Role of Intranasal Topical Steroid in Pediatric Sleep Disordered Breathing and Influence of Allergy, Sinusitis, and Obesity on Treatment Outcome

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INTRODUCTION

Sleep-disordered breathing (SDB) in childhood describes a spectrum of abnormalities ranging from primary snoring to obstructive sleep apnea syndrome (OSAS). Chronic sleep-related airway obstruction results in repetitive hypoxemia and sleep disturbance that can cause neurocognitive disturbance, growth failure, and cor pulmonale (1).

The most common symptoms associated with this disorder are habitual snoring, difficulty breathing, witnessed apneas, restless sleep, and daytime neurobehavioral problems (2). Frequent snoring was observed at 3.2% and occasionally at 16.7% in an epidemiological study (3). Sleep apnea has been reported at between 1% and 3% of children and occurs most frequently in children between 2 and 6 years old (4). Pediatric SDB is usually managed with adenotonsillectomy which needs general anesthesia and sometimes is associated with complication including bleeding and perioperative respiratory compromise. As adjunctive treatments, nonsurgical alternatives for reduction of adenoid size are limited. However, recent studies showed that topical nasal corticosteroid spray reduced adenoid size and improved symptoms of nasal airway obstruction and OSAS (1, 2). Topical nasal corticosteroid spray is considered to be the first line treatment for allergic rhinitis which is also associated with sleep disturbance through nasal obstruction, enlargement of tonsils and adenoids, and an elongated face (5, 6). However, there are few results which show its effect in the SDB children irrespective of allergic rhinitis, sinusitis and body weight.

This study was aimed to evaluate the efficacy of short term

mometasone furoate in pediatric SDB patients with parental questionnaire (obstructive sleep apnea-18, OSA-18) and lateral neck X-ray and to identify the effect of allergy, sinusitis, and obesity on treatment result.

MATERIALS AND METHODS

Study population
This prospective, observational study was approved by the Institutional Review Board of the Samsung Medical Center. Forty one (32 males, 9 females), two to eleven year-old children, who visited otolaryngology clinic due to sleep disordered breathing were recruited between March 2006–July 2007, based on the following inclusion criteria: 1) history of habitual snoring for the last 3 months or longer, and 2) adenoid hypertrophy confirmed with simple X-ray findings or endoscopic examination by otolaryngologist. Children were excluded from the study if they met any of the exclusion criteria: 1) presence of symptoms of acute respiratory infection; 2) use of nasal or systemic corticosteroid or antibiotics within 4 weeks prior to the study; 3) prior tonsil or adenoid surgery; and 4) a history of craniofacial, neuromuscular, or genetic disorders.

Diagnostic criteria and method
Informed consent for participation in this study was obtained from the parent or legal guardian of each child enrolled. Initial assessment of each patient upon entering the study included the following: history and physical examination (including body weight and height), parental questionnaire (OSA-18), sinus X-ray, adenoid X-ray, and skin prick test or Pharmacia CAP system for detecting allergy. Allergic rhinitis was diagnosed in case that each child complaining typical allergic symptoms showed positive result in allergic test.

We checked paranasal sinus X-ray for detecting the presence of sinusitis and categorized into three group: no evidence of sinusitis, unilateral haziness, and bilateral haziness. For the evaluation of obesity, body weight was checked and we judged each child for obesity with their body weight, height, and age according to Korean pediatric standard growth curve. We regarded each child as obese in case that body weight belong to upper 10 percentile according to growth curve. Body weight was checked at before and after treatment for identification of bias according to change of body weight. All patients received 4 weeks course of single intranasal administration in each nostril with mometasone furoate (100 μg). After 4 weeks course of therapy, all patients were re-assessed to evaluate the efficacy of treatment.

Outcome measures
The primary outcome was measured with the OSA-18 survey (Table 1), a valid and reliable discriminative quality of life (QOL) measure for children with varying levels of SDB (7, 8). The OSA-18 has been previously shown to possess satisfactory test-retest reliability and internal consistency (7). The survey consists

| Evaluation of sleep-disordered breathing | None | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|-----------------------------------------|------|---|---|---|---|---|---|---|
| Sleep disturbance (S)                   | 1    | 2 | 3 | 4 | 5 | 6 | 7 |
| Loud snoring?                           | 1    | 2 | 3 | 4 | 5 | 6 | 7 |
| Breath holding spells or pause in breathing at night? | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| Chocking or gasping sounds while a sleep? | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| Restless sleep or frequent awakening from sleep? | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| Physical suffering (P)                  | 1    | 2 | 3 | 4 | 5 | 6 | 7 |
| Mouth breathing because of nasal obstruction | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| Frequent colds or upper respiratory obstruction? | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| Nasal discharge or runny nose?          | 1    | 2 | 3 | 4 | 5 | 6 | 7 |
| Difficulty in swallowing foods?         | 1    | 2 | 3 | 4 | 5 | 6 | 7 |
| Emotional distress (E)                  | 1    | 2 | 3 | 4 | 5 | 6 | 7 |
| Mood swings or temper tantrums?         | 1    | 2 | 3 | 4 | 5 | 6 | 7 |
| Aggressive or hyperactive behavior?     | 1    | 2 | 3 | 4 | 5 | 6 | 7 |
| Discipline problems?                    | 1    | 2 | 3 | 4 | 5 | 6 | 7 |
| Daytime problems (D)                    | 1    | 2 | 3 | 4 | 5 | 6 | 7 |
| Excessive daytime drowsiness or sleepiness? | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| Poor attention span or concentration?  | 1    | 2 | 3 | 4 | 5 | 6 | 7 |
| Difficulty getting out of bed in the morning? | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| Caregiver congress (C)                  | 1    | 2 | 3 | 4 | 5 | 6 | 7 |
| Caused you to worry about child’s general health? | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| Created concern that child is not getting enough air? | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| Interfered with your ability to perform daily activities? | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| Made you frustrated?                    | 1    | 2 | 3 | 4 | 5 | 6 | 7 |

OSA-18: Obstructive sleep apnea-18.
of 18 items grouped into 5 domains: sleep disturbance (4 items), physical suffering (4 items), emotional distress (3 items), daytime problems (3 items), and caregiver concerns (4 items). Items are scored on a 7-point ordinal scale and have excellent test-retest reliability.

After completing questionnaire, OSA-18, they were evaluated for measuring adenoidal-nasopharyngeal (AN) ratios by using lateral radiographs of nasopharynx. Lateral radiographs of the nasopharynx were exposed with the patient in the erect position and the head fixed with a wall-mounted cephalostat and oriented with the Frankfort horizontal plane. The exposures were made with 70 kV, and the exposure time varied between 0.4 and 0.6 depending on the age of the children. For each of the radiographs, the AN ratio was computed according to the method of Fujioka et al. (9) (Fig. 1).

Statistics
The AN ratio was obtained by dividing the measurement for A by the value for N. A commercially available statistical program (SPSS ver. 11.5, SPSS Inc, Chicago, IL, USA) was used to perform the statistical analysis. Statistical comparisons of changes in OSA-18 score between before and after topical intranasal mometasone furoate treatment employed Wilcoxon signed rank test. A paired t-test was used for comparison of changes in AN ratio and body weight. Spearman rank correlation analysis was employed to analyze the correlation between change in OSA-18 score and change in AN ratio. Mann-Whitney U-test was used to analyze the effect of allergy, obesity and sinusitis on the change of OSA-18 score. A P-value of less than 0.05 was considered statistically significant.

RESULTS

Table 2 summarizes the demographic data including the patient’s age, sex, body weights, and history of allergy. All 41 children

| Characteristics | Values |
|-----------------|--------|
| No. of subjects | 41     |
| Mean age (year)| 6.4 (2-11) |
| Sex (male)     | 31 (75.6%) |
| Obesity        | 8 among 20 patients* |
| History of allergy | 17 among 37 patients† |
| Presence of sinusitis | No haziness (17), unilateral (5), and bilateral (19) |

*20 of 41 children were checked body weight and height. We regarded each child as obese in case that body weight belongs to upper 10 percentile according to growth curve. †37 of 41 children were checked for allergy.

Table 3. Parental questionnaire (OSA-18) results before and after intranasal corticosteroid treatment

|                                | Before treatment | After treatment | P-value |
|--------------------------------|-----------------|----------------|---------|
| Sleep disturbance              | 13.58±4.82      | 10.85±5.46     | <0.001  |
| Loud snoring                   | 5.53            | 3.90           | <0.001  |
| Breath holding/pause           | 2.87            | 2.26           | 0.004   |
| Choking or gasping             | 2.12            | 2.09           | NS*     |
| Fragmented sleep               | 3.04            | 2.58           | 0.034   |
| Physical symptom               | 15.85±4.78      | 13.19±5.00     | 0.001   |
| Mouth breathing                | 5.24            | 4.07           | 0.001   |
| Frequent URI                   | 4.31            | 3.51           | 0.004   |
| Rhinorrhea                     | 4.04            | 3.48           | 0.044   |
| Dysphagia                      | 2.24            | 2.12           | NS      |
| Emotional distress             | 8.39±4.29       | 8.00±4.18      | NS      |
| Mood swings or tantrums        | 2.97            | 3.00           | NS      |
| Aggression/hyperactive         | 2.82            | 2.56           | NS      |
| Discipline problems            | 2.58            | 2.43           | NS      |
| Daytime function               | 8.85±3.76       | 8.53±3.64      | NS      |
| Daytime drowsiness             | 2.39            | 2.41           | NS      |
| Poor attention span            | 3.04            | 2.82           | NS      |
| Difficulty awaking             | 3.41            | 3.29           | NS      |
| Caregiver concerns             | 12.19±6.01      | 10.68±4.80     | NS      |
| Worried over child health      | 4.00            | 3.73           | NS      |
| Concerned not enough air       | 3.82            | 3.14           | 0.017   |
| Missed activities              | 2.21            | 1.97           | NS      |
| Frustration                    | 2.14            | 1.82           | NS      |
| Total                          | 58.87±13.26     | 51.26±12.87    | 0.003   |

*No statistically significant difference.

URI: upper respiratory infection; OSA-18: obstructive sleep apnea-18.
completed the 4-weeks course of intranasal mometasone furoate treatment. Compliance with daily nasal spray was comparable and there was no significant side effect such as dry nose and epistaxis.

The changes of OSA-18 survey score after treatment are shown in Table 3. Sleep disturbance and physical suffering were the highest rated domains, followed by caregiver concerns, daytime problems, and emotional distress.

There was significant reduction in score of sleep disturbance domain \( (P < 0.001) \) and physical symptom domain \( (P = 0.001) \) after treatment. Also, total OSA-18 score decreased significantly \( (P = 0.003) \) after the treatment (Fig. 2). Among 41 patients, 37 children were tested for allergy and 17 patients were proved to have allergic rhinitis based on their symptom and allergy test. And we could obtain the information of body weight and height in 20 children, and 8 children were proved to be obese. But, presence of allergy \( (P = 0.065) \) and obesity \( (P = 0.851) \) didn’t affect the effect of nasal steroid on total OSA-18 score. There was no significant change in body weight between before and after treatment \( (P = 0.954) \).

Sinus X-ray was checked in all children and sinusitis were detected in 24 children. 19 children showed bilateral haziness of sinus on X-ray and 5 children showed unilateral haziness. Change in OSA-18 score showed no significant difference according to presence of sinusitis \( (P = 0.488) \).

The mean AN ratio was \( 0.63 \pm 0.11 \) before the treatment and \( 0.59 \pm 0.12 \) after the treatment. There was a statistically significant difference \( (P = 0.006) \) between before and after treatment (Fig. 3). There was no significant correlation between the changes of AN ratio and improvement of symptom score \( (P = 0.858) \).

**DISCUSSION**

This prospective, observational study shows a significant improve-
radiographs in evaluation of adenoid size, and Major et al. (16) in 2006 systematically reviewed lateral cephalometric diagnosis in adenoid hypertrophy, and proved that the results of lateral neck X-ray showed good correlation with actual adenoid size.

Acoustic rhinometry have been known as useful tool in evaluating nasopharyngeal cross-sectional area and volume after adenoidectomy (17, 18). But short term use of mometasone nasal spray couldn’t make so much reduction of adenoid size comparing with adenoidectomy. Considering the effect of nasal cycle on acoustic rhinometry and reduction of adenoid size after application of intranasal spray, we didn’t employ acoustic rhinometry as a tool to evaluate efficacy of short term nasal steroid spry for pediatric sleep disordered breathing.

In our study, 22 of 31 children (71%) who had tested with lateral neck radiography, showed decreased AN ratio after 4 weeks course of treatment ($P=0.006$). Demain and Goetz (19) in 1995 reported a study of standard dose aqueous nasal beclomethasone in treatment of adenoid hypertrophy. All Adenoid size was decreased in all enrolled patients after 8 weeks treatment and mean reduction in AN ratio was 29%. Cengel and Akyol (20) in 2006 studied change of adenoid size after 6 weeks course of intranasal mometasone furoate treatment. 67.2% of enrolled children showed reduction of adenoid size after treatment. However there has been no proven mechanism about shrinkage of adenoid. Existence of inflammation had been proved in mucosal surface at soft plate in OSAS patients (21, 22). 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 steroid for 4 weeks might reduce the inflammation of covering mucosa of adenoid. Therefore, application of intranasal steroid can be effective treatment option for reducing adenoid size.

We chose OSA-18 as the measuring tool for assessing the efficacy of intranasal steroid. In 2000, Franco et al. (23) proposed OSA-18 as a practical mean of office-based determination of quality-of-life impact for obstructive sleep apnea syndrome in children. In 2005, Michell and Kelly (24) used OSA-18 as indicator for treatment response after adenotonsillectomy in SDB children and mentioned that it was so useful. OSA-18 is composed of easily applicable 18 questions and has relatively high reproducibility (4), and it is known that OSA-18 shows good correlation with respiratory disturbance index (RDI) (25).

In our study, parents or caregivers could easily carry out the questionnaire and it takes only few minutes to fill up the form. For this reason, we thought that OSA-18 can be excellent tool for evaluating SDB children after treatment in office-based clinics or other clinics without polysomnography (PSG). Moreover, in the case of tertiary care clinics with PSG, OSA-18 can have a additional role in children not suitable for PSG.

There are a few options for evaluating the adenoid size in pediatric SDB patients. Among them lateral neck radiography and direct video rhinoscopy has been used widely. Mlynarek et al. (25) in 2004 reported that direct video rhinoscopy is better correlated to the severity of symptoms than are values obtained by lateral neck radiography. But fiberoptic examination of child’s nasopharynx can be challenging and might not be suitable for all patients. In some children it is impossible to exam nasopharynx due to patient’s noncooperation (26). For this reason we selected lateral neck radiography for assessing adenoid size. But we could not get data from all enrolled children. Some patients refused to let their children be exposed radiation in spite of harmless dose.

As the result of our study, allergic rhinitis and sinusitis had no influence on degree of change in adenoid size and in OSA-18 score. According to other report, adenoid size decreased significantly after intranasal steroid and there was notable difference in improvement after treatment according to allergy status (27). But there are not so many reports about effect of allergy on efficacy of intranasal steroid in pediatric SDB patients, so further research is required with large sample size.

We assumed that improvement in quality of life of SDB children is due to not only decreased AN ratio but also other factors such as increase nasal airway patency. Considering this result, intranasal steroid can be used in SDB children regardless of allergic status or sinusitis.

There are some limitations to this study. We could not have a control group due to lack of consent. At early period of this study, we wanted to have control group using placebo. But most parents and caregivers refused to participate in our study because using placebo. The other limitation is that we didn’t confirm the increased nasal airway patency with objective tool. In general, acoustic rhinometry has been used as popular tool for assessing nasal airway. But most cohorts of our study were under 5 years old, so it was impossible to get patient’s cooperation during acoustic rhinometry.

In conclusion, We believe that 4-weeks course of intranasal steroid (mometasone furoate) can be a effective treatment option in pediatric SDB patients without significant complications. And this treatment works effectively regardless of allergic status, sinusitis, and obesity.

Future placebo controlled study will be required to ascertain the effect of short term steroid use for pediatric sleep disordered breathing.

**CONFLICT OF INTEREST**

No potential conflict of interest relevant to this article was reported.

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