young LW, Girdany BR. Radiographic evaluation of adenoidal size in children: adenoidal-nasopharyngeal ratio. *AJR Am J Roentgenol*. 1979; 133: 401-404.
14. Craig TJ, Teets S, Lehman EB, Chinchilli VM, Zwillich C. Nasal congestion secondary to allergic rhinitis as a cause of sleep disturbance and daytime fatigue and the response to topical nasal corticosteroids. *J Allergy Clin Immunol*. 1998; 101: 633-637.
15. Demain JG, Goetz DW. Pediatric adenoidal hypertrophy and nasal airway obstruction: reduction with aqueous nasal beclomethasone. *Pediatrics*. 1995; 95: 355-364.
16. Brouillette RT, Manoukian JJ, Ducharme FM, Oudjhane K, Earle LG, Ladan S, et al. Efficacy of fluticasone nasal spray for pediatric obstructive sleep apnea. *J Pediatr*. 2001; 138: 838-844.
17. Cengel S, Akyol MU. The role of topical nasal steroids in the treatment of children with otitis media with effusion and/or adenoid hypertrophy. *Int J Pediatr Otorhinolaryngol*. 2006; 70: 639-645.
18. Salib JR, Howarth PH. Safety and tolerability profiles of intranasal antihistamines and intranasal corticosteroids in the treatment of allergic rhinitis. *Drug Saf*. 2003; 26: 863-893.
19. Storms WW, Pearlman DS, Chervinsky P, Grossman J, Halverson PC, Freitag JJ, et al. Effectiveness of azelastine nasal solution in seasonal allergic rhinitis. *Ear Nose Throat J*. 1994; 73: 382-386, 390-394.
20. Ratner PH, Findlay SR, Hampel F Jr, van Bavel J, Widlitz MD, Freitag JJ. A double-blind, controlled trial to assess the safety and efficacy of azelastine nasal spray in seasonal allergic rhinitis. *J Allergy Clin Immunol*. 1994; 94: 818-825.
21. Crof CB, Thomson HG, Samuels MP, Southall DP. Endoscopic evaluation and treatment of sleep-associated upper airway obstruction in infants and young children. *Clin Otolaryngol Allied Sci*. 1990; 15: 209-216.
22. Wang D, Clement P, Kaufman L, Derde MP. Fiberoptic evaluation of nasal cavity and nasopharynx in children. *Int J Pediatr Otolaryngol*. 1992; 24: 35-44.
23. Kubba H, Bingham BJ. Endoscopy in the assessment of children with nasal obstruction. *J Laryngol Otol*. 2001; 115: 380-384.
24. Cassano P, Gelardi M, Cassano M, Fiorella ML, Fiorella R. Adenoid tissue rhinopharyngeal obstruction grading based on fibroendoscopic findings: a novel approach to therapeutic management. *Int J Pediatr Otorhinolaryngol*. 2003; 61: 1303-1309.
25. Feres MF, Hermann JS, Sallum AC, Pignatari SS. Endoscopic evaluation of adenoids: reproducibility analysis of current methods. *Clin Exp Otorhinolaryngol*. 2013; 6: 36-40.
26. Bitar MA, Birjawi G, Youssef M, Fuleihan N. How frequent is adenoid obstruction? Impact on the diagnostic approach. *Pediatr Int*. 2009; 51: 478-483.
27. Parikh SR, Coronel M, Lee JJ, Brown SM. Validation of a new grading system for endoscopic examination of adenoid hypertrophy. *Otolaryngol Head Neck Surg*. 2006; 135: 684-687.
28. Salturk Z, Yucesan S, Atar Y, Bal M, Ucar K. Concordance of lateral radiological measurements and quality of life in adenoid hypertrophy. *J Clin Analytical Med*. 2014; 5: 110-112.
29. Mlynarek A, Tewfik MA, Hagr A, Manoukian JJ, Schloss MD, Tewfik TL, et al. Lateral neck radiography versus direct video rhinoscopy in assessing adenoid size. *J Otolaryngol*. 2004; 33: 360-365.
30. Caylakli F, Hizal E, Yilmaz I, Yilmazer C. Correlation between adenoid-nasopharynx ratio and endoscopic examination of adenoid hypertrophy: a blind, prospective clinical study. *Int J Pediatr Otorhinolaryngol*. 2009; 73: 1532-1535.