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Article

Efficacy and safety of fluticasone propionate nasal spray in treatment ofadenoidal hypertrophic snoring in children

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This study investigatedthe efficacy and safety offluticasone propionate nasal spray in treatment of adenoidal hypertrophic snoring in children.Fifty-six children with adenoidal hypertrophic snoring were enrolled. According to adenoidal-nasopharyngeal ratio (ANR) in lateral nasal X-ray examination,the children were assigned in moderategroup (23 cases) and severegroup (33 cases).The fluticasone propionate nasal spray was used for all patientsfor 4 weeks.In 56 patients, after treatment, compared with before treatment, the snoring, sleep apneaand nasal obstruction scores in moderategroupand the nasal obstruction score in severegroupwere significantly decreased,respectively ($P < 0.05$).The decreases of snoring, sleep apnea, mouth breathing and nasal obstruction scores after treatment in moderate group were significantly higher than those in severe group, respectively ($P <0.001$).After treatment, in 18 patients with ateral nasal X-ray examination,the adenoid size was obviously reduced, and the nasopharynx airway was obviously enlarged. The meanANRdropped from 0.76±0.10 to 0.72±0.09($P <0.001$).Duringtreatment, only 2 of 56 patients were reported with intranasal dryness and occasional epistaxis, which were self-healed without treatment.Fluticasone propionate nasal spray is effective and safe for treatment of children's snoring caused by adenoidal hypertrophy.

Keywords: Adenoidal hypertrophy. Snoring. Fluticasone propionate. Children.

INTRODUCTION

There are various causes of snoring in children, including adenoidal hypertrophy, enlarged tonsil, acute and chronic rhinitis and sinusitis, obesity, etc.. The adenoidal hypertrophy is the most commonproblem affecting the pediatrichealth, and the adenoidectomy is one of the most frequently performed treatment procedures (Mlynarek *et al.*, 2004). In recent years, the age of children undergoing adenoidectomy is decreasing, and thesurgery may lead to complications such as early or late bleeding (4%-5%), adenoid tissue recurrence (10%-20%),postoperative dyspnea (27%)(Shokouhi *et al.*, 2015), andeven death and other complications(Gerhardsson *et al.*, 2016).In addition, the risk caused by anesthesia is also an important factor of adenoidectomy. Meanwhile,the adenoids, like tonsils, are the important immune organs in the upper respiratory tract, and the surgical indications are still controversial (Paulussen *et al.*,2000). Therefore, for treatment of children with adenoid hypertrophy, the intranasal steroidtherapy alternativeto adenoidectomy is importantand must be tried before surgery (Yilmaz *et al.*, 2013). The reliability of application of nasal steroids to children has been reported in many studies (Wandalsen, Mendes, Solé, 2010; Emin *et al.*, 2011). Among the steroid drugs, the fluticasone propionate is proved to be a reliable drug in children over 3 years old (Brouillette *et al.*, 2001). Only a few adverse reactions of fluticasone propionate have been reported(Boner *et al.*, 2010),but whetherthis is due to poor reports or

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indeed fewadverse effectis not clearly known. Can the nasal steroid therapy prevent childrenwith adenoidal hypertrophic snoring from surgery? In this study, the efficacy and safety of fluticasone propionate nasal spray in treatment of adenoidal hypertrophic snoring in children was investigated. The objective was to provide a reference for the furtherapplication of this strategyin treating adenoidal hypertrophic snoring in children.

SUBJECTS AND METHODS

Subjects

Fifty-six children with adenoidal hypertrophic snoring who were treated in the Department of Otolaryngology, Zhejiang Xiaoshan Hospital from January 2016 to September 2018 were enrolled in this study. There were 44 males and 12 females. Their age was 3-12 years, with mean age of 7.34±2.56 years. This study was approved by the Institutional Review Board of the Zhejiang Xiaoshan Hospital. The detailed information about the study was given to the participant' parents or legal guardians. The informed consent for participation in the study was obtained before the initiation of study.

Inclusion criteria and exclusion criteria

The inclusion criteria were as follows: i) thepatients presenteddifferent degrees of sleep snoring,with or without sleep apnea, chronic mouth breathingand nasal obstruction; ii) the adenoidal-nasopharyngeal ratio (ANR) was no less than 0.61by lateral nasal X-ray examination; iii) the patients had no previous adenoidectomy.The exclusion criteria were as follows: i) the patients had upper respiratory infection or tonsillar hypertrophy (grade II and higher) within the past two weeks; ii) the patients had nasal anatomic anomalies or sinonasal diseases; iii) the patients had history of epistaxis; iv) the patients had craniofacial malformations or immunodeficiency; v) the patients were hypersensitive to steroids; vi) the patients had received the intranasal, topicalor systemic steroid or antibiotic treatment within the past 4 weeks.

Treatmentmethod

Fluticasone propionate nasal spray was used for all patients once per day, 2 sprays per nostril (4 sprays per day; total 200μgper day). The treatment was continued for4 weeks.It is informed that the nozzle should not be directed towards the nasal septum when spraying.

X-ray examination

The lateral nasal X-ray examination was made in all patients in the supine position during nasal inspiration, with their necks slightly extended and the mouths closed toradiation tube with 1 m distance. The childwho could not stand alone was hold by one parent. Both the parent and child were covered with lead aprons. The X-ray films were stored in the computer in the radiology unit. The ANR0.61-0.70 in lateral nasal X-ray examination presented the moderate adenoidal hypertrophy, and ANR ≥0.71 presented the severe adenoidal hypertrophy(Acar *et al.*, 2014).According to this, the children were assigned in moderategroup (23 cases) and severegroup (33 cases).The lateral nasal X-ray examination was performed again at the end of treatment.The films were assessed by the same physicianaccording to previously described methods.

Sleep symptom questionnaire and observation of side effects

Before and the end of treatment, a questionnaire including a numerical grading scale for duration of sleep symptoms (snoring, sleep apnea, mouth breathing, nasal obstruction) was filled in by the participant' parents or legal guardians.The numerical grading scale was evaluatedusing a clinical scoring system(Brouilette *et al.*, 1984) ranging from 0 to 3 points (0 point: no symptom;1 point: mild symptom;the symptom continued for 1/4-1/2 of the whole night;2 points: moderate symptom;the symptom continued for 1/2-3/4 of the whole night;3points: severe symptom;the symptom continued for 3/4-1/1 of the whole night). Thevalues of symptom of snoring, sleep apnea, mouth breathing and nasal obstructionwere added together to give a total symptom score for each patient.During the

follow-up, the side effects such as intranasal dryness and occasional epistaxis were observed.

Statistical analysis

All statistical analysis was carried out using SPSS 18.0 software (SPSS Inc., Chicago, IL, USA). According to the type of analyzed variables, the baseline characteristics were presented as median (interquartile range) and percentile,which were analyzed using Mann-Whitney non-parametricU-test and Chi-square test, respectively. In addition, the symptomscores and ANR were presented as mean±SDfor the comparison between before and after treatment and between two groups using t test. $P < 0.05$ was considered as statistically significant.

RESULTS

Baseline demographics, symptom scores and ANR of patients

Fifty-six children took part in this study. In moderate group, there were 19 (33.9%) males and 4 (7.2%) females. In severe group, there were 25 (44.6%) males and 8 (14.3%) females. The baseline demographics, symptom scores and ANR of patients in two groups were summarized in Table I.There was no significant difference in age, gender, height, weight or mouth breathing score between two groups. The snoring score ($P = 0.012$), sleep apnea score ($P = 0.009$), nasal obstruction score ($P = 0.032$) and ANR ($P < 0.001$) in severe groupwere significantly higher than those in moderate group, respectively.

TABLE I - Baseline demographics, symptom scores and ANR in groups

Parameter n	Moderate group 23	Severe group 33	P
Age ((median (IQR), years)	9.0 (5.0-10.0)	7.0 (5.0-10.0)	0.547
Gender (n (%), male)	19 (82.6)	25 (75.8)	0.488
Height (M (IQR), cm)	130.0 (110.0-145.0)	120.0 (108.5-147.5)	0.799
Weight (M (IQR), kg)	34.0 (20.0-45.0)	25.0 (19-45.5)	0.977
Snoring score (M (IQR), points)	2 (2-3)	3 (2-3)	0.012
Sleep apnea score (M (IQR), points)	1 (0-2)	2 (1-2)	0.009
Mouth breathing score (M (IQR), points)	2 (1-3)	3 (2-3)	0.076
Nasal obstruction score (M (IQR), points)	2 (1-2)	2 (2-3)	0.032
ANR (M (IQR))	0.67 (0.63-0.68)	0.85 (0.80-0.90)	< 0.001

M (IQR), median (interquartile range); ANR, adenoidal-nasopharyngeal ratio.

Treatment efficacy

After 4 weeks of treatment, the symptomsof 56 childrenwere reported by their parents or legal guardians. In moderate group, compared with before treatment, after treatmentthe snoring score ($P = 0.022$), sleep apnea score ($P = 0.031$) and nasal obstruction score ($P < 0.001$) were significantly decreased, respectively, but the mouth breathing score was not significantly changed. In severe group, compared with before treatment, after treatment the nasal obstruction score was significantly decreased ($P = 0.002$), but the snoring score, sleep apneascore and mouth breathing scorewere not significantly changed(Table II).Thedecreases of symptom scores after treatment in two groups were shown in Table III.

The decrease of snoring score, sleep apnea score, mouth breathing score and nasal obstruction scoreafter treatment in moderate group were significantly higher than those in severe group, respectively (all P < 0.001).

TABLE II - Symptom scores before and after treatment in two groups (points)

Symptom	Moderate group (n = 23)			Severe group (n = 33)		
	Before treatment	After treatment	P	Before treatment	After treatment	P
Snoring	2.09±0.73	1.87±0.81	0.022	2.58±0.66	2.42±0.71	0.096
Sleep apnea	1.13±0.87	0.83±0.72	0.031	1.76±0.83	1.52±0.79	0.103
Mouth breathing	1.96±0.98	1.70±0.70	0.110	2.39±0.83	2.21±0.82	0.136
Nasal obstruction	1.83±0.94	1.13±0.81	< 0.001	2.30±0.68	1.85±0.91	0.002

TABLEIII - Decrease of symptom scores after treatment in two groups

Symptom	Decrease of score (points)		P
	Moderate group (n = 23)	Severe group (n = 33)	
Snoring	0.22±0.02	0.16±0.02	< 0.001
Sleep apnea	0.31±0.03	0.23±0.04	< 0.001
Mouth breathing	0.25±0.03	0.19±0.02	< 0.001
Nasal obstruction	0.69±0.08	0.45±0.04	< 0.001

After treatment, 38 cases in 56 patientswere excluded from the radiographic comparison due to the refusing from their parentsor legal guardians. The remaining 18 patients received the lateral nasopharynxX-ray examination. After treatment the adenoid size was obviously reduced, and the nasopharynx airway was obviously enlarged (Figure 1). Excepting 3 cases, the ANR decreased in varying degrees in other 15 cases (Figure 2). In these 18 patients, after treatment the mean ANR of 18 patients dropped from 0.76±0.10 to 0.72±0.09, with significant difference between them (P < 0.001). In addition, the sleep apnea score dropped from 2.33±0.77 points to 2.06±0.94 points (P = 0.020), the snoring score dropped from 1.67±0.91 points to 1.17±0.79 points (P = 0.015), and the nasal obstruction score dropped from 1.83±0.86 points to 1.06±0.87 points (P = 0.002). There was no significant improvement of mouth breathing score (P = 0.542) (Table IV).

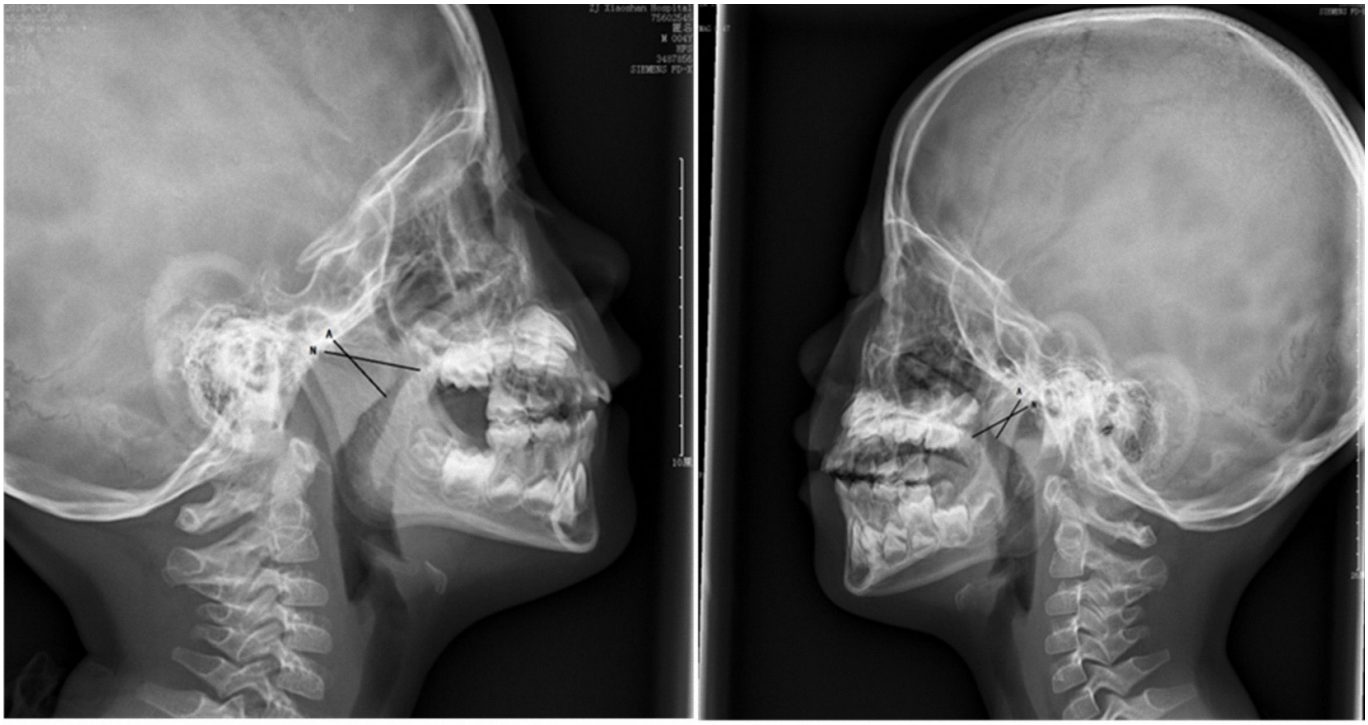

FIGURE 1 -Lateral nasopharynx X-ray examination of one patient before treatment (A) and after treatment (B).

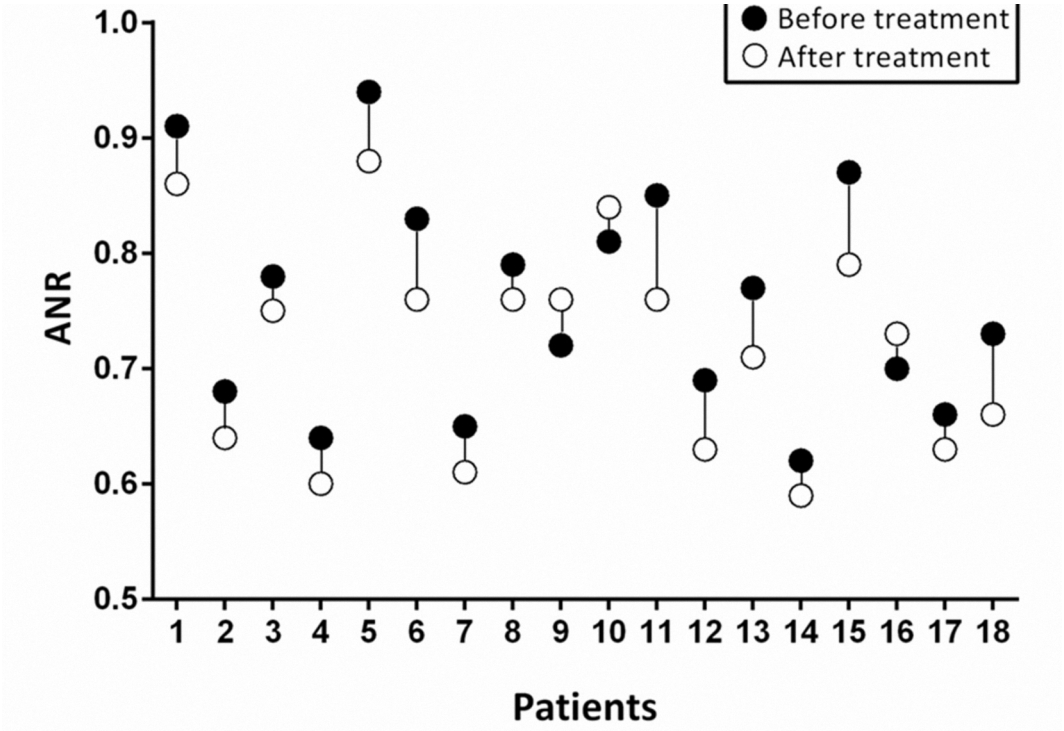

FIGURE 2 - Change of ANR before treatment and after treatment in 18 patients. ANR, adenoidal-nasopharyngeal ratio.

TABLE IV - Symptom scores and ANR before and after treatment in 18 patients

Index	Before treatment	After treatment	P
Sleep apnea score	2.33±0.77	2.06±0.94	0.020
Snoring score	1.67±0.91	1.17±0.79	0.015
Mouth breathing score	1.94±0.10	1.83±0.92	0.542
Nasal obstruction score	1.83±0.86	1.06±0.87	0.002
ANR	0.76±0.10	0.72±0.09	< 0.001

ANR, adenoidal-nasopharyngeal ratio

Side effects

During the treatment, the side effectsof therapy were observed by the parents or legal guardians of children. Only two patientswere reported with intranasal dryness and occasional epistaxis, respectively, which were self-healed without treatment. There was no obviousside effect in other patients.

DISCUSSION

Adenoidal hypertrophy is a common disease in children. The hypertrophic adenoidblocksthe nasopharyngeal airway which leads tothe anterior open bite and adenoid face(Reda, Kamel, Abdel, 2013), withemergence ofmouth breathing, nasal obstruction, snoring, sleep apneaand otitis media(Shi, Li, Wu, 2009), and even serious mentalproblem, learning difficulty and memory loss(Song, Ji,2009).Therefore, in recent years the adenoidectomy has become one of the most common surgery in childhood, but the risks of postoperative bleeding anddisease recurrence haveattracted more and more attention from clinicians(Contencin,Guilleminault, Manach, 2003).How to use effective drugs for the treatment of adenoid hypertrophy is a concern for the clinicians.Goldbart *et al.* (2005) have confirmed that, the glucocorticoid receptors are expressed in the adenoid tissue of children. Zhang *et al.*(2007) havefound that, in the adenoidal hypertrophy children, especiallywith snoring, the glucocorticoid receptor subtypeis expressed in the adenoid tissue, and the atomization inhalation therapy can make the steroid drugs to reach the target organs with highconcentration and fastspeed. This makes it possible to use nasal steroid spraytherapyto treat the adenoid hypertrophy.

Themechanisms of nasal steroid treatment for adenoidal hypertrophymay be that, the steroid drugs combine to the glucocorticoid receptors in the adenoidal tissue, and directly damage the lymphocytes, reduce the inflammatory reaction in nasal cavity and nasopharynx, change the adenoidal colony state, thereby reducing the inflammatory adenoidal hypertrophy (Criscuoli *et al.*, 2003). Demirhan *et al.*(2010) have found that,in adenoidal hypertrophy children, after excessive administration with fluticasone propionate nasal spray (400μg/day) for 8 weeks, the initial adenoid/choanaratiodrops from 87% to 56%,with a total decrease of 35.6%.On the contrary, Brouillette *et al.* (2001) have reported that,the reduction in adenoid size caused by fluticasone propionate nasal sprayshows no significant difference with placebo. Results of the present study showed that, in 18 children with adenoidal hypertrophy, after treatment the adenoid size was obviously reduced, and the nasopharynx airway was obviously enlarged.In addition, the ANR after treatment was significantly lower than that beforetreatment. This indicates that, the fluticasone propionate nasal spray can effectively reduce the adenoid size.There were 3 cases in which the ANR was not significantly decreased after treatment. There 3 cases hadupper respiratory tractinfection during the treatment period, which might affect the treatment outcome. In addition, this may be related to the shorter medication time and smaller dosage. Therefore, thefurther treatment and follow-up are necessary.

Ngamphaiboon *et al.* (1997) have evaluated the efficacy and safety of fluticasone propionate nasal spray (100μg/day) intreatment of children with perennial allergic rhinitis. Results show that, in 4 weeks of treatment, the adrenal function of patients is not inhibited by the drug. This suggests that fluticasone propionate nasal spray is safe for children. In the

present study, during the treatment, only 2 patients were reported with intranasal dryness and occasional epistaxis, which were self-healed without treatment. There was no obvious side effect in other patients.This further confirms that the fluticasone propionate nasal spray has good safety.

It is reported that fluticasone propionate nasal spraycan significantly mitigate respiratory disturbance in children with obstructive sleep apnea syndrome(Brouillette *et al.*, 2001).The present study has achievedsimilar beneficial effects.In addition, thenasal steroids not only has the vasoconstriction and decongestant effect, but also has the effectof stabilizing vascular endothelial barrier, reducing vascular permeability, relieving nasal mucosal edema, and controlling nasal congestion by inhibiting the glandsecretion. Therefore, the nasal steroids have the long and stable curative effect. Several studies have demonstrated that, the topical use of nasal steroidsis the best choice to improve nasal obstruction (Zhang *et al.*, 2008;Ferrante *et al.*, 2017). In the survey in our study, the improvement of nasal obstructionis also the most recognized by the parents of children. The follow-upfound that, thenasal congestion in children was alleviated after one week offluticasone propionate nasal spray treatment, and the rest of the symptoms were relieved in varying degrees after about two weeks. At the same time, we found that the mouth breathing symptom was not obviously alleviated in two groupsafter treatment.We consider that this may be related to children's habit of mouth breathing at sleep.At last, our results suggest that, the symptom improvements in moderate adenoid hypertrophy group werebetter than those in severe adenoid hypertrophy group.

In conclusion, thefluticasone propionate nasal spray is effectiveand safe fortreatment of children's snoring caused by adenoidal hypertrophy. The therapeutic effect is more obvious in children with moderate adenoidal hypertrophy. For children with severe adenoidal hypertrophy, it is also a good strategy before the adenoidectomy (if the treatment is invalid).There are some limitationsof this study: i) the blind method is not adopted; ii) the sample size is relatively small; iii) the long-term efficacy was not observed. The future research direction is to increase the sample size and employ the randomized controlled studiesfor observing long-term efficacy, inorder to obtain more reliable results.

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