Treatment Outcomes of Adenotonsillectomy for Children with Obstructive Sleep Apnea: A Prospective Longitudinal Study

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Objective: To evaluate the efficacy of adenotonsillectomy (AT) in the treatment of children with obstructive sleep apnea (OSA) in a 3-y prospective, longitudinal study with analysis of risk factors of recurrence of OSA.

Study Design: An investigation of children (6 to 12 y old) with OSA documented at entry and followed posttreatment at 6, 12, 24, and 36 mo with examination, questionnaires, and polysomnography.

Multivariate generalized linear modeling and hierarchical linear models analysis were used to determine contributors to suboptimal long-term resolution of OSA, and Generalized Linear Models were used for analysis of risk factors of recurrence.

Results: Of the 135 children, 88 terminated the study at 36 months post-AT. These 88 children (boys = 72, mean age = 8.9 ± 2.7 y versus boys 8.9 ± 2.04 y, girls: 8.8 ± 2.07 y; body mass index [BMI] = 19.5 ± 4.6 kg/m²) had a preoperative mean apnea-hypopnea index (AHI) of 13.54 ± 7.23 and a mean postoperative AHI at 6 mo (AHI6) of 3.47 ± 8.41 events/h (with AHI6 > 1 = 53.4% of 88 children). A progressive increase in AHI was noted with a mean AHI6 = 6.48 ± 5.57 events/h and AHI36 > 1 = 68% of the studied group. Change in AHI was associated with changes in the OSA-18 questionnaire.

The residual pediatric OSA after AT was significantly associated with BMI, AHI, enuresis, and allergic rhinitis before surgery. From 6 to 36 mo after AT, recurrence of pediatric OSA was significantly associated with enuresis, age (for the 24- to 36-mo period), postsurgery AHI (severity), and the rate of change in BMI and body weight.

Conclusions: Adenotonsillectomy leads to significant improvement in apnea-hypopnea index, though generally with incomplete resolution, but a worsening over time was observed in 68% of our cases.

Keywords: adenotonsillectomy, comorbidity, obstructive sleep apnea, polysomnography, treatment outcomes

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INTRODUCTION

Obstructive sleep apnea (OSA) syndrome is a highly prevalent condition in children and characterized by snoring, witnessed apnea, unrefreshing sleep, and excessive daytime sleepiness.1-12 Children with OSA experience recurrent periods of elevated upper airway resistance during sleep due to partial or complete upper airway obstruction, which results in snoring, episodic oxyhemoglobin desaturation, hypercapnia, and repeated arousals.3,4 The respiratory disturbance of recurrent hypoxia-reoxygenation episodes during the night is associated with an increased risk of suboptimal growth, poor sleep quality, neurocognitive dysfunction, behavioral problems, overweight status, and cardiovascular disease in childhood.5-8 The prevalence of OSA is approximately 2-3% in children,9,10 and current studies have evaluated the influence of OSA on various associated morbidities5-8,11 and tried to identify the factors predicting poor treatment outcome.12

The choice of therapy for OSA is predicated on the etiology, severity, and individual history of the increased upper airway resistance. The timely diagnosis and appropriate treatment of OSA is especially important, because untreated OSA can account for markedly increased health care costs.13-15 Adenotonsillar hypertrophy is considered an important factor in the development of OSA in otherwise healthy children. Adenotonsillectomy (AT) is recommended as the first line of treatment for childhood OSA by the American Academy of Pediatrics.1 and the effectiveness of AT in the treatment of children with OSA has been confirmed by several studies.15-17 However, some studies examining the efficacy and outcomes of AT in pediatric OSA showed incomplete resolution of OSA after surgery.12-17 For example, nonobese children with severe OSA and chronic asthma were found to be at higher risk of residual OSA in a recent multicenter retrospective study.12 In addition, few studies have evaluated the overall long-term efficacy of AT in the treatment of children with OSA. Thus, this 3-y prospective, longitudinal study aimed to delineate factors contributing to potential post-AT OSA through careful examination of demographic and pre- and post-AT polysomnography (PSG) information. In our geographical location, the mean age for AT at the time of the study was approximately 8 y, and such age for surgery was based on two factors: usual recommendations made by ear, nose, and throat (ENT) surgeons when AT was considered, and reluctance of parents in our culture to have their children undergo nonemergency surgery.

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METHODS

Starting in August 2007, children between the ages of 6 and 12 y with signs and symptoms of a sleep disturbance, including snoring, mouth breathing, and witnessed breath holding, lasting for at least 3 mo, were evaluated prospectively using a standardized history and physical examination, neurocognitive and psychological testing, and PSG in the sleep center of Chang Gung Memorial Hospital (CGMH). The CGMH sleep clinic is a multidisciplinary clinic with expertise in the management of pediatric sleep apnea and is the only accredited pediatric sleep laboratory in Taiwan.

The inclusion criteria for subjects, based on PSG, were an obstructive apnea-hypopnea index (AHI, the number of apnea and hypopnea events per hour of sleep) greater than one event/h or a respiratory disturbance index (RDI) of more than five events/h with clinical symptoms. Both parents and patients agreed to participate in this longitudinal study and were willing to sign informed consent.

Exclusion criteria for the children were previous AT, craniofacial abnormalities, neuromuscular disease, or other significant medical, psychiatric, or genetic disorders, and obesity (obesity was defined based on Taiwan general public health tables, taking into consideration age and body mass index (BMI) in kg/m$^2$).18

This prospective study was approved by the institutional review board of CGMH, and the caregivers (parents) signed informed consent before their children were enrolled for study.

Procedure

All subjects underwent a routine medical history and physical examination by an otolaryngologist, a craniofacial surgeon, a pediatrician, and a child psychiatrist for assessment of associated comorbidities.

A standardized datasheet for patient demographic data, including age, sex, height, weight and all systemic comorbidities, was checked by child psychiatrists.

The ENT examination was performed by an otolaryngologist and a craniofacial surgeon. Tonsillar size was graded as follows: (1) small tonsils confined to the tonsillar pillars; (2) tonsils that extended just outside the pillars; (3) tonsils that extended outside the pillars but did not meet at the midline; (4) large tonsils that met at the midline.19 Adenoid tissue was examined with a lateral x-ray film of the neck or a flexible fiberoptic endoscope. The amount of obstruction was categorized into four grades (grade 0 = 0-25%, grade 1 = 25-50%, grade 2 = 50-75%, and grade 3 = 75-100%). Allergic rhinitis was confirmed by a pediatrician and a craniofacial surgeon. Tonsillar size was graded as

statistical analyses

Descriptive statistics were performed. Considering the missing data in longitudinal studies and the evolution of AT over time, multivariate generalized linear model (GLM) and hierarchical linear models (HLM) analyses were used to determine contributors to residual sleep apnea at various time points post-AT. GLM statistics were used to analyze the risk factors for OSA recurrence after AT looking at the entire follow-up period. We used HLM analyses to investigate the changes during the different follow-up points (AT$_{6,12,24,36}$): because there were different numbers of subjects at each follow-up point, a two-level model was used. We analyzed fixed effects in level one, and random effects in level two. The coefficient of level one (fixed effects) was the intraclass correlation (ICC) which was, in our model, the proportion of group level variance from the total variance.

RESULTS

During the study period, 135 pediatric OSA subjects who underwent AT were enrolled. Eighty-eight children (64.6%) completed all preoperative and postoperative evaluations and were included in the analysis. The dropout rate was 17.8% in the first year, 28.9% in the second year, and 35.4% in third year, indicating the reluctance of parents to participate in long-term follow-up. The mean age at the time of screening was 8.9 ± 2.7 y. Boys were predominant in this sample (n = 72, 81.8% mean age 8.9 ± 2.04). The mean AHI before AT (AHI$_0$) was...
13.53 ± 7.23 events/h and the mean BMI was 19.54 ± 4.64 kg/m². The BMI-z score revealed that our subjects were not obese. We compared the characteristics of subjects that completed the study and those that did not, and found there was no significant difference between these two groups (Tables 1 and 2).

A comparison of PSG data before and after AT showed that the baseline AHI₀ (13.53 ± 7.23 events/h; median = 6.85, range 1.2 to 49.4 events/h) had improved significantly at all post-AT yearly time points (AHI₁₂ < 0.001, AHI₂₄ P < 0.001, AHI₃₆ P = 0.004, respectively). Rapid eye movement (REM) sleep also showed a significant increase at all post-AT yearly time points (P = 0.04, 0.016, 0.003, respectively), as did the percentage of slow wave sleep (P = 0.03, 0.02, 0.006, respectively). Median AHI also was significantly improved at all post-AT yearly time points (Tables 3 and 4).

Overall, these data indicate the positive results of surgery but do not represent the real postsurgical evolution of the AHI over time. Using a multivariate Generalized Linear Model (GLM) analysis we found a significant improvement in the AHI (mean AHI₀ = 13.54 to mean AHI₆ = 3.47 events/h) during “period 1” (pre-AT-AHI₀ to 6 mo post-AT-AHI₆). The success rate of AT in this study at 6-mo postsurgery is therefore 46.6%. The remaining 53.4% of the children had an AHI₆ greater than one event/h

During period 2 (6 to 36 mo post-AT) there was an AHI elevation beginning at the 6-mo time point: from mean AHI₆ = 3.47 to mean AHI₃₆ = 6.48 events/h (range: AHI₆ = 0 to 35.5 events/h to AHI₃₆ = 0 to 42.3 events/h). Though all values were significantly less than the baseline AHI (AHI₀), the mean AHI showed a significant increase from 6 to 36 mo postsurgery (Tables 3 and 4 and Figure 1). Using GLM analysis, we found persistence of a significant difference between presurgery and postsurgery PSG data, but this effect varied between different time sequences: With HLM analysis and the two-level model calculations, the coefficient in level one (fixed effects) showed again that the value of the AHI was significantly reduced during the period (AHI₀ to AHI₆), and that the significant positive gains covered not only AHI but also apnea index (AI), mean oxygen saturation, sleep latency, wake after sleep onset (WASO), and percentage of REM sleep. But in period 2, the proportion of the AHI was significantly increased: from 6 mo posttreatment to later time points (up to AHI₃₆). This AHI rebound starting 6 mo postsurgery was associated with a worsening of nocturnal sleep (WASO, sleep latency, and sleep efficiency).

Subgroup Analyses

We divided the post-AT patients into two groups. Group 1 (the successful group, n = 41) had an AHI₆ < 1 at AT+6 mo. The analysis of this subgroup, considered as initially fully treated, revealed that the recurrence rate was 35.3% after AT+12 mo, 50% after AT+24 mo, and 66.7% after AT+36 mo. Group 2 (the nonsuccessful group, n = 47) had an AHI₆ > 1 at AT+6 mo and also showed a progressive increase in the residual AHI at +36 mo. Overall, when considering worsening and recurrence, 68% of the children followed had an abnormal AHI and abnormal sleep at AT+36 mo. The mean AHI₃₆ was 6.48 ± 5.57 events/h.

Determination of risk factors for OSA recurrence after AT was based on GLM of repeated measure analysis: AHI₀ was significantly associated with BMI, body weight, AHI, and the presence of enuresis and allergic rhinitis before surgery: the risk factor of residual pediatric OSA 6 mo after AT was significantly related to BMI and body weight, severity of pediatric OSA, enuresis and rhinitis before surgery. The analyses performed in period 2 (from post-AT+6 mo to +36 mo) showed that the recurrence of pediatric OSA was significantly associated with age, persistence of enuresis, the AHI post-AT+6 mo, and a fast and abnormal increase of BMI and body weight (from

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### Table 1—Clinical characteristics of children completing the longitudinal study versus those who dropped out during the 3 y of follow-up

<table>
<thead>
<tr>
<th></th>
<th>Completed group</th>
<th>Dropout group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of subjects</td>
<td>n = 88</td>
<td>n = 47</td>
<td></td>
</tr>
<tr>
<td>Mean age at time of screening (y old)</td>
<td>8.9 ± 2.7</td>
<td>8.6 ± 2.11</td>
<td>0.908</td>
</tr>
<tr>
<td>Number of males</td>
<td>72 (81.8%)</td>
<td>39 (83%)</td>
<td>0.375</td>
</tr>
<tr>
<td>BMI (kg/m²) (mean ± SD) at entry</td>
<td>19.54 ± 4.64</td>
<td>20.10 ± 6.29</td>
<td>0.369</td>
</tr>
<tr>
<td>BMI z score at entry</td>
<td>-0.75 ± 1.00</td>
<td>-0.78 ± 0.99</td>
<td>0.358</td>
</tr>
</tbody>
</table>

BMI, body mass index; SD, standard deviation.

### Table 2—Comorbidities of children completing the longitudinal study versus those who dropped out during the 3 y of follow-up

<table>
<thead>
<tr>
<th>Comorbidity</th>
<th>Completed group</th>
<th>Dropout group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PLM disorder</td>
<td>10 (11.4%)</td>
<td>1 (2.1%)</td>
<td>0.203</td>
</tr>
<tr>
<td>Learning disorder</td>
<td>14 (15.9%)</td>
<td>2 (4.3%)</td>
<td>0.068</td>
</tr>
<tr>
<td>ADHD</td>
<td>33 (37.5%)</td>
<td>21 (44.7%)</td>
<td>0.838</td>
</tr>
<tr>
<td>Enuresis</td>
<td>17 (19.3%)</td>
<td>2 (4.3%)</td>
<td>0.049</td>
</tr>
<tr>
<td>Other physical comorbidity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asthma</td>
<td>4 (4.5%)</td>
<td>1 (2.1%)</td>
<td>0.651</td>
</tr>
<tr>
<td>Allergic rhinitis</td>
<td>44 (50%)</td>
<td>28 (59.6%)</td>
<td>0.665</td>
</tr>
<tr>
<td>Eczema</td>
<td>4 (4.5%)</td>
<td>1 (2.1%)</td>
<td>0.713</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>6 (7.9%)</td>
<td>1 (2.1%)</td>
<td>0.514</td>
</tr>
<tr>
<td>Dermatitis</td>
<td>1 (1.1%)</td>
<td>0 (0%)</td>
<td>0.796</td>
</tr>
<tr>
<td>Findings of ENT examination</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tonsil hypertrophy (more than grade 2)</td>
<td>86 (97.7%)</td>
<td>40 (85.1%)</td>
<td>0.108</td>
</tr>
<tr>
<td>Adenoid hypertrophy</td>
<td>74 (84.1%)</td>
<td>41 (87.2%)</td>
<td>0.956</td>
</tr>
<tr>
<td>Turbinate hypertrophy</td>
<td>10 (11.4%)</td>
<td>2 (4.3%)</td>
<td>0.067</td>
</tr>
<tr>
<td>Nasocelept deviation</td>
<td>4 (5.4%)</td>
<td>1 (2.1%)</td>
<td>0.528</td>
</tr>
</tbody>
</table>

*Diagnosed according to criteria of Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition. **Confirmed and diagnosed by pediatricians. ENT, ear, nose and throat; ADHD, attention deficit hyperactivity disorder; PLM, periodic limb movement.
Six months after AT, the OSA-18 analyses showed significant improvement in the items of sleep disturbance (mean: 4.06 ± 1.52 to 2.40 ± 1.22), physical suffering (mean: 3.82 ± 2.02 to 2.79 ± 1.92), daytime problems (mean: 4.12 ± 1.98 to 3.33 ± 2.03), caregiver concerns (mean: 4.44 ± 1.78 to 3.01 ± 1.91) and total quality of life (mean: 5.12 ± 2.08 to 6.01 ± 2.95) (higher scores indicated greater severity, except the item of total quality of life, which was the reverse). However, the items of sleep disturbance, daytime problems, and caregiver concerns worsened again at +36 mo post-AT. The results of the sleep questionnaire were similar to the results of the PSG.

**DISCUSSION**

The limitations of this study include: (1) a somewhat small sample size, ending with 88 children and a male predominance; the dropout rate was 36% with only 88 subjects completing the 36-mo follow-up; (2) age (6 to 12 y) was taken into consideration when AT would usually be performed in Taiwan; (3) because of our institutional review board, this was not a randomized controlled trial; (4) the lack of obese children (a deliberate choice); and (5) the fact that craniofacial structure imaging data (i.e., three-dimensional computed tomography)
was not performed on every child. Although a 1-y follow-up study of sleep disordered breathing with AT\textsuperscript{5} has discussed the recurrence issue, our study, to the best of our knowledge, is the first prospective 3-y longitudinal study of pediatric OSA after AT. Also, the long-term follow-up of these patients was performed in the same hospital sleep center using the same recording techniques and PSG scoring criteria. Clinical evaluation was a systematic evaluation that was based on criteria established prior to the beginning of the study, and repeated psychiatric and neurocognitive testing was administered by the same team.

AT is the treatment of choice for pediatric OSA and our results showed significant improvements post-AT. However, incomplete resolution of pediatric OSA was noted in many of our children. Our results show that post-AT OSA does not spontaneously remit, and although the effect size was relatively small (66.7\% of subjects), AHI did worsen over time, even if surgery was successful at 6 months posttreatment. A recent study has reported some mechanisms by which this worsening may occur:\textsuperscript{15} Asthma was not a predictive factor for post-AT OSA in our study group, but our rate of asthma was low at the outset. This polysomnographic finding is associated with a subjective and objective demonstration of poor sleep, and a demonstration of the worsening of symptoms associated with attention and daytime hyperactivity.

Our study outlines some risk factors, such as severe pediatric OSA, obesity, and a large increase in BMI after AT, rhinitis, enuresis, and older age for recurrence of OSA, but we do not claim to have identified all of the risk factors. Finally, an obvious conclusion of our work is that children in whom OSA is diagnosed require long-term follow-up.

**ACKNOWLEDGMENTS**

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**DISCLOSURE STATEMENT**

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**REFERENCES**