Evaluating the Management of Obstructive Sleep Apnea in Neonates and Infants

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Objectives: To investigate interventions used in treating obstructive sleep apnea in neonates and infants and to report their efficacies.

Design: Retrospective medical record review.


Patients: Neonates and infants aged 0 to 12 months at the time of obstructive sleep apnea diagnosis by polysomnography.

Main Outcome Measures: Demographic data, comorbidities, polysomnography data, and intervention data.

Results: In total, 126 patients (86 [68.3%] male and 40 [31.7%] female) were included in the study. The most common interventions (and the mean age at the time of intervention) were anti–gastroesophageal reflux disease treatment (88 patients [69.8%] at age 7 months), observation (33 patients [26.2%] at age 6 months), supplemental oxygen (31 patients [24.6%] at age 4 months), adenoidectomy (30 patients [23.8%] at age 15 months), other surgical (25 patients [19.8%] at age 7 months), continuous positive airway pressure/bilevel positive airway pressure (CPAP/BiPAP) (18 patients [14.3%] at age 16 months), supraglottoplasty (11 patients [8.7%] at age 6 months), tonsillectomy and adenoidectomy (9 patients [7.1%] at age 24 months), tracheostomy (7 patients [5.6%] at age 10 months), and other nonsurgical (7 patients [5.6%] at age 15 months). Among neonates and infants, nonsurgical interventions were performed in most cases, although those aged 0 to 3 months underwent more surgical interventions (19.7%) than those aged older than 3 to 9 months (11.7%). The mean objective improvement, measured as a percentage decrease in preintervention apnea-hypopnea index, was greatest in neonates and infants receiving CPAP/BiPAP, followed by those undergoing tracheostomy.

Conclusions: Anti–gastroesophageal reflux disease treatment is the most common intervention in each age group. Although adenoidectomy is the most common surgical intervention overall, the prevalence increases with age. Supraglottoplasty is the most common surgical intervention in neonates and infants aged 0 to 3 months and offers the greatest objective improvement in this age group. Overall, the use of CPAP/BiPAP is associated with the greatest objective improvement.


Sleep-related breathing disorder describes a collection of conditions characterized by an abnormal respiratory pattern or a diminished breathing frequency during sleep. Obstructive sleep apnea (OSA) is the most common form of sleep-related breathing disorder and has an estimated prevalence among the pediatric population of between 1% and 4%.1,2 Evidence in the literature shows that sleep-related breathing disorder in the pediatric population has significant negative effects on health, as well as on behavior later in childhood, including depression, failure to thrive, neurocognitive impairment, excessive daytime sleepiness, increased risk for systemic and pulmonary hypertension, and behavioral issues suggestive of attention-deficit/hyperactivity disorder.3,4 This argues for the need for early intervention in this population.

CME available online at www.jamanetwork.com/cme.aspx and questions on page 116

As OSA becomes an increasingly more common pediatric concern, data have begun to emerge about the management of infants and school-aged children with OSA. Despite the wide variation in documented success with tonsillectomy and adenoidectomy (T&EA) (range, 27.2%-82.9%),3 this surgical management has become the preferred first-line treatment for many physicians.5,6 Unfortunately, this management strategy fails to sufficiently address OSA management in the neonate.
and infant population, in whom T&A is rarely performed owing to concern about potentially higher complication rates. Results of studies further suggest a predilection for the youngest children to have more severe sleep apnea. Therefore, although technology has made diagnosis of OSA possible through polysomnography (PSG) regardless of age, the youngest and potentially most severely affected patient subgroup remains neglected with respect to data regarding intervention course and efficacy.

Because the origin of sleep apnea in these patients is poorly defined and OSA therapy is directed toward the underlying cause, treatment strategies cannot be assumed to be analogous to those used in older children. Potential surgical interventions include T&A, tongue reduction, tracheostomy, and supraglottoplasty, while medical strategies include oral appliances, nasal corticosteroid use, and continuous positive airway pressure (CPAP). However, little is known about the frequency of use or the efficacy of these interventions.

In this study, we investigated the outcomes of non-surgical and surgical interventions aimed to treat neonates and infants diagnosed as having OSA. All study participants were diagnosed by an in-laboratory PSG performed when the child was younger than 12 months. After diagnosis, the neonates’ and infants’ medical records were analyzed for the full extent of their follow-up periods with the otolaryngology or pulmonology clinic. Institutional review board approval was obtained to search the pulmonology records for all children aged 0 to 12 months undergoing his or her first PSG at our institution between January 1, 2007, and December 31, 2010. Of these 218 patients, 126 met the criteria for inclusion in the study. Inclusion criteria were patients diagnosed between 0 and 12 months of age as having OSA by an abnormal PSG result, defined as an apnea-hypopnea index (AHI) of at least 1.5, with documented follow-up results in the otolaryngology or sleep and pulmonology clinic for at least 6 months following diagnosis. Patients with a known infectious origin at the time of PSG in whom OSA symptoms abated on resolution of the infectious process were excluded from the study.

Collected outcome measures included demographic data, comorbidities, interventions targeted to treat OSA, and the subjective improvement of OSA symptoms following the intervention. Interventions that occurred after age 12 months and subjective improvement measures were also collected to assess longer-term efficacy of treatment and the symptomatic improvement associated with later interventions. Collected PSG data included AHI; hypopneas; oxygen nadir; arousal index; total sleep time; severity of snoring; percentage of total sleep time with oxygen saturations of less than 89%; and central, obstructive, and mixed apneas; as well as the presence or absence of hypoventilation, periodic breathing, and stridor or stertor. With respect to comorbidities, gastroesophageal reflux disease (GERD) was included as a comorbid disease if it was clinically diagnosed by the child’s primary care physician and was medically treated. Although criteria for grading the severity of OSA among the pediatric population vary in the literature, our study used the following 4-level grading system based on the AHI: an AHI of less than 1.5 was considered normal, an AHI of 1.5 to 4.9 was considered mild, an AHI of 5.0 to 14.9 was considered moderate, and an AHI of 15.0 or higher was considered severe. The cutoff values chosen were consistent with other studies examining the pediatric population with OSA. An arousal index of 12 or higher and oxygen desaturations of less than 89% for at least 2% of total sleep time were also considered abnormal.

Because this study is retrospective, the subjective improvement of each intervention was determined by us from the follow-up appointment medical record to objectively grade family members’ or caregivers’ reports of symptomatic improvement using the following Likert-type scale: 1 for worsening, 0 for no change, 1 for mild improvement, 2 for moderate improvement, and 3 for significant improvement or resolution. The intervention outcome was then measured objectively by calculating the percentage change in the AHI between preintervention and postintervention PSG. For patients with more than 2 PSG studies, the final PSG recorded was used to determine the objective improvement. The specific methods of PSG data collection, interpretation, and scoring are discussed in an earlier publication.

### METHODS

In total, the study inclusion criteria were met by 126 patients, of which 86 (68.3%) were male and 40 (31.7%) were female. Further distribution based on age, sex, and OSA severity is summarized in Table 1. Table 2 gives the mean AHI scores compared with abnormal arousal indexes and oxygen desaturations.

Table 3 gives the 10 most common comorbidities observed in our patient population. Gastroesophageal reflux disease (GERD) was the most common comorbidity, with 68.3% of neonates and infants being affected. As summarized, 46 patients (36.5%) were affected by a congenital syndrome or craniofacial malformation, with Down syndrome (7.9%) and cleft palate (7.1%) being most common.
In total, 259 interventions were performed, with some patients undergoing multiple interventions. As summarized in Table 4, the most common interventions (and the mean age at the time of intervention) were anti-GERD treatment (88 patients [69.8%] at age 7 months), observation (33 patients [26.2%] at age 6 months), supplemental oxygen (31 patients [24.6%] at age 4 months), adenoidectomy (30 patients [23.8%] at age 15 months), other surgical (25 patients [19.8%] at age 7 months), CPAP/bilevel positive airway pressure (CPAP/BiPAP) (18 patients [14.3%] at age 16 months), supraglottoplasty (11 patients [8.7%] at age 6 months), T&A (9 patients [7.1%] at age 24 months), tracheostomy (7 patients [5.6%] at age 10 months), and other nonsurgical (7 patients [5.6%] at age 15 months). Of the other nonsurgical interventions, caffeine and blood transfusion were used in the setting of prematurity, after which the children required no further intervention. Other surgical interventions included neurosurgical decompression, among patients who underwent ventriculoperitoneal shunt placement (2 patients), meningomyelocele closure (2 patients), Chiari decompression (1 patient), and an intraventricular cyst fenestration (1 patient).

A comparison of 209 nonsurgical interventions and 92 surgical interventions by age at the time of intervention demonstrated a high percentage (>75%) of nonsurgical interventions in each age group. The numbers (and percentages) of nonsurgical interventions and surgical interventions, respectively, for each age group were as follows: 53 (80.3%) and 13 (19.7%) for 0 to 3 months, 51 (91.1%) and 5 (8.9%) for older than 3 to 6 months, 26 (86.7%) and 4 (13.3%) for older than 6 to 9 months, 70 (77.8%) and 20 (22.2%) for older than 9 to 12 months, and 9 (15.3%) and 50 (84.7%) for older than 12 months. Of 13 surgical interventions that were performed between 0 and 3 months of age, 9 (69.2%) were performed following diagnosis of severe OSA. These surgical interventions were performed in 10 neonates, 7 of whom had a craniofacial malformation (Pierre Robin sequence in 5 patients and Down syndrome in 2 patients). After age 12 months, the percentage of nonsurgical interventions decreased to 15.3%. This is shown in Figure 1, which plots the mean age at the time of intervention based on the severity of OSA at the time of diagnosis. This is further shown in Figure 2 and Figure 3, which show anti-GERD treatment to be the most common intervention regardless of OSA severity or age at the time of intervention.

Subjective measures of intervention outcome were based on parental and caregiver responses to OSA-related symptoms documented during follow-up appointments and were measured on a scale of −1 (indicating worsening) to 3 (indicating significant improvement or resolution). Table 5 summarizes that observation was the most subjectively effective intervention, with a mean value of 2.8 on this scale. Similarly, tracheostomy had a mean subjective rating of 2.7. For those patients who underwent both preintervention and postintervention PSG studies, CPAP/BiPAP showed the highest mean percentage decrease in the AHI (a 67.2% decrease), followed by tracheostomy (67.0%), observation (65.6%), and supraglottoplasty (65.3%).

Among 126 patients, 235 PSG studies were performed. Polysomnography was repeated in 41.3% of the study population (52 patients), of whom 10 patients (19.2%) had an initial PSG that showed mild OSA, 14 patients (26.9%) had an initial PSG that showed moderate OSA, and 28 patients (53.8%) had an initial PSG that showed severe OSA. Of the patients undergoing repeat PSG studies, complete resolution of OSA (AHI, <1.5) was achieved in 8 patients (15.4%). While more than half of the patients undergoing repeat PSG studies were initially diagnosed as having severe OSA, these neonates and infants comprised only 2 of 8 patients who experienced complete resolution. Four patients underwent nonsurgical interventions, including 3 with observation and 1 with CPAP/BiPAP, while the remaining 4 patients underwent surgical interventions, including 1 tracheostomy, 1 supraglottoplasty, 1 adenoidectomy, and 1 tonsillectomy. For children treated with a positive airway pressure (PAP) device, the appliance was used during the repeat PSG studies. Although in theory the appliance should be adjustable to remove all obstructive events, some children could not tolerate the higher pressures and

Table 2. Number of Patients in Each Age Group With an Arousal Index of 12 of Higher and at Least 2% TST With Oxygen Saturations of Less Than 89% by Obstructive Sleep Apnea (OSA) Severity at the Time of Diagnosis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Age, mo</th>
<th>0 to 3</th>
<th>&gt;3 to 6</th>
<th>&gt;6 to 9</th>
<th>&gt;9 to 12</th>
<th>Total</th>
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<td>AHI, mean</td>
<td>2.8</td>
<td>3.3</td>
<td>3.4</td>
<td>3.2</td>
<td>3.2</td>
</tr>
<tr>
<td></td>
<td>Arousal index ≥12, No.</td>
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<td>2</td>
<td>4</td>
<td>7</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>≥2% TST with oxygen &lt;89%, No.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>35</td>
</tr>
<tr>
<td>Moderate OSA</td>
<td>AHI, mean</td>
<td>8.9</td>
<td>8.2</td>
<td>7.8</td>
<td>6.6</td>
<td>8.2</td>
</tr>
<tr>
<td></td>
<td>Arousal index ≥12, No.</td>
<td>7</td>
<td>9</td>
<td>5</td>
<td>4</td>
<td>25</td>
</tr>
<tr>
<td></td>
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<td>5</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>9</td>
</tr>
<tr>
<td>Severe OSA</td>
<td>AHI, mean</td>
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<td>16.5</td>
<td>26.1</td>
<td>28.3</td>
</tr>
<tr>
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<td>8</td>
<td>6</td>
<td>1</td>
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<td>21</td>
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Abbreviations: AHI, apnea-hypopnea index; TST, total sleep time.
orders, it remains unclear whether a causal relationship exists between the 2 or if the processes simply share common risk factors and tend to occur in the same children. The presence of GERD in about 68% of neonates and infants in our study is comparable with its prevalence of up to 67% during the first 6 months of life and is consistently observed in the setting of OSA. Data showing that anti-GERD treatment decreases OSA severity and ameliorates the AHI of 45.5%. These results suggest that, while anti-GERD treatment was the most common therapy in our study. Treatment yielded mild to moderate subjective improvement and a mean decrease in the AHI of 45.5%. These results suggest that, while anti-GERD treatment may decrease OSA severity and ameliorate disease, it alone does not offer a cure.

Furthermore, GERD has a strong association with laryngomalacia and is seen in 65% to 100% of cases of laryngomalacia. Of 36 neonates and infants in our study with laryngomalacia, 33 (91.7%) had concomitant GERD for which they were being treated. Because the severities of both components have been found to improve with anti-GERD therapy, current recommendations stress the importance of treating GERD to improve concomitant disease. Therefore, anti-GERD treatment was the most appropriate intervention for this subgroup in our study. However,
while anti-GERD treatment may lessen the severity of laryngomalacia by decreasing mucosal irritation and edema, the anatomical abnormality still exists.

Our data also showed that the youngest neonates and infants (age range, 0-3 months) were managed with more surgical interventions than those aged older than 3 to 9 months. This must be considered in the context of a large percentage (36.5%) of neonates and infants also having a congenital syndrome or craniofacial malformation. The anatomical anomalies present in these children necessitate the need for OSA diagnosis and surgical interventions at a younger age. In total, 52.4% of all severe OSA was diagnosed in the subgroup aged 0 to 3 months, a group that composed only 38.9% of the study population, demonstrating that the most severe OSA tends to occur in the youngest patients.

**TREATMENT EFFICACY**

It is impossible to control for compliance with nonsurgical interventions. This is likely most exaggerated in the setting of PAP appliances, where discomfort commonly leads to noncompliance. Marcus et al demonstrated that, while the use of CPAP/BiPAP was efficacious in the setting of pediatric OSA, a high dropout rate and parental overestimation of actual time spent using the device were also observed. Our study showed moderate improvement by subjective response and a large mean decrease in the AHI of 67.2%. While PAP directly creates a more patent airway and reduces soft-tissue obstruction, this positive effect observed in our study may be partially attributable to the previously observed effect of PAP in ameliorating GERD symptoms, which would be significant in our study owing to the large proportion of patients with GERD. Regardless, PAP appliances proved to be the most objectively efficacious intervention herein.

In our study population, supraglottoplasty also showed both subjective and objective improvement, with a mean subjective assessment of moderate improvement and a mean decrease in the AHI of 65.3%. This is the only surgical intervention that showed a steady decrease rather than an increase in prevalence with age. The prevalence of supraglottoplasty increased with greater severity of OSA, and no major surgical complications occurred. These results suggest that supraglottoplasty performed in the first 3 months of life is efficacious for neonates and infants with severe OSA, despite fears about surgical interventions in the newborn period.

While Valera et al found supraglottoplasty to be efficacious in alleviating sleep apnea in infants with severe laryngomalacia, it becomes less efficacious when comorbidities are present. Infants receiving the earliest surgical intervention are presumably the most medically complex. Therefore, our finding of supraglottoplasty benefit increasing with age at the time of inter-
vention is consistent with these previous results and should not deter physicians from early surgical management because children undergoing the procedure later in life likely have fewer medical complexities and will have more favorable OSA outcomes simply owing to the nature of less severe disease.

For the most efficacious treatment strategies, observation was subjectively superior to all interventions. However, the percentage of patients undergoing observation decreased dramatically as severity of disease increased, from 23.5% in the mild OSA group to 2.9% in the severe OSA group. Therefore, selection bias confounds the results in that the least severely affected patients were more likely to undergo observation rather than any given intervention.

Both nonsurgical and surgical treatments provided complete resolution of OSA. Because of the nature of the study, it can be inferred that many patients who experienced complete resolution did not follow up with a repeat PSG to confirm resolution.

Physicians consider and prefer alternative methods before resorting to tracheostomy. In children with Pierre Robin sequence or isolated micrognathia, evidence supports mandibular distraction osteogenesis as a generally safe and effective alternative to tracheostomy.23,24 Our study population further supports these findings because the most objectively efficacious intervention in the group aged 0 to 3 months was mandibular distraction osteogenesis. The subjective improvement was also moderate to significant. While only 1 infant who underwent the procedure returned for a repeat PSG, all had documented subjective improvement in the follow-up period. The overall improvement seen in our patients who underwent mandibular distraction osteogenesis lends further support to early surgical intervention in these medically complex neonates and infants to prevent the need for future tracheostomy.

USEFULNESS OF PSG

Although PSG is the standard criterion for diagnosis of OSA in all age groups, the usefulness of PSG extends beyond diagnostic capabilities by also guiding therapeutic decision making. The incidence of OSA in children with craniofacial syndromes is much higher than that in the general population, demonstrating that the full capabilities of PSG are most dynamic in the newborn population. Current recommendations are straightforward, advising that all children with craniofacial abnormalities should undergo PSG early in life, regardless of whether symptoms suggestive of OSA are present.27 In our study, most children who underwent surgical intervention in the first 3 months of life had a craniofacial malformation. In these patients, PSG was performed early and guided the decision to intervene surgically, supporting the use of PSG in medically complex neonates and infants in whom surgical interventions are a consideration.

LIMITATIONS

The lack of normative data with respect to normal-range PSG results in the neonate and infant population represents the main limitation of our study. Severity criteria based on AHI cutoffs vary in the literature.28,29 This is magnified in the neonate population, among whom the effect of physiologic central apneas is not fully understood. To date, no means exist to delineate these physiologic apneas from pathologic apneas. Future studies establishing normal-range PSG results and subsequent AHI criteria in the neonate and infant population are warranted.

As mentioned earlier, selection bias is inherent in retrospective studies and confounds our results for treatment strategies. Furthermore, the nature of the study ren-
ders it impossible to assume that all parents were offered similar treatment options, adding additional bias and conceivably confounding the subjective measurement of each intervention outcome.

Our results are also affected by the limited number of repeat PSG studies. While studies\(^{19,30}\) show that subjective response tends to overestimate the objective improvement, many patients do not obtain a postintervention PSG, especially in the case of significant improvement in symptoms.

## CONCLUSIONS

Many factors influence intervention selection and timing in the pediatric population with OSA. Age at the time of diagnosis is a powerful factor. While T&A is the first-line treatment for OSA in children older than 12 months, the distinction is much less clear in neonates and younger infants. Our data suggest that in all age groups studied herein observation is a suitable decision for mild OSA. As OSA severity increases, surgical management should be considered regardless of age. The youngest neonates and infants (age range, 0–3 months) represent many of the most severe cases of OSA and show strong improvement after surgical interventions, despite their young age. These positive effects are demonstrated by our results, specifically with respect to considering supraglottoplasty in severe laryngomalacia, as well as mandibular distraction in children with micrognathia. Adenoidectomy, tonsillectomy, and T&A are used with increasing frequency as children age.

Gastroesophageal reflux disease is an important comorbidity to recognize and treat in this population. While our data show subjective and objective improvement with anti-GERD treatment, the extent of this treatment alone cannot be fully appreciated because multiple interventions were commonly used in a single patient. A prospective, con-

<table>
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<th>0 to 3</th>
<th>&gt;3 to 6</th>
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<th>&gt;9 to 12</th>
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<td></td>
</tr>
<tr>
<td>Subjective (n = 9)</td>
<td>3.0</td>
<td>3.0</td>
<td>3.0</td>
<td>2.0</td>
<td>2.5</td>
<td>2.7</td>
</tr>
<tr>
<td>Objective (n = 2)</td>
<td>NA</td>
<td>NA</td>
<td>91.6</td>
<td>NA</td>
<td>42.3</td>
<td>67.0</td>
</tr>
<tr>
<td>Other surgical</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subjective (n = 16)</td>
<td>2.5</td>
<td>NA</td>
<td>2.0</td>
<td>2.3</td>
<td>1.8</td>
<td>2.0</td>
</tr>
<tr>
<td>Objective (n = 3)</td>
<td>78.0</td>
<td>NA</td>
<td>23.0</td>
<td>NA</td>
<td>−16.9</td>
<td>28.0</td>
</tr>
</tbody>
</table>

Abbreviations: CPAP/BiPAP, continuous positive airway pressure/bilevel positive airway pressure; GERD, gastroesophageal reflux disease; NA, not available; T&A, tonsillectomy and adenoidectomy.

\(^{a}\)Subjective improvement is based on a scale of −1 (indicating worsening) to 3 (indicating significant improvement or resolution). Objective improvement is based on the percentage decrease in preintervention to postintervention apnea-hypopnea index; a negative value refers to an increase in preintervention to postintervention apnea-hypopnea index.
trolled study is needed to determine the efficacy of anti-
GERD treatment with respect to OSA management.

Our data support the usefulness of PSG in medically
complex children at an early age not only to diagnose OSA
but also to guide management. For this reason, physi-
cians should obtain PSG in patients with craniofacial ab-
normalities or symptoms suggestive of OSA regardless of
age. This is especially important in medically com-
plex children in whom surgical interventions are being
considered. Finally, while our data support the benefit
of early surgical intervention in moderate to severe OSA
among all age groups, it is also important to encourage
families to obtain postintervention PSG to verify the ob-
jective improvement, despite subjective improvement.

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Author Contributions: Ms Leonardis and Drs Robison
and Otteson had full access to all the data in the study
and take responsibility for the integrity of the data and
the accuracy of the data analysis. Study concept and de-
sign: Leonardis, Robison, and Otteson. Acquisition of data:
Leonardis and Robison. Analysis and interpretation of data:
Leonardis. Critical revision of the manuscript for impor-
tant intellectual content: Leonardis and Otteson. Statistical
analysis: Leonardis. Administrative, technical, and material
support: Robison and Otteson. Study supervision: Robi-
son and Otteson.

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