Effect of Adenotonsillectomy on Central and Obstructive Sleep Apnea in Children with Down Syndrome

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Abstract

Objectives. To determine and quantify changes in both central and obstructive sleep apnea in patients with Down syndrome (DS) after adenotonsillectomy (AT).

Study Design. Case series with chart review.

Setting. Tertiary care children's hospital.

Subjects and Methods. The records of all patients with DS who underwent AT for sleep-disordered breathing between November 2008 and December 2014 were examined. In total, 113 patients were identified, and 36 of these patients had pre- and postoperative polysomnograms (PSGs) that were analyzed for obstructive and central components. Wilcoxon signed-rank test, paired *t* test, and McNemar test were used to examine pre- and postoperative PSG differences. Logistic regression and multivariate analysis of variance of patient characteristics (between subjects) and PSG results (within subjects) were conducted.

Results. The mean (SD) patient age was 5.5 (4.0) years (range, 0.9-15 years); 50.0% were male. After AT, significant reductions were identified in both obstructive apnea-hypopnea index (AHI) ($P < .001$) and overall AHI ($P < .001$). Among the 15 patients with severe obstructive sleep apnea, 86.7% experienced a significant AHI reduction to moderate or mild disease ($P < .001$). In addition, of the 15 patients with central sleep apnea (central apnea index [CAI] >1), 66.7% had resolution of central sleep apnea postoperatively ($P = .004$). There was also a significant interaction identified between CAI reduction, preoperative CO_2 retention, and adenoid size, $F(2, 20) = 6.87$, $P = .05$.

Conclusion. Children with DS who underwent AT demonstrated significant reductions in both obstructive and central apneic indices on PSG. A significant number of patients with central sleep apnea demonstrated resolution postoperatively. Additional analysis demonstrated a significant interaction between CO_2 retention, adenoid size, and postoperative CAI reduction.

Keywords

central sleep apnea, central apnea index, obstructive sleep apnea, sleep-disordered breathing, polysomnogram, Down syndrome, trisomy 21, pediatrics

Down syndrome (DS) is the most common chromosomal abnormality in the United States and is estimated to occur in 1 in 750 infants born in the United States every year.[1] Sleep-disordered breathing (SDB) is a common disorder in children with DS and is defined by physiological changes in breathing during sleep secondary to respiratory disturbances.[2] Sleep-disordered breathing can be separated into obstructive sleep apnea (OSA) and central sleep apnea (CSA).[3,4]

It is estimated that up to 80% of patients with DS have OSA compared with 1% to 4% in the nonsyndromic population.[5-9] Relative macroglossia, microstomia, midface hypoplasia, and a narrowed pharyngeal inlet are some of the dysmorphic features that, along with adenotonsillar encroachment and generalized hypotonia, are believed to contribute to the increased prevalence of OSA in patients with DS.[10,11]

Central sleep apnea is an event in the absence of inspiratory effort that lasts for at least 20 seconds or the duration of 2 breaths and is associated with an arousal or a >3% oxygen desaturation.[4] Theorized to be due to a derangement of central nervous system ventilatory control, CSA response to adenotonsillectomy (AT) has not been studied extensively in the pediatric or adult DS patient population.[12,13]

Adenotonsillectomy has been a documented treatment for OSA in both nonsyndromic and DS children for many years. Recently, AT has been suggested to reduce and in some cases resolve CSA.[14] While some data document the

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effectiveness of AT for the treatment of both OSA and CSA in nonsyndromic children, data examining SDB response to AT in patients with DS are limited.[14-16] The objectives of this current study were to determine and quantify both OSA and CSA responses to AT in children with DS.

Materials and Methods

We retrospectively reviewed patients younger than 18 years with DS who underwent AT for SDB between 2008 and 2014 at our tertiary care children's hospital. Institutional review board approval was obtained from the University of Pittsburgh Medical Center prior to beginning this research project. Patients were identified through the electronic database of patient records using *International Classification of Diseases* code 758.0 for DS along with procedural codes 42820, 42821, 95810, and 95811 for AT and PSG.

Children with DS who underwent AT for SDB and had full-night pre- and postoperative PSGs were included in this study. All children demonstrated a preoperative PSG apnea-hypopnea index (AHI) >1 and confirmed diagnosis of trisomy 21 status.[4] Children older than 18 years or with central hypoventilation syndrome, cerebral palsy, or other associated neurological disorders were excluded from this study. Patient age, sex, weight, body mass index (BMI), and tonsil grade (1-4) were recorded upon preoperative visit. Adenoid size (0%-100%) was recorded intraoperatively. The PSG data were extracted both pre- and postoperatively and included total AHI, obstructive AHI (O-AHI), central apnea index (CAI), lowest oxygen saturation, highest carbon dioxide (CO_2) saturation, and the presence of CO_2 retention. Central, obstructive, and hypopneic events were defined, recorded, and scored in accordance with the American Academy of Sleep Medicine (AASM) scoring manual. Children with a CAI greater than or equal to 1 on preoperative PSG were considered to have CSA.[14] Sleep apnea and OSA were defined as AHI or O-AHI scores of greater than 1 and were further categorized as mild (1-5), moderate (5-10), or severe (>10).[14,17] Carbon dioxide levels were recorded by end-tidal and transcutaneous measurement. Retention was defined as sustained CO_2 levels higher than 50 mm Hg for at least 25% of total sleep time (TST).

Pre- and postoperative PSGs were performed in accordance with the AASM 2007 guidelines at a dedicated pediatric sleep laboratory with the Somnostar z4 Sleep System (Carefusion, San Diego, California).[4] Respiratory events and associated data were scored and interpreted using the Somnostar 9.1G diagnostic platform (Carefusion). Physicians board-certified in sleep medicine interpreted all PSGs conducted in this study.

Demographic data and PSG variables were recorded. All baseline characteristics of the subject population were not normally distributed and are therefore presented as median (range). The difference between postoperative and preoperative PSG parameters (Δ) was calculated. One-sample Wilcoxon signed-rank tests were used to assess the significance of PSG differences for parameters, which violated the assumption of normality, including AHI, O-AHI, CAI, and lowest oxygen saturation. A 1-sample *t* test was used to examine the change

in highest CO_2 saturation, which was normally distributed, and McNemar tests were used to examine differences in categorical variables. Logistic regression and multivariate analysis of variance (MANOVA) of patient characteristics (between subjects) and PSG results (within subjects) was conducted. A *P* value <.05 was considered significant.

Results

A total of 113 patients with DS were investigated in this study. Of these, 36 had pre- and postoperative PSGs and were included. The patients' median age was 5.0 years (range, 0.9-15.0 years), and 50.0% were male. The median BMI was 17.3 kg/m^2 (range, 10.8-43.0 kg/m^2). The median patient tonsil and adenoid sizes were 3 (range, 1-4) and 55% (range, 0-100%), respectively.

Preoperative AHI ranged from 1.1 to 59.5, with a median of 10.4. Postoperative AHI ranged from 0.4 to 59.4, with a median of 3.5. The difference between post- and preoperative AHI ranged from –58.1 to 42.2, with a median of –6.1, indicating that AHI was significantly reduced following AT (*P* < .001) (**Table 1**). Nineteen (53.7%) children had severe sleep apnea (AHI ≥10) before AT. Of these children, only 2 (10.5%) continued to have severe sleep apnea postoperatively. The other 17 (89.5%) children with preoperative severe sleep apnea experienced a reduction to mild or moderate disease after AT (**Table 2**). One child with a preoperative AHI of 59.4 had an AHI of 1.4 postprocedure. Overall, only 2 (5.5%) of the 36 patients had complete resolution of apnea (AHI <1).

Preoperative O-AHI ranged from 0.9 to 59.3, with a median of 8.7. Postoperative O-AHI ranged from 0.4 to 59.3, with a median of 2.6. The difference between post- and preoperative O-AHI ranged from –58.7 to 42.2, with a median of –4.7, indicating that AT significantly reduced O-AHI (*P* < .001) (**Table 1**). Fifteen (41.6%) children had severe OSA before AT (O-AHI ≥10), but only 2 (13.3%) of these children remained severe postoperatively. Obstructive sleep apnea was reduced to mild or moderate in the remaining 13 (86.6%) of the 15 patients with severe OSA (**Table 2**). Six (16.6%) of the 36 patients experienced complete resolution of OSA (O-AHI <1).

With regard to central sleep apnea, preoperative CAI ranged from 0 to 8.3, with a median of 0.8. Postoperative CAI ranged from 0 to 6.6, with a median of 0.3. The difference between post- and preoperative CAI ranged from –7.6 to 4.4, with a median of –0.2, indicating that CAI was significantly reduced by AT (*P* = .007) (**Table 1**). After AT, 23 (63.9%) children had a reduction in CAI, and 6 (16.7%) had an increase in CAI. Prior to surgery, 15 (41.6%) of the children had CSA (CAI ≥1). The median CAI of those with CSA before AT was 1.5 (range, 1-8.3), and after surgery, the median was 0.6 (range, 0-6.6) (*P* = .004). Ten (66.7%) of the 15 patients with diagnosed CSA demonstrated resolution (CAI <1) postoperatively, while CSA persisted in 5 (33.3%) patients (**Table 2**).

Other PSG parameters included lowest oxygen saturation, highest CO_2 saturation, and the presence of CO_2 retention.

Table 1. Pre- and Postoperative Polysomnogram Indexes.

Characteristic	Preoperative	Postoperative	Δ[a]	P Value[b]
AHI, median (range)	10.4 (1.1 to 59.5)	3.5 (0.4 to 59.4)	−6.1 (−58.1 to 42.2)	<.001[c]
O-AHI, median (range)	8.7 (0.9 to 59.3)	2.6 (0.4 to 59.3)	−4.7 (−58.7 to 42.2)	<.001[c]
CAI, median (range)	0.8 (0 to 8.3)	0.3 (0 to 6.6)	−0.2 (−7.6 to 4.4)	.007[c]
Lowest O_2, median (range), %	86 (50 to 91)	88 (60 to 93)	2 (−13 to 38)	.020[c]
Highest CO_2, mean (SD), %	52 (7)	52 (5)	0 (7)	.637[d]

Abbreviations: AHI, apnea-hypopnea index; CAI, central apnea index; O-AHI, obstructive apnea-hypopnea index.
[a]Postoperative minus preoperative values.
[b]$P < .05$ indicates statistical significance.
[c]Significance evaluated using 1-sample Wilcoxon signed-rank tests on Δ values.
[d]Significance evaluated using a 1-sample *t* test on Δ values.

Table 2. Number of Patients Displaying Severe Obstructive Sleep Apnea, Central Sleep Apnea, or CO_2 Retention.

Characteristic	Preoperative	Postoperative	P Value[a]
AHI ≥10	19	2	<.001
O-AHI ≥10	15	2	<.001
CAI ≥1	15	5	.004
CO_2 retention	11	8	.549

Abbreviations: AHI, apnea-hypopnea index; CAI, central apnea index; O-AHI, obstructive apnea-hypopnea index.
[a]$P < .05$ indicates statistical significance evaluated using the McNemar test with a binomial distribution.

Preoperative lowest oxygen saturation ranged from 50% to 91%, with a median of 86%. Postoperative lowest oxygen saturation ranged from 60% to 93%, with a median of 88%. The difference between post- and preoperative oxygen nadir ranged from –13 to 38, with a median of 2, indicating that AT significantly increased the oxygen nadir ($P = .018$) (**Table 1**). In contrast, highest CO_2 saturations were comparable before (mean [SD], 52% [7%]) and after surgery (52% [5%]) (**Table 1**). In addition, CO_2 retention was similar before and after AT (**Table 2**).

MANOVA was conducted to assess the influence of patient characteristics (age, sex, BMI, tonsil size, and adenoid size) on changes in PSG parameters before and after AT. Larger tonsils (size >2) ($F(1, 29) = 9.36$, $P = .005$) and adenoid tissue obstructing greater than 50% of the nasopharynx ($F(1, 29) = 4.47$, $P = .043$) were associated with a significant reduction in CAI postoperatively. Despite the association between obstructive tissues and CAI, logistic regression, univariate analysis of variance (ANOVA), and correlation analyses revealed no association between OSA severity and pre- or postoperative CAI. Logistic regression adjusted for baseline characteristics revealed that each 10% increase in adenoid size was associated with a 76% higher odds of preoperative CO_2 retention (95% confidence interval [CI], 1.17-2.65; $P = .007$). There was also a significant interaction identified between CAI reduction, preoperative CO_2 retention, and adenoid size, $F(2, 20) = 6.87$, $P = .05$.

Discussion

Sleep-disordered breathing and associated obstructive PSG patterns are commonly associated with patients with DS, but to date, little data exist examining CSA. The identification of CSA during PSG can provide additional challenges to the management of the patient with DS who has SDB. In this current study, we sought to examine both obstructive and central responses to AT in the DS population with SDB through objective PSG measurements.

In 2007, Merrell and Shott[18] examined pre- and postoperative PSG data of 21 children with DS and reported that 12 (52%) demonstrated normal AHIs after AT or tonsillectomy alone. A recent publication evaluating pre- and postoperative obstructive PSG findings in 11 children with DS noted that AT decreased AHI by an average of 6.1, and only 2 (18.2%) patients reported a normal AHI postoperatively.[16] A similar average AHI reduction of 6.2 was demonstrated in our analysis (**Table 1**), with only 2 of our 36 patients demonstrating a postoperative AHI <1. These findings reiterate AT is effective in AHI reduction but often noncurative in patients with DS.

The present study found a statistically significant postoperative decrease in O-AHI, with 86.6% of patients with severe obstruction having reduction of their O-AHI to less than 10 postoperatively (**Table 2**). Patients also exhibited an increase in oxygen nadir post-AT, demonstrating at least partial resolution of the obstructive component. Historically, oxygen saturation has been associated with OSA symptomatology.[19] These findings demonstrate only partial resolution/improvement of obstructive components by AT in DS-associated OSA.

In the general pediatric population, CSA was recently reported to be present in 14.9% of children with OSA.[14] Another analysis examining CSA in patients with DS without obstructive disease reported CSA in 89.4% of the patients reviewed.[20] In our current study of DS children with OSA, 41.6% demonstrated a CAI ≥1 consistent with CSA. Although little data exist on the significance of these findings, they suggest that CSA events may occur more often in neurodevelopmentally impaired populations such as DS.[20]

In our study, 66.7% of children with CSA demonstrated resolution postoperatively (**Table 2**). This finding is similar

to the 73.3% resolution rate of CSA reported by Baldassari et al[14] when examining the general pediatric population's response to AT. The mechanism underlying CAI reduction and CSA resolution after AT is currently unclear.[14] In our study, both adenoid and tonsil size influenced CAI reduction. This suggests that although CSA is a disorder perceived to be primarily associated with central nervous system respiration control, there is often a connection with airway obstruction in children with diagnosed CSA and OSA.

There is a paucity of data examining the cause of CSA and the physiology of resolution after obstruction surgery. One predominant theory on obstruction-associated CSA relates to CO_2 retention and elevation. Studies have suggested that increased airway resistance contributes to increased CO_2 levels and that elevated CO_2 can trigger central chemoreceptors resulting in increased upper airway relaxation and unstable inspiratory/expiratory muscle activity.[12,21,22] In our study, patients with larger adenoids were more likely to experience CO_2 retention preoperatively and demonstrated a significant postoperative reduction in CSA. These findings support the theory that by altering obstruction-associated CO_2 retention and elevation, respiratory stability is restored to some patients, and CAI reduction or CSA resolution occurs.[14] This finding may be more evident and critical in patients with DS since their narrowed nasopharyngeal and oropharyngeal anatomy gives rise to relatively greater encroachment by adenotonsillar tissue.

This study does have some limitations. It was a retrospective study, so clinical findings and validated quality-of-life sleep questionnaires were not used pre- or postoperatively. Anatomical evaluations of tonsillar size were recorded from clinical evaluation and not intraoperatively, which could have further limited this subjective assessment. In addition, neither Mallampati nor Friedman classifications were recorded. Being retrospective in nature, we did not control for why postoperative PSGs were conducted on 36 of 114 patients, making it susceptible to inclusion bias. When examining median differences of pre- and postoperative CAI and O_2 nadir in all patients with DS investigated, slight improvements were demonstrated postoperatively (**Table 1**). The benefits of these minor improvements are unknown but unlikely to have clinical value.

Patients with DS are known to have numerous associated comorbidities that could have contributed to the results found in this study, and very little literature exists on CSA, making both underlying cause and significance a topic of debate. With the above in mind, this study used predominantly objective findings to examine the effect of AT on SDB in a complex patient population.

Conclusion

The utilization of PSG data in the diagnosis and treatment of SDB has expanded in recent years with an emphasis on use in the DS population.[10,17,18] In DS children with SDB, the presence of both obstructive and central events is demonstrated on PSGs. Unfortunately, there is a paucity of literature on the relationship between OSA, CSA, and their responses to AT in the DS population. In our current study, most patients demonstrated a significant reduction of both obstructive and central apnea after AT. Additional analysis demonstrated a significant interaction between CO_2 retention, adenoid size, and postoperative CAI reduction. To our knowledge, this is one of the largest studies examining pre- and post-AT PSG changes in pediatric DS. It is also the first to examine in detail CSA response to AT in the DS population.

Author Contributions

Prasad John Thottam, conception, data analysis, drafting, final approval, accountability for all aspects of the work; **Sukgi Choi**, data analysis, revising critical portions, final approval, accountability for all aspects of the work; **Jeffrey P. Simons**, conception, revising critical portions, final approval, interpretation of data, accountability for all aspects of the work; **Dennis J. Kitsko**, conception, design, data analysis, revising critical portions, final approval, accountability for all aspects of the work.

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