

CLINICAL REVIEW

Treatment of obstructive sleep apnea in children: do we really know how?

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KEYWORDS

obstructive sleep apnea, tonsils, adenoids, upper airway, pharynx, snoring, hypertension, CPAP, corticosteroids

Summary Obstructive sleep apnea syndrome (OSAS) is a frequent, albeit underdiagnosed problem in children. If left untreated, OSAS may lead to substantial morbidities affecting multiple target organs and systems. The immediate consequences of OSAS in children include behavioral disturbance and learning deficits, pulmonary hypertension, as well as compromised somatic growth. However, if not treated promptly and early in the course of the disease, OSAS may also impose long-term adverse effects on neurocognitive and cardiovascular function, thereby providing a strong rationale for effective treatment of this condition. This review provides a detailed description of the current treatment modalities for pediatric OSAS, and uncovers the potential limitations of the available data on these issues. Furthermore, we postulate that OSAS will persist relatively often after tonsillectomy and adenoidectomy, and that critical studies need to be conducted to identify such patients and refine the clinical management algorithm for pediatric OSAS.

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INTRODUCTION

The prevalence of obstructive sleep apnea syndrome (OSAS) in the pediatric population is currently estimated at up to 2% of all children [1]. However snoring, the hallmark symptom of OSA in the pediatric population is much more frequent, and has been found to range from 8 to 27% [2–5]. Since snoring and obstructive apnea represent the two extremes of a wide spectrum of upper airway resistance, the transition from normal to pathological must clearly occur

somewhere along this continuum. However, the definition of what constitutes pathology in a snoring child is yet to be defined [6]. For example, there is general consensus today that any child presenting with 10 obstructive apneic events per hour of sleep needs treatment because his condition is distinctly pathological. However, if such a child had only two obstructive apneic events per hour of sleep, though outside the normative range, there would be disagreement as to whether this situation is clinically significant [7]. It is clear however, that the decision to treat OSAS is dependent on a thorough understanding of the morbidity associated with this problem. Similarly, information regarding the efficacy and safety of any given therapeutic modality will dictate the clinical standards for the management of such patients. In this review we will initially provide a brief review of the available evidence for OSAS-associated morbidity, which ultimately determines the overall rationale for

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treatment of OSAS, and then critically assess how our current clinical management guidelines are substantiated by evidence-based approaches.

MORBIDITY OF OSAS IN CHILDREN OR THE WHY SHOULD WE TREAT QUESTION

The primary rationale for treating any disorder is the prevention or cessation of morbidities associated with the disease. It therefore appears necessary to initially analyze in more detail the potential consequences of OSAS in children such as to provide the framework that justifies the need for treatment of this disorder. The morbidity of OSAS can be divided into three major categories, namely neurobehavioral, cardiovascular, and somatic growth.

Neurobehavioral morbidity

Frank disruption of sleep architecture leading to sleep fragmentation is considered to be relatively unusual in children with OSAS [8]. Nevertheless, more subtle alterations in EEG spectral characteristics do occur even when arousal is not immediately apparent during an obstructive apnea [9]. Similarly, excessive daytime sleepiness (EDS) does not appear to be a major symptom in children with OSAS as reported by parental observations [10] or when objectively defined using multiple sleep latency testing [11]. Indeed, when we defined EDS as a mean sleep latency < 10 min, only 13% of children with OSAS had EDS. However, overall sleep latencies were mildly, albeit significantly reduced in OSA patients [11]. Interestingly, the increase in daytime sleep propensity exhibited linear dependencies on apnea index, arousal index, degree of nighttime hypoxemia, and BMI, but was not related to patient age and degree of obstructive hypoventilation [11]. Thus in contrast with adult patients, EDS is not a predominant feature of OSAS in children. Despite the apparent relative absence of EDS, OSAS and even snoring appear to be associated with significant behavioral and learning problems. Indeed, the link between OSAS and behavioral disturbances has long been recognized and reported in case series or observational studies [12–20]. Two more recent studies have further demonstrated that effective treatment of OSAS is associated with at least partially reversible neurobehavioral and learning deficits [21, 22]. Indeed, in a large cohort of first graders who were failing in school we found not

only a 6–9 fold increase in the incidence of OSAS when compared with the predicted prevalence of OSAS in the general pediatric population, but more importantly that the overall school performance was significantly improved one year later in those children undergoing surgical removal of the hypertrophic adenotonsillar tissue causing OSAS. We have further found that young children who snore loudly and frequently during their sleep are at higher risk for lower grades in school several years after the sleep disordered breathing has resolved. Thus, OSAS may impose adverse and sustained neurocognitive outcomes and diminished academic achievement, particularly when OSAS develops during critical phases of brain growth and development. Such recent findings clearly provide a strong impetus to achieve early recognition of the disorder and to effectively treat the underlying causes, such as to prevent long-lasting deleterious consequences.

Cardiovascular morbidity

Normally, the circulatory effects of breathing are small. In adults however, the presence of OSAS is clearly associated with an increased risk for systemic hypertension, that has been undisputedly attributed to cyclical hypoxia during sleep with consequent alterations in the renin-angiotensin axis and enhanced sympathoadrenal discharge [23–25]. Thus, it is now clear that heightened sympathetic tone develops during OSAS and is detectable even during waking [26]. Very few studies have addressed this area in children. Marcus and colleagues showed that diastolic blood pressure elevations occurred in OSAS children and persisted after awakening [27]. Similarly, changes in left ventricular wall thickness indicative of elevated afterload were found in a high proportion of children with OSAS, suggesting that these changes may be due to systemic blood pressure elevations in these patients [28]. Furthermore, autonomic regulatory mechanisms may also be affected by the recurrent upper airway obstruction during sleep both during the night [29], as well as during daytime [30]. Although additional studies are clearly needed to better delineate the overall short-term and long-term implications of the autonomic alterations associated with OSAS in children, it is possible that such changes may predispose to earlier occurrence of more severe hypertension and consequent long-term associated morbidities.

In addition to systemic circulatory effects, recurrent hypercapnia and hypoxia can elicit vasomotor recruitment of the pulmonary circulation, and lead to pulmonary vascular hypertension. Evidence to this

effect in children has particularly emerged in the last decade. Tal and colleagues clearly showed that a substantial proportion (37%) of children with OSAS had evidence of right ventricular dysfunction commensurate with elevated pulmonary artery pressures [31, 32]. Although we assume that such pulmonary vascular changes are reversible with treatment, we are unaware of any study addressing this issue in the literature. However, it is possible that exposure to hypoxia during childhood may exacerbate the pulmonary vascular response to subsequent hypoxia during adulthood, and more readily lead to pulmonary hypertension [33].

Somatic growth

One of the better known consequences of OSAS in children is the higher risk for failure to thrive. However the incidence of this problem has not been systematically assessed, and has clearly changed in more recent years with increased awareness and less severe cases being more readily diagnosed. Further, the mechanisms underlying the development of growth retardation in OSAS are not fully defined. It is possible that dysphagia due to enlarged tonsils and adenoids may play a role in a minority of cases, and that decreased appetite due to changes in olfactory acuity may also contribute in some cases. However, it has been postulated that the increased respiratory effort during sleep will lead to increased metabolic expenditure and contribute to slower weight gain in these children, since OSAS treatment is associated with decreases in energy expenditure concomitant with weight gain [34]. More recently, a potential hormonal mechanism has been advanced, whereby decreased insulin growth factor-I levels may account for slower linear growth in some children with OSAS [35]. Interestingly, weight gain has been reported after treatment even in obese children with OSAS [36].

In summary, OSAS in children is associated with important short-term and long-term morbidity the full implications of which have not been completely determined. Nevertheless, the currently available information on the adverse consequences of OSAS in children clearly mandate the institution of early and effective therapy for this condition.

METHODS

A computerized Medline search was conducted on English-language-published peer-reviewed studies

focusing on treatment of OSAS in children. Case reports were included only if they were considered to significantly add to the knowledge base. Bibliographies of review articles on these topics were also scanned for additional references. The data were extracted from the articles and tabulated so as to itemize relevant methodologies and study results. Letter and numerical grades were assigned to each study according to the methodological design and strength of the scientific evidence using a modified version of the system employed by Hudgel and Thanakitcharu [37]. In brief, the following grades were used: (A) blinded, controlled trials; (B) observational prospective studies; (C) observational retrospective studies; (D) case reports or expert opinion. Also, a numerical score was given for the literature of each study reviewed, so that the quality of the literature could be compared across the various studies reviewed. An A study was given 20 points; a B study was given 10 points, a C study was given 5 points, and a D study was assigned 1 point. In order to weigh this grade for the number of subjects included, one tenth (0.1) of a point was added to the score of each study for each subject within a given study. The major purpose of the score was to indicate the level of scientific rigor of a given study rather than to indicate that the value of the intervention or outcome was better when compared to studies assigned lower scores. We further modified the score based on the diagnostic algorithms employed prior to the intervention as well as on the post-treatment assessment approach. For example, if the initial diagnosis of OSAS was based on clinical history and physical examination the overall score derived above was multiplied by 0.5, if a single or multiple channel home recording was conducted, the overall score was multiplied by 0.75, and when formal overnight polysomnography in the sleep laboratory was conducted, the score was multiplied by 1. This approach was justified on the basis that for the otherwise normal child, the principal parental complaint is snoring during sleep, and that occasionally parents will comment on breathing difficulties during sleep, unusual sleeping positions, morning headaches, daytime fatigue, irritability, poor growth and weight gain, and behavioral problems. Nevertheless, even when the diagnostic interview is conducted by a sleep specialist, the accuracy of OSAS prediction is relatively poor with at least 30% false negative rates [10, 38–42]. In addition, although overnight home recording improve the diagnostic accuracy of OSAS, they are still less sensitive than formal sleep studies in the sleep laboratory [43]. To enable assessment of outcome

measures following intervention, if outcome was based on parental history, then the study score was multiplied by 0.5, if a reduced overnight study was conducted, the score was multiplied by 0.75, and if a polysomnographic evaluation was used for determination of treatment outcome then the score was multiplied by 1.

TONSILLECTOMY AND ADENOIDECTOMY (T&A)

It is widely accepted that once the diagnosis of OSAS has been established, the first line of treatment should involve surgical removal of enlarged tonsils and/or adenoids (T&A). We identified a total of 21 studies in which sufficient information on T&A outcomes could be obtained. The summary of the studies and some of their salient features and findings are provided in Table I.

It becomes evident from Table I, that the available data are marred by substantial limitations that preclude any definitive conclusions on the overall efficacy of surgical intervention in this disorder. First and foremost, there was no study which employed a prospective randomized design. Although it is obvious that such a design would presently be rather difficult, if not impossible, to implement because of ethical considerations [61] there is still room for comparisons between different surgical modalities. In fact, we were unable to determine from the reviewed literature whether tonsillectomy alone, tonsillotomy alone, adenoidectomy alone, or a combination of these surgical approaches will provide a superior outcome. For example, Niemenen and colleagues reported that a proportion of children who underwent adenoidectomy alone later required the addition of tonsillectomy [46]. However, no details are provided as to what proportion of children undergoing adenoidectomy alone had recurrence of OSAS. Alternatively, in studies using several surgical approaches, pooled outcomes are provided which preclude accurate determination of improvement or cure rates for any given surgical technique [58]. In the only study comparing combined tonsillectomy and adenoidectomy with adenoidectomy alone, Shintani and colleagues found similar improvements in both the respiratory disturbance index (RDI) and in the lowest oxyhemoglobin saturation [44]. However, only 13 children were included in the adenoidectomy alone group compared to 114 patients in the T&A group.

The severity of OSAS is a potentially important consideration that could affect the impact of T&A.

Only one study has addressed this issue, albeit not specifically. Suen *et al.* reported that $RDI > 19$ was more likely associated with a post-operative $RDI > 5$, i.e., with an abnormal sleep study after treatment [45]. However, this conclusion was based on a very small patient cohort totaling 26 patients. In addition, a very recent study published thus far only in abstract form suggested that children belonging to ethnic minorities, obese children, and those with a family history of sleep-disordered breathing were at higher risk for having residual OSAS after T&A [62]. These are important issues because they indicate that residual OSAS may be more frequent than previously anticipated, and may lead to changes in the currently restricted indications for post-T&A polysomnographic evaluation. In other words, identification of at-risk patients for non-curative T&A based on pre-operative polysomnography and/or other risk factors would mandate follow-up objective assessments that are not currently done in most pediatric centers. To further address this issue, we examined the literature for evidence of OSAS cure after T&A. Although most of the studies suggest that T&A is associated with significant clinical improvement, the rate of cure, defined as disappearance of symptoms and normalization of overnight respiratory measures, was documented in only 11 studies [44–46, 49–53, 58, 101]. The cumulative cure rate for such studies was 80% and included a total of 401 patients. This figure is strikingly similar among studies, and therefore suggests that surgery has a residual OSAS rate of approximately 20%. Since the data from such studies did not partition for severity, it is possible that T&A “failures” may in fact correspond to the very same risk factors associated with sustained OSAS reported above. These findings contrast with those emanating from studies in which post-operative symptoms served as the outcome measure. We identified a total of 8 studies which included 251 patients [46, 48, 50, 55, 56, 58–60]. Reported improvement in the patients’ condition occurred in 97% of cases. These data can be viewed as further demonstration that parentally-reported symptoms constitute a poor predictor of OSAS in children both before and after T&A [10].

In summary, T&A emerges as the leading treatment approach for OSAS in children. However, post-operative persistence of the disease is more frequent than expected. In addition, it needs to be stressed that the published literature was usually obtained in tertiary pediatric centers, and therefore the effectiveness of T&A under routine conditions remains to be determined.

Table 1 Summary of studies on tonsillectomy and adenoidectomy for pediatric obstructive sleep apnea

Author	Year	Methods	Subjects	Results	Conclusions	Comments	Grade	Score
Shintani <i>et al.</i> [44]	1998	Referrals for snoring and apnea, inductance plethysmography, SaO ₂ and cephalometrics pre and 2 months post T&A, not randomized, blinded, or controlled	92 male, 42 female, 1–9 yrs, 74 pts with AHI > 10, 114 pts with T&A	75.4% of T&A pts improved with mean AHI decreased from 18–7.5, lowest SaO ₂ increased from 79–85%, unimproved pts tended towards smaller tonsils, narrower epipharyngeal space, and less mandibular protrusion; greater tonsillar hypertrophy associated with greater improvement	T&A effective, facial morphology and tonsillar hypertrophy affect results	Cephalometrics not statistically significant, AHI and “improvement” poorly defined, incomplete PSG	B	13.2
Suen <i>et al.</i> [45]	1995	Prospective; referrals to ENT for suspected OSA; 16 channel PSG, T&A if RDI > 5, F/U PSG > 6 wks post tx; PSG partially blinded, not randomized or controlled	41 male, 28 female, 1–14yrs, otherwise healthy, all with tonsillar hypertrophy and snore, all with apnea and/or daytime somnolence, 30 tx'd with T&A; 26 with PSG post tx	51% with RDI > 5, larger tonsils than RDI < 5 group; RDI decreased 18.1–4.5, min SaO ₂ increased 70.9–88.0%, obstructive hypopnea, longest apnea, arousals all decreased; sleep time increased; 4/26 still with RDI > 5	85% cure with T&A; all pts showed improvement; RDI only preoperative predictor of success; PSG necessary for OSA dx	No randomization or control	B	12.6
Niemenen <i>et al.</i> [46]	2000	Controlled, prospective, not randomized or blinded; all referrals to ENT for T&A; 6 channel PSG if sx of OSA, normal exam, and otherwise healthy; AHI > 2 T&A, AHI < 2 no T&A; sx score and PSG pre and 6 mos post T&A	58 healthy snorers (31 male, 27 female), 3–10 yrs, 21 with AHI > 2; 30 healthy controls (17 male, 13 female)	T&A: mean AHI decreased 6.9–0.3, median sx score decreased 12–1, mean OSA score decreased 3.4–3.1. PS and control groups: 15 without change in sx, 16 with decreased sx, PSG unchanged	T&A curative, PSG necessary for OSA dx, observation sufficient if PSG normal	Not blinded or randomized; no electroencephalography or electrooculography	B	12.1

Table I continued

Author	Year	Methods	Subjects	Results	Conclusions	Comments	Grade	Score
Helfaer <i>et al.</i> [47]	1996	Prospective; referrals to ENT for PSG dx'd OSA; all tx'd with T&A; randomized anesthesia type; post-op PSG in ICU (day of surgery)	15 pts, 1–12 yrs, 1–15 OA/hr, otherwise healthy	Obstructive events decreased 5–2/hr; total respiratory events decreased; minimum SaO ₂ (REM) increased 78–92%; min SaO ₂ (NREM) increased 90–94%	Normal children with mild OSA have improvement on the night of surgery and do not need intensive monitoring; anesthesia choice does not matter	Small size; no randomization or control of T&A; no post-acute F/U	B	11.5
Zucconi <i>et al.</i> [48]	1993	Prospective; consecutive referrals to sleep center for snoring; PSG: 25 nocturnal, 35 diurnal; T&A or T&monotonsillectomy; F/U PSG at 3–18 mos in 14 of nocturnal and 15 of diurnal; not randomized, blinded, or controlled	nocturnal: 13 male, 12 female; diurnal: 23 male, 12 female; 16–103 mos; 19 of nocturnal group, 15 of diurnal group tx'd	Nocturnal PSG: AHI decreased 11.1–3.4 min SaO ₂ increased 81–89%, elimination of pathological respiratory events in all but 3, reduction or elimination of snoring, nocturnal agitation, daytime sx's; similar results for T&M subset Diurnal PSG: relief of apnea/hypopnea in 13/15 Adenoidectomy alone ineffectual (5 pts total)	A&T, A&Monotonsillectomy < 4 yrs reduces AHI and snoring in pts with mild-moderate OSA	No control or randomization, diurnal studies of questionable validity	B	11.4
Bar <i>et al.</i> [35]	1999	Prospective; referrals to sleep clinic for signs/sxs of OSA; T&A; pre/3–10 mos post 13-channel PSG or oximetry; weight, height, IGF-I, IGF-BP3 levels	11 male, 2 female, 1.6–10.8 yrs	RDI decreased 7.8–1.0; no change in mean SaO ₂ or time below 90%; paradoxical breathing decreased 37.4–18.6% of total sleep time; weight standard deviation score increased 0.86–1.24 at 18 mos; no change in height standard deviation score; IGF-I increased 70%; no change in IGF-BP3	RDI improves after T&A in OSA pts; IGF-I increases after T&A; wt increases after T&A; IGF-I axis is affected in children with OSA	Small n; no randomization or control of T&A; some children with persistent sleep disturbance	B	11.3

Table 1 continued

Author	Year	Methods	Subjects	Results	Conclusions	Comments	Grade	Score
Wiet <i>et al.</i> [49]	1997	Retrospective case series; pts with “unclear” history and or physical exam or complicated OSA; T&A and/or uvulopharyngopalatoplasty (31 T&A alone); pre/post 14 channel PSG; AHI > 5 = OSA	48 pts; 1.5–20 yrs; 22 African-American; 13 healthy, 20 obese, 5 trisomy 21, 4 asthma 2 cerebral palsy, 4 other	All: AHI decreased 27–6, time SaO ₂ < 90% decreased 17.9–1.4%, time ET/CO ₂ > 50 mmHg decreased 22.3–12.6%. Healthy pts: AHI decreased 23–6, time SaO ₂ < 90% decreased 8.0–0.5%, time ET/CO ₂ > 50 mmHg decreased 32.0–15.2%. Obese pts: AHI decreased 33–4, time SaO ₂ < 90% decreased 20.1–0.5%, time ET/CO ₂ > 50 mmHg decreased 14.9–10.1%.	T&A effective in complicated pts	Uvulopharyngopalatoplasty results not separated from T&A	C	9.8
Agren <i>et al.</i> [50]	1998	Consecutive referrals to ENT for OSA sx; pre-operative PSG and questionnaire; post-operative apnea mattress and oxymetry; orthodontic exam; OAI > 1 = OSA	12 male, 8 female, 4–9 yrs, otherwise healthy; 16 T&A, 3 T, 1 A; AHI > 1 in 17/20, > 5 in 10/20.	Snoring eliminated; minimum SaO ₂ increased 87–93%; > 4% SaO ₂ dip rate decreased 3/hr–0/hr; periodic breathing decreased from 34–8% of total sleep time; 15/20 with normal recording; 19/20 sx free, mandible growth more horizontal at F/U	T&A effective in reducing signs and sx of OSA and changing oral growth/shape	Multichannel study; nonstandard interpretation of PSG; unvalidated postoperative studies; no randomization or control	B	9.5
Stradling <i>et al.</i> [51]	1990	Prospective; referral to ENT for T&A + snoring; tonsillectomy and/or adenoidectomy; pre and 6 mo post tx home oximetry and video; height measurement and sx questionnaire; not randomized or blinded	31 male, 30 female, 2–14 yrs; 31 healthy controls; 46 T&A, 7 T, 8 A	> 4% decrease in SaO ₂ > 3/hr: decreased from 61–13% of pts.; mean > 4% SaO ₂ dip rate decreased 3.6–1.5/hr; heart rate 10.7 beats per minute > controls, normalized after tx; movement: 65% with > 8% of time moving—decreased to 4% after tx; height velocity and weight % increased post tx; sx comparable to control after tx	T&A relieves signs and sx of OSA; improved growth after tx	Multichannel recordings; no randomization	B	9.1

Table 1 *continued*

Author	Year	Methods	Subjects	Results	Conclusions	Comments	Grade	Score
Lind <i>et al.</i> [52]	1982	Referrals to ENT clinic for nocturnal breathing difficulties or recurrent ear/throat infection; included if hx of apnea or kissing tonsils; overnight ETCO ₂ and observation; T + /-A; repeat ETCO ₂ 4 wks post tx; growth F/U at 10–42 mos	14 pts, 2.8–7.6 yrs; 6 controls (normal tonsils, no apnea)	Apnea > 20 sec in 5 pts; no apnea post tx; increased appetite and alertness; mean ETCO ₂ decreased 6.6–5.7 kPa; no difference between post tx and control ETCO ₂ ; weight increased –0.7 standard deviation score to 0.3 standard deviation score; height increased from –0.2 standard deviation score to 0.4 standard deviation score	CO ₂ , growth, sxs improve post T&A	Small size; no PSG; criteria for dx of OSA unclear	B	7
Kudoh <i>et al.</i> [53]	1996	Obese pts referred for sleep disordered breathing; respisomnogram and SpO ₂ pre and 5–6 days post T&A; weight loss; not randomized, blinded, or controlled	21 male, 10 female, 2–14 yrs, all with adenotonsillar hypertrophy and % expected body weight 130–260%	Irregular breathing decreased from 34.4–0%, SaO ₂ > 90% increased from 1.7–95% of total sleep time to >95% in all	T&A effective even if still obese, partial improvement with weight loss	No statistical tests reported, poorly defined parameters and methods	B	6.6
Harvey <i>et al.</i> [54]	1999	Prospective cohort of OSA referrals; questionnaire (blinded), PSG, developmental study (Griffith); mild = 1 < AHI < 5, severe = AHI > 5; PS (AHI < 1) excluded; developmental test and sxs reassessed 6 mo after; self-selection to T and/or A; not randomized	39 pts; 35 ± 16 mos; 29 neurologically normal; 24 pts tx'd	Sxs improved in neurologically normal tx'd pts; no change in developmental score or temperament; improvement in untreated children with neurological abnormalities	Surgery does not alter development and temperament at 6 mos	Unconventional AHI (desaturation not linked to events); no post tx PSG	B	6.2

Table 1 *continued*

Author	Year	Methods	Subjects	Results	Conclusions	Comments	Grade	Score
Brouillette <i>et al.</i> [55]	1982	Sleep clinic referrals over 3 yrs for suspected OSA; PSG or nap study; 8 T&A, 11 tracheostomy, 3 T or A	15 male, 7 female; 19/22 < 5 yrs; 10 neurologically abnormal, 6 with craniofacial abnormality, 14 with enlarged T&A	5 with failure-to-thrive – all with catch-up after tx; 12 with cor pulmonale – all improved after tx; all pts with subjective improvement in sx (dyspnea, arousals, activity, development)	Tx improves morbidity	Case series of varied pts with varied dx, tx, and F/U	C	6.1
Frank <i>et al.</i> [56]	1982	Retrospective; pts tx'd in sleep clinic for OSA; T&A; pre/6 wk post PSG	15 male, 17 female, 2–12 yrs; 23 with adenotonsillar hypertrophy, 3 trisomy 21, 6 with other medical dx; 17 tx'd with T&A; post tx PSG in 7	Mean obstructive apnea decreased from 194–7/night; all snoring and restless sleep resolved; sleep efficiency and increased; arousals normalized	T&A effective in reducing OSA sx and obstructive events	Small study; non-standard PSG criteria	C	5.7
Ali <i>et al.</i> [21]	1996	Prospective; matched healthy controls; questionnaire of consecutive pts on T&A waiting list; those with sx studied with home oximetry and video, Conner's behavior scale, WISC-R, Continuous Performance Test (CPT), Matching Familiar Figures Test (MFFT); studies repeated 3–4 mos after tx	6–12 yrs; 12 subjects, 10 control; 11 snoring control subjects with normal oximetry/video; male : female 1 : 1	Mean > 4% SaO ₂ dip rate decreased 2.9–1.4/hr; time spent moving decreased 6.1–4.2%; snorers also had significant decrease in movement; normalization of movement and oximetry after tx; snorers and OSA pts both with decreased sx after tx; Conners: no baseline difference, but OSA group improved in all scales; CPT: no baseline difference, but OSA group and snorers improved; MFFT: no baseline difference, improvement for OSA group and snorers only if groups combined	Behavior and vigilance significantly improve in OSA pts after T&A; snorers also improve, but less so; sleep disturbance normalizes in OSA pts after T&A	Multichannel recordings	B	5.6

Table I continued

Author	Year	Methods	Subjects	Results	Conclusions	Comments	Grade	Score
Potsic et al [57]	1986	Prospective; referral to ENT for T&A secondary to airway obstruction from hyperplasia; questionnaire and sonography pre/6 wks post T&A	100 pts, mean age 5.8 yrs, 50 controls; sonography in 50 pts.	decreased "breath-holding", snoring, daytime somnolence, mouth breathing, and cough after tx; 86% improved by sonography (mean score decreased from 3.5–1.55 on scale of 1–6)	T&A curative	No valid measure of obstruction; no validation of sonography; no randomization or symptomatic controls	B	5
Nishimura et al. [58]	1996	3 yr retrospective review of OSA surgery pts, PSG pre/post, not randomized, blinded, or controlled	27 male, 8 female, 1–13 yrs, AHI > 5, T&A for most	75% decreased In AHI or AHI < 5 in 86%, all sxs reduced (snoring, apnea, oral breathing, labored breathing, night terrors, enuresis)	T&A effective in reducing AHI and sxs	No statistical tests reported	C	4.8
Ahlqvist-Rastad et al. [59]	1988	Consecutive referrals to ENT clinic, sx & physical exam scores pre/post surgery, not randomized, blinded, or controlled	85 pts, 1.5–14 yrs, 76 tonsillectomy, 9 T&A	9% spontaneous improvement, snoring decreased 83–9.5%, restless sleep decreased 55–13%, OSA decreased 82–0%, weight gain, decreased fatigue	Tonsillectomy improves sxs, especially snoring apnea, and restlessness	No PSG, no statistical analysis	B	4.6

Table 1 *continued*

Author	Year	Methods	Subjects	Results	Conclusions	Comments	Grade	Score
Soultan <i>et al.</i> [36]	1999	Retrospective cohort of OSA pts with adenotonsillar hypertrophy tx'd by T&A; nap study in 20/45; weight and height compared pre/post tx, mean F/U time 15 mos (6–36 mos); not randomized, controlled, or blinded	32 male, 13 female, most AA, 1.4–10.25 yrs	Weight increased in 65% obese and morbidly obese pts. As well as all underweight pts (69% of all pts); body mass index increased in 62% of all pts	T&A may increase weight in OSA pts including obese ones.	Inadequate PSG; criteria for dx of OSA unclear	C	2.4
Hultcrantz <i>et al.</i> [60]	1999	Randomized, prospective study of tonsillectomy vs. tonsillotomy; pts scheduled for T&A for snoring and/or OSA, mouth breathing, and/or eating problems; 6 mo and 12 mo F/U questionnaire	26 male, 15 female, 3.5–8 yrs; all with tonsillar hyperplasia; 20 tonsillectomy; 21 tonsillotomy	Less pain, better feeding and weight gain in tonsillotomy group; no difference in snoring or satisfaction at 6 or 12 mos; no observed apnea in either group	Tonsillotomy has less morbidity than and equal efficacy to T&A	No PSG; criteria for dx of OSA unclear	C	2.3

AHI, OAI: apnea hypopnea index, obstructive apnea index; dx, dx'd: diagnosis, diagnosed; ENT: otorhinolaryngologist; ETCO₂: end tidal CO₂; F/U: follow up; hr: hour; mos: months; OSA: obstructive sleep apnea; PSG: polysomnography; pts: patients; RDI: respiratory disturbance index; SaO₂: hemoglobin saturation; sxs: symptoms; T&A, T, A: tonsillectomy and adenoidectomy, adenoidectomy, tonsillectomy; tx, tx'd: treatment, treated; wks: weeks; yrs: years.

Potential complications of T&A in OSAS

Table 2 lists the potential complications associated with T&A. Both the frequency and type of complications are based on retrospective analyses, such that specific morbidity data on children with OSAS undergoing surgical treatment are unavailable. The overall mortality for all indications of tonsillectomy and/or adenoidectomy is variably reported from 1 in 4000 to 1 in 27 000 cases [63]. In addition, morbidity for T&A ranges from 5 to 10% in the general indication studies; however, more recent studies report higher morbidity rates in patients with OSAS, ranging from 18 to 34% [64–69]. While the intra-anesthetic complications of T&A in OSAS patients have not been specifically examined, the increased prevalence of post-operative complications frequently involves respiratory insufficiency secondary to upper airway edema/obstruction or pulmonary edema. The antecedent risk factors for post-operative complications in this group have been identified by various authors, and include age < 2 years, craniofacial anomalies affecting the pharynx particularly midfacial hypoplasia and retrognathia, failure-to-thrive or thin body habitus, hypotonia, cor pulmonale, morbid obesity, previous upper airway trauma, severe OSAS by PSG criteria, concomitant uvulopharyngopalatoplasty, and history of prematurity [65, 68, 69]. Close post-operative monitoring of these patients in an intensive care unit is therefore currently recommended. In addition, when upper airway-induced respiratory difficulty supervenes during the post-operative period, CPAP and/or bilevel positive airway pressure (PAP) appear to be useful in the prevention of intubation [65, 70].

Table 2. Complications of tonsillectomy and adenoidectomy in children

Anesthesia-related complications including death
Hemorrhage (immediate, delayed)
Airway obstruction
Nasopharyngeal stenosis
Pulmonary edema
Nausea and Emesis
Pain (local, odynophagia, otalgia)
Infection
Velopharyngeal insufficiency
Dehydration
Fever
Hypersomnolence

NON-SURGICAL THERAPIES

Despite the popularity of T&A as the mainstay of OSAS treatment, there have been some studies examining alternative approaches. Most of these studies however, have addressed the particular intervention either as a temporary palliative measure prior to T&A or as a second line of treatment once T&A has failed to resolve OSAS. We found no studies beyond the occasional case report using pharmacological agents that have been employed in adult patients with OSAS such as progesterone, acetazolamide, theophylline, protryptilline, opioid antagonists in children [37, 71]. Thus, this portion of our paper will focus on corticosteroids, supplemental oxygen, and CPAP in children with OSAS.

Corticosteroids

We found only one study examining the role of systemic steroids in OSAS [72]. The aim of the prospective open-label study was to assess whether OSAS secondary to adenotonsillar hypertrophy could be treated by a short course of oral prednisone. Ten otherwise healthy children with PSG-proven OSAS were treated with a 5-day course of 1 mg/kg given once daily. No significant reduction in symptoms or home PSG indices was found. A marginal reduction in radiographically assessed adenoid size was noted, but other airway pharyngeal measures were unchanged, such that T&A was avoided in only one child. It is possible that this overall unsatisfactory response to systemic steroids may have been related to either the short duration of treatment or to the need for higher doses of prednisone to achieve the desired reduction in lymphoid tissue size.

In a subsequent study by the same group, the efficacy of topical intranasal steroids in treating OSAS was assessed [73]. Twenty-five otherwise healthy children with PSG-proven mild to moderate OSAS were randomized in a triple-blinded fashion to placebo or 50 mcg fluticasone bilaterally twice a day for 1 week followed by once a day administration for 5 weeks. Mean AHI decreased from 11/h to 6/h, and the number of oxygen desaturation events per hour of sleep decreased from 7 to 3 h. Movement arousals were also significantly decreased. In contrast, polysomnographic indices were unchanged in the placebo group. In fact, 12 of 13 patients treated with fluticasone showed improvement in the AHI, but 46% ultimately required T&A, and there was no significant difference

between groups with respect to symptom score or airway radiography. In a different study, Demain and colleagues showed reduction of adenoidal size and improvement in symptoms of nasal obstruction after 24 weeks of intranasal steroid therapy [74]. However, efficacy for OSAS was not considered. Thus, topical intranasal steroid therapy does seem to have some temporary benefit in otherwise healthy patients with mild-moderate OSAS, and could have a role in some selected cases. Nevertheless, before such approach can be implemented more extensively, the rate of OSAS recurrence after discontinuation of intranasal steroid therapy and the actual failure rate, i.e., the percentage of children ultimately requiring T&A despite topical steroids, need to be established in larger cohorts.

Supplemental oxygen

Supplemental oxygen via nasal cannula (SuppOx) has been proposed as a temporary measure in severe OSAS patients awaiting surgery. The two available studies examined 39 children and found that SuppOx improved oxygenation during sleep in all cases, and was associated with some decrease in RDI in a small proportion of the children [75, 76]. However, in two children significant alveolar hypoventilation developed ($PETCO_2 \geq 75$ mmHg) [76] thereby prompting the use of extreme caution when using SuppOx in OSAS patients. We are currently unaware of any study examining this treatment modality as the sole approach for OSAS.

Noninvasive mask ventilation

In the past, when surgery failed to relieve the degree of sleep-associated respiratory disturbance, a tracheotomy was frequently performed. This alternative is now rarely pursued due to the development of noninvasive approaches to maintain upper airway patency during sleep. In more recent years, positive pressure administered via a noninvasive interface (CPAP or bilevel PAP) has become the second line of treatment in children and infants with unresolved OSAS after T&A.

Before we proceed with a critical review of the published evidence on CPAP in children, we feel that it is important to emphasize the patient-machine interface in these interventions. Although no controlled studies address this issue, it is evident that the use of nasal prongs, nasal masks, or face masks requires individualized, case by case consideration. When a

silicone mask is selected, particular care to ensure that the mask fits snugly and is comfortable to the patient is essential for ensuring successful intervention. Pediatric masks are becoming increasingly available in several sizes, and for particular clinical conditions such as craniofacial syndromes, custom-made masks can be ordered to fit the facial contours. Inappropriately fitted masks will inevitably leak, and efforts to seal such leaks will frequently result in pressure sores, particularly on the bridge of the nose. Bubble-cushioned masks have been developed and can sometimes palliate the severity of the air leak while adding to the patient's comfort. In addition, air leaks will more frequently be directed upwards, and may irritate the conjunctiva and lead to increased lacrimation and eye discomfort. Attention needs also to be given to the mask manifold to ensure that no pressure vectors are generated. A multiplicity of techniques may be used to secure the mask, and primarily include Velcro or elastic straps or a tissue cap. Again, the importance of patients' comfort can not be overemphasized. Adequate parental training and behavioral techniques designed to improve the acceptance and tolerance to these devices are being developed in various centers and clearly need to be implemented to attempt to improve the compliance of the family and the patient [77].

Over the last decade CPAP has been increasingly used in children as a successful alternative to upper airway surgery or tracheotomy. While the studies noted below identified only minor complications, many practitioners have speculated that mid-facial hypoplasia may develop with long-term use, particularly in children with neuromuscular weakness, and one possible case has been reported [78].

The cumulative information on the use of CPAP in children is shown in Table 3. Most of the studies were retrospective in nature and demonstrate feasibility rather than efficacy. Marcus and colleagues initially reported the cumulative retrospective "multicenter" experience on the use of CPAP in children [80]. Although the criteria for implementation of CPAP and the patient selection differed from participating center to participating center, the major take home message from this study was that nasal mask ventilation could be successfully implemented in young and older children with a wide variety of underlying conditions including OSAS, and that the procedure appeared to be safe. Nonetheless, poor compliance emerged as a major problem [80]. In the same year, Waters and colleagues reported their experience in 80 patients [82]. As in the Marcus *et al.* study, the vast majority of

Table 3 Summary of studies on continuous positive pressure ventilation for the management of pediatric obstructive sleep apnea

Author	Year	Methods	Subjects	Results	Conclusions	Comments	Grade	Score
Marcus <i>et al.</i> [80]	1995	Retrospective review; multicenter survey of CPAP usage; all pts dx'd by PSG; tx deemed effective if: sxs resolved, normoxia, improvement of other PSG abnormalities; not randomized or controlled	94 pts: 3% < 1 yr, 29% 1–5 yrs, 36% 6–12 yrs, 32% 13–19 yrs; 64% male, 27% obese, 25% craniofacial anomaly, 18% idiopathic (16/17 post T&A), 13% trisomy 21, 5% mental retardation, 5% neuromuscular disease	CPAP used in pts with sxs and PSG anomalies; 2nd line tx after T&A in 76%; also used if T&A not indicated or no evidence of hypertrophy; poor compliance (<50% prescribed use) in 13%; effective in all but 1 compliant pt; minor complications only	Safe; effective; well tolerated	Multicenter retrospective study; varied criteria for dx and implementation of tx; varied CPAP techniques and equipment	C	14.4
Waters <i>et al.</i> [82]	1995	Retrospective review of all pts tx'd at 1 center; PSG in all; CPAP recommended if T&A not indicated or failed; CPAP titrated by PSG; tx failure defined as no regular CPAP use 6mos after initiation; not randomized or controlled	57 male, 23 female; 12 days–15.3 yrs; 40% with syndrome, 12.5% with malformation, 19% with isolated adenotonsillar hypertrophy, 13% with lower respiratory tract disease, 8% with obesity, 8.8% cerebral palsy, 6% chronic lung disease, 7% other disease; 81.3% post T&A	Successful in 86% of pts completing training; 12.5% failed to continue tx (70% secondary to patient or parent intolerance); 1 patient deteriorated; 11% died (expected consequence of underlying disease); RDI decreased 27.3–2.55; Complications: hypoventilation and central apnea at high pressures (25%), local irritation	Effective; high prevalence of complex patients in CPAP cohort	Dropouts during training omitted from analysis without explanation; transient users not separated in analysis	C	13
McNamara <i>et al.</i> [83]	1999	Prospective trial of CPAP in infants referred to sleep clinic; dx and titration by PSG; multiple F/U PSG; included if > 5 apneas/hr (mixed and obstructive)	15 male, 9 female; 1–51 wks; 16 term, 8 premature; 3 with syndrome; 8 with anatomic abnormality; 8 with ALTE	NREM: OAI decr. 14.6–0.1/hr, desaturation index decr. 37.8/hr, mean NREM length incr. 15.9–21.6 min REM: OAI decr. 43.6–0.4/hr, desaturation index decr. 63.4–9.8/hr, mean REM length incr. 6.3–13.2/hr; 6 pts d/c'd secondary to parent noncompliance or inadequate family support	Safe and effective in 85%; OAI and sleep normalized; family training and support important		B	12.4

Table 2 continued

Author	Year	Methods	Subjects	Results	Conclusions	Comments	Grade	Score
Guilleminault <i>et al.</i> [81]	1995	Retrospective review of pts tx'd at 1 center; PSG dx and /titration; pts followed for 5 mo–12 yrs; not randomized or controlled	35 male, 39 female; 9 wks–12 mos; average birth weight 2.68 kg; 77% with craniofacial anomaly; 51% syndromic; referral reason: abnormal sleep 66%, ALTE 23%, failure-to-thrive 11%	72/74 tx'd successfully; failures related to complex underlying disease and parental refusal; minor complications only	Safe; effective; well tolerated	Families screened prior to being offered CPAP	C	12.4
McNamara <i>et al.</i> [84]	1999	Prospective; PSG dx, titration, and several weeks after start of tx; follow up study with and without CPAP; age matched symptomatic and normal controls; not randomized or blinded	8 term infants per group; 6–18 wks at dx; 50% male/female	OAI decreased 22.2–0.3 (NREM), 51.8–1.1 (REM); decrease OAI also off CPAP and in OSA controls (but still elevated); increased REM with tx; increased spontaneous arousals (to control levels) and arousals after apnea during REM in tx'd pts.	CPAP effective in normalizing OAI; CPAP normalizes sleep architecture and arousals during REM		B	10.8
Rains [77]	1995	Prospective; PSG dx and titration; behavioral training of parent and patient; questionnaire and F/U at 1, 3, 9 mos.; not controlled or randomized	2 male, 2 female, 3–12 yrs; all with craniofacial anomalies and multisystem syndromes; 3 with mental retardation	Mean total respiratory disturbances decreased 175–36; lowest SaO ₂ increased 73–89%; normalization of sleep architecture; all using CPAP at 3 mos, 1 discontinued prior to 9 mos for other medical reason; all with marked sx improvement	CPAP safe and effective in complex pts; behavioral intervention effective	Small size	B	10.4
Downey <i>et al.</i> [79]	2000	Retrospective chart review; PSG diagnosis and titration; OSA = AI > 1; not randomized or controlled	18pts < 2 yrs, 6 with tracheostomy, 2 post T&A; 3/18 with idiopathic OSA	12pts successfully tx'd including 4/6 with tracheostomy and 2/2 prior T&A; 4 pts refused; 5 pts also required supplemental O ₂ ; no change in arousal index (16.3 pre/16.1 post)	CPAP improves OSA and is effective tx; accepted and tolerated in pts < 2 yrs	Not randomized or controlled;	C	6.8

AHI, OAI: apnea hypopnea index, obstructive apnea index; dx, dx'd: diagnosis, diagnosed; ENT: otorhinolaryngologist; ETCO₂: end tidal CO₂; F/U: follow up; hr: hour; mos: months; OSA: obstructive sleep apnea; PSG: polysomnography; pts: patients; RDI: respiratory disturbance index; SaO₂: hemoglobin saturation; sxs: symptoms; T&A, T, A: tonsillectomy and adenoidectomy, adenoidectomy, tonsillectomy; tx, tx'd: treatment, treated; wks: weeks; yrs: years.

children had complex disorders leading to OSAS in whom T&A had previously been ineffective. These authors also found that parental and patient training could be achieved in the vast majority of patients (86%), but that compliance was reduced and that higher pressures were associated with more frequent side effects such as skin and eye irritation [82]. In the third study appearing in 1995, Guilleminault and colleagues summarized their experience at Stanford Medical Center and their findings and conclusions in 72 pediatric patients essentially duplicated those of the two other studies [81]. More recently, McNamara and Sullivan found that application of CPAP was possible in infants with OSAS due to either syndromic conditions or identified in association with apparent life threatening events (ALTE) [83, 84]. Although CPAP was highly effective in normalizing sleep architecture and gas exchange in these infants, the authors also stressed the substantial need for training of parents and infants such as to increase the tolerability of the intervention. Nevertheless, and as seen with older children, poor compliance rates were reported. From these and other smaller studies [77, 79], the overall impression at this point is that CPAP is primarily reserved for children with OSAS in association with other medical conditions, and for a few otherwise normal children with OSAS in whom T&A failed and the post-operative residual OSAS remains severe. In addition, CPAP intervention in children appears to be safe but requires extensive behavioral training such as to achieve reasonable compliance rates. At this point in time, we are unaware of prospective studies aiming to determine criteria for the application of noninvasive ventilation to children with post-T&A OSAS and whether specific ventilatory approaches such as bilevel PAP are associated with improved outcomes. A multicenter study that is currently underway comparing CPAP versus bilevel PAP may clarify the latter point.

SPECIAL APPROACHES TO SPECIAL CASES WITH OSAS

There is an abundance of case-series studies involving children with a variety of syndromic conditions associated with OSAS. In this mixed group of children, patients with Down syndrome, Crouzon and Apert syndromes, Treacher-Collins syndrome, Pierre-Robin sequence, cerebral palsy, and multiple other rare craniofacial disorders were included. Most of these studies were retrospective in nature, and the majority did not assess outcomes using polysomnography. The

heterogeneity of underlying conditions and surgical approaches precludes critical analysis of the results. Nevertheless, the overall consensus emerging from the cumulative review of these papers suggests that pre- and post-operative sleep studies need to be combined with a carefully tailored and individualized surgical approach to the patient such as to optimize outcome and prevent tracheotomy [85–100].

Surgical techniques that have been advocated in addition to T&A include uvulopalatopharyngoplasty, uvulectomy, epiglottoplasty, distraction osteogenesis, mandibular advancement, tongue reduction, septoplasty, and turbinectomy. In the largest series published, 70 children with a variety of conditions were treated with individualized surgery [86]. Tracheostomy was avoided in 90.4% and the average RDI decreased from 25.9 to 4.4 after surgery while the average lowest recorded oxygen saturation increased from 61 to 92% after surgery. Prospective data from a subset of this population suggest that surgical management is more likely to be successful at ages greater than 12 months [87]. Similarly, in a prospectively-studied series of 18 patients with OSA and cerebral palsy treated surgically, 83% avoided tracheostomy, RDI decreased from 7.0 to 1.4, and lowest recorded oxygen saturation rose from 73.7 to 88.2% [88].

CONCLUDING REMARKS

In this review, we have provided a comprehensive and critical analysis of the published literature on the morbidity and treatment of OSAS in children. Despite more than 20 years of treating children with this condition, we have only very limited information on the long-term consequences of pediatric OSAS. Furthermore, we are still unable to define the appropriate cost-effective guidelines for treatment, and have widely adopted an intervention that emerges as relatively ineffective. It is therefore imperative that we do not wait another 20 years to answer such questions, and urgently institute the necessary efforts to develop novel and effective therapies while defining which children should receive them.

Practice Points

OSAS in children is associated with potentially long-lasting neurobehavioral, cardiovascular and somatic growth consequences.

Tonsillectomy and adenoidectomy (T&A) remains the first line of treatment for pediatric OSAS;

however, its effectiveness is not yet fully established by appropriate methodology.

Steroids play little if any role in the management of pediatric OSAS.

Non-invasive mask ventilation emerges as a viable secondary line of treatment in children with residual OSAS.

Research Agenda

Multicenter studies are needed to establish:

The respiratory disturbance index at which T&A is indicated.

The patient subsets in whom a polysomnographic evaluation should be obtained following T&A.

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