Review Article

The Asian Paediatric Pulmonology Society (APPS) Position Statement on Childhood Obstructive Sleep Apnea Syndrome

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Abstract

With recognition of the importance of obstructive sleep apnea syndrome (OSAS) in children, practice guidelines have been developed for the management of OSAS in the USA and Europe. A panel of experts in pediatric OSAS in Asia were appointed by the Asian Paediatric Pulmonology Society (APPS) to prepare a position statement for management of childhood OSAS in Asia. The purpose of this statement is to provide a reference standard in the diagnosis and management of childhood OSAS for doctors working in Asia. The expert panel determined the scope of this statement. Focused literature search related to the key topics was conducted by panel members. The final content of this statement was agreed on by all panel members and approved by the council of APPS. The current statement covered diagnostic approach, diagnostic criteria, management algorithm, drug-induced sleep endoscopy, medical treatment including medications and positive pressure ventilation, surgical treatment including adenotonsillectomy, orthodontic treatment, and orofacial myofunctional therapy (OMT). Diagnostic criteria of childhood OSAS from 1 year to 18 years were presented that include both clinical (criteria A) and polysomnography findings (criteria B) in the diagnosis of childhood OSAS. The use of nocturnal pulse oximetry as a screening tool was suggested using the McGill oximetry score. Management of OSAS with medical treatment, tonsillectomy and adenoidectomy (TandA), positive airway pressure, orthodontic devices, nasal valves, and OMT were reviewed. Management of persistent OSAS after TandA was addressed, and the importance of weight control was emphasized. The position statement provides a guideline to the management of childhood OSAS in Asia.

Keywords: Child, polysomnography, sleep apnea syndrome, snoring

Introduction

Obstructive sleep apnea syndrome (OSAS) was reported to affect 1%–6% of prepubertal children.[1,2] While standard management guideline has been developed for use in the developed countries in the USA and Europe, management of childhood OSAS in Asia has not been standardized.[1,3,4] The aim of this position statement is to provide guidance to the management of childhood OSAS in Asian children for general pediatricians and general practitioners. To this aim, a group of experts in pediatric OSAS gathered in 2015 during the 1st Annual Scientific Meeting of the Asian Paediatric Pulmonology Society (APPS) held in Hong Kong in October 2015. A panel was formed and was given the task to prepare the position statement based on the current literature, especially that from Asia and the consensus among the group. The group presented the drafted statement in the International Paediatric Sleep Association in Taiwan in March

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2016 and comments were received and the group developed the second draft which was presented in the 2nd Annual Scientific Meeting of APPS in Singapore in November 2016. Further comments were received and revision was done. The final draft was presented to the guideline committee of APPS which recommended the statement to be presented to the executive committee of APPS and approval was granted for the statement to be released as the official position statement of APPS in March 2017.

Definition of Obstructive Sleep Apnea Syndrome

The diagnostic criteria of childhood OSAS are defined in Table 1. The current definition does not cover children younger than 1 year old as infants, especially those younger than 3 months, have different types of breathing disorders during sleep.[5]

Risk Factors for Childhood Obstructive Sleep Apnea Syndrome

Adenotonsillar hypertrophy is the most recognized risk factor of OSAS in children.[6,7] Allergic rhinitis and obesity are other common risk factors.[8-12] Other risk factors include well-known structural abnormalities of the airway, such as micrognathia and midfacial hypoplasia, Down syndrome, Prader–Willi syndrome, achondroplasia, and less well-known and subtle defects such as congenital teeth agenesis and septum deviation, short lingual frenulum, and chronic mouth breathing.[13-18] Neuromuscular disorders such as muscular dystrophies, cerebral palsy, and Chiari malformation are at high risk for OSAS. Other factors include gastroesophageal reflux and premature birth.[19-21] Children with a family history of OSAS are at an increased risk for OSAS. Environmental tobacco smoke exposure was also associated with OSAS.[22,23]

Table 1: Diagnostic criteria of childhood OSAS (1- to 18-year-old)

Criteria A and B must be met
Criteria A: 1 or more of the followings
Habitual snoring, i.e., ≥3 nights per week
Labored breathing (snorting), or observed obstructive apnea during the child's sleep
Daytime sleepiness, hyperactivity, attention deficit, behavioral problems, learning problems, academic deterioration
Hypertension or nocturnal hypertension
Nocturnal enuresis (primary or secondary)
Excessive sweating during sleep
Chronic NREM parasomnias
Criteria B: PSG demonstrates one or both of the following
One or more obstructive apneas, mixed apneas, or hypopneas, per hour of sleep, i.e., AHI ≥1# or
A pattern of obstructive hypoventilation, defined as at least 25% of total sleep time with hypercapnia, i.e., $PaCO_2$ (or validated surrogate marker like $TcCO_2$*) >50 mmHg together with signs of partial obstruction like paradoxical breathing and/or out of phase between chest and abdominal recordings and/or flow limitation

#For children older than 12 years, AHI >5 might be used as the cutoff at the discretion of the attending pediatric respirologist, *$TcCO_2$ should be done with a validated transcutaneous CO_2 monitor with *in vivo* calibration by arterial CO_2 or arterialized capillary CO_2. PSG: Polysomnography, NREM: Non rapid eye movement

Complications of Childhood Obstructive Sleep Apnea Syndrome

Childhood OSAS is associated with neurological and cardiovascular morbidities.[24-29] These neurological morbidities include attention deficit/hyperactivity disorder, hypersomnolence, parasomnia (confusional arousals, sleep terrors, sleep walking, nightmares, and bruxism), depression, aggression, somatization, abnormal social behaviors, and nocturnal enuresis.[30-39] Cardiovascular morbidities include elevated systolic and diastolic blood pressure, dysfunction of autonomic regulation, reduced cerebral blood flow, left ventricular remodeling, and endothelial dysfunction.[25,29,40-46] Childhood OSAS is also associated with growth impairment.[47,48]

Diagnostic Approach

Children of all ages should be screened by their family physicians or pediatricians for the presence of snoring, especially habitual snoring, i.e. 3 or more nights per week and symptoms suggestive of OSAS during routine health checkup [Tables 2 and 3]. If positive, further focused evaluation should be performed.[1]

If there is reported habitual snoring with signs and/or symptoms suggestive of OSAS, further evaluation and management is advised. The approach may vary, depending on the resources available. An algorithm for the evaluation of children with suspected OSAS is suggested in Figure 1.

Sleep polysomnography (PSG), wherever available, is considered the gold standard for diagnosis of OSAS. Attended PSG in the sleep laboratory is preferred, especially for children younger than 4 years old. Several studies demonstrated the validity of unattended study in children but these unattended studies should involve monitoring of electroencephalogram or a way to monitor autonomic nervous system disruption, for example, electrocardiogram + SpO_2 plethysmography.[42,49,50] Nap studies should not be used to substitute these overnight studies.

When PSG, attended or otherwise, is not available, analysis of nocturnal pulse oximetry would provide the second best objective assessment of the child's condition. This monitoring underscores abnormal breathing during sleep as it misses the hypopnea with only arousal. Nocturnal pulse oximetry is a useful diagnostic test only when the OSAS is associated with significant oxygen desaturation. A positive diagnostic test is made when there are 3 or more desaturation clusters (defined as 5 or more desaturations to <90% occurring in a 10–30 min period) [Table 4].[47-49] The positive predictive value and negative predictive value (NPV) of the test were 96.8% and

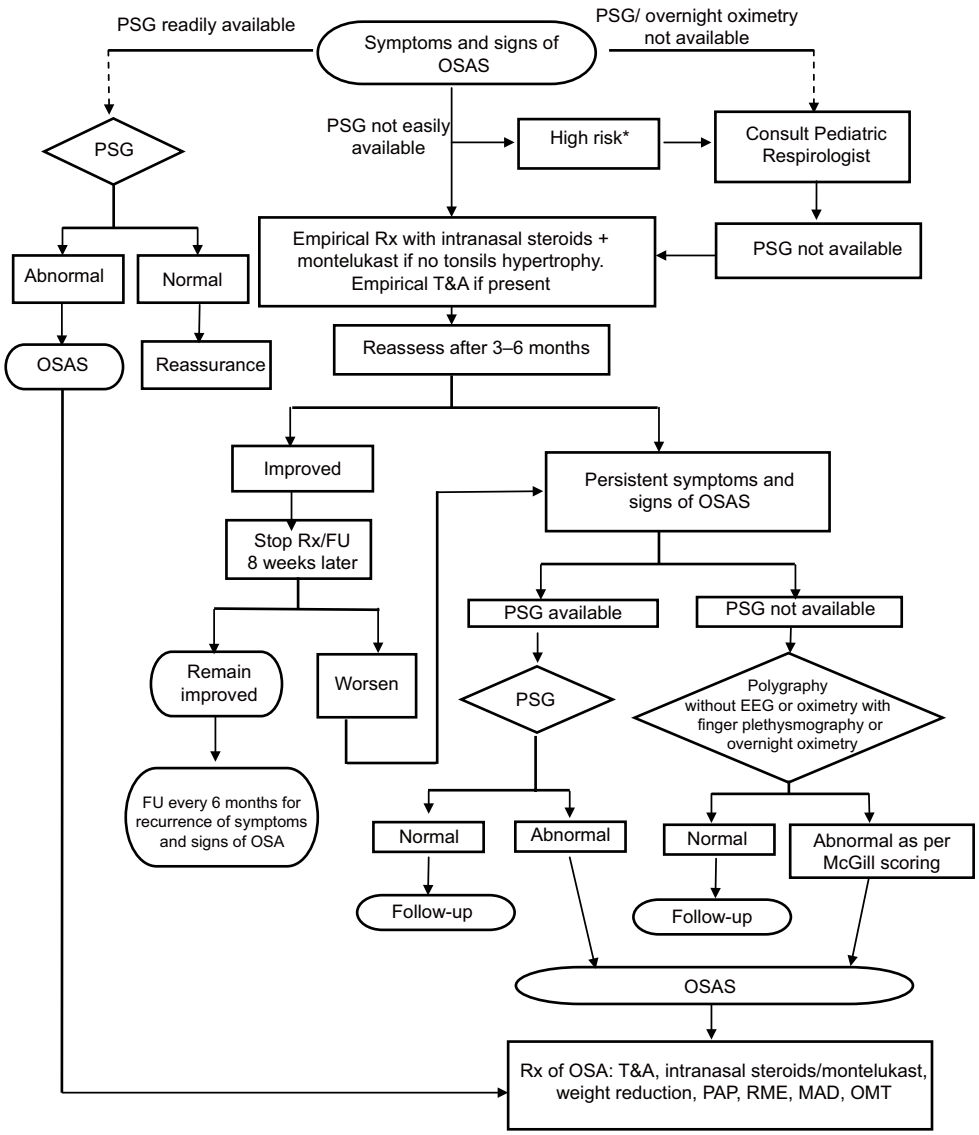

Figure 1: Management algorithm of children with suspected obstructive sleep apnea syndrome. *High-risk group: age <3 years, obesity, chronic mouth breathing, syndromic or nonsyndromic craniofacial growth disorders, chronic gastroesophageal reflux, chronic upper airway allergies, trisomy 21, cerebral palsy, neuromuscular disorders, chronic lung disease, sickle cell disease, genetic/metabolic diseases. Abbreviations: T and A: Tonsillectomy and adenoidectomy; PAP: Positive airway pressure; RME: Rapid maxillary expansion; MAD: Mandibular advancement device; OMT: Orofacial myofunctional therapy.

58.11%, respectively.[51-53] The major limitation of nocturnal pulse oximetry monitoring is the low NPV when OSAS could not be ruled out.

Drug-induced Sleep Endoscopy

Endoscopy has been used to evaluate the upper airway for a long time.[54-56] Good sedation is essential and medications such as midazolam, fentanyl, or propofol are commonly used. As OSAS children are prone to have obstructive apnea/hypopnea with sedation, it is important to have a competent medical practitioner to provide sedation and intervene whenever necessary. Structured reporting format for the findings of endoscopy is important.[57] There are often multilevel obstructions found in patients with sleep-disordered breathing (SDB).[58-62]

Evaluation of four-site "VOTE" was suggested.[63,64] However, this missed out the adenoids in children. Hence, evaluation of six sites was suggested [Figure 2].[65,66]

At the retrolingual level, the degree of hypertrophy of lingual tonsils and features of reflux laryngitis which were commonly associated with obstructive sleep apnea (OSA) should also be noted.[67] Having knowledge of number of sites of obstruction will help to plan management.

Medical Treatment of Childhood Obstructive Sleep Apnea Syndrome

Intranasal corticosteroids

The use of intranasal corticosteroids was shown in a case series by Alexopoulos *et al*. that their use could improve

Table 2: Symptoms of obstructive sleep apnea syndrome

Labored breathing during sleep
Gasps/snorting noises/observed episodes of apnea
Nocturnal enuresis (especially secondary enuresis)
Sleeping in a seated position or with the neck hyperextended
Chronic observed episodic cyanosis during sleep
Headaches on awakening
Daytime sleepiness
Attention-deficit/hyperactivity disorder
Learning problems
Unexplained mood swing
Confusional arousal/sleep walking
Somniloquy

Table 3: Sign of obstructive sleep apnea syndrome

Underweight or overweight
Tonsillar hypertrophy
Adenoidal facies
Micrognathia/retrognathia
High-arched palate
High Mallampati score
Cross or open bite
Increased overjet
Short lingual frenulum
Loud pulmonary component of the second heart sound
Hypertension

PSG findings and OSA symptoms in children with mild SDB.[68]

Later, randomized placebo-controlled trials involving the use of different intranasal corticosteroids, mometasone furoate, budesonide, and fluticasone propionate aqueous spray were shown to decrease apnea-hypopnea index (AHI) [Table 5].[69-71]

A meta-analysis of the above studies conducted by Liu *et al*. in 2016 showed a reduction of AHI by 1.1 with the use of intranasal corticosteroids in children with OSA.[72]

Leukotriene receptor antagonist

Montelukast given for 16 weeks at a dosage of 4 mg/day for <6 years old or 5 mg/day for >6 years old was shown by Goldbart *et al*. in an open-label case–control study involving 46 children aged between 2- and 10-years to be effective in reducing AHI significantly in treatment group, pretreatment 3.0/h to posttreatment 2.0/h, when compared to control group, pretreatment 3.2/h to posttreatment 4.1/h.[73]

Subsequently, Goldbart *et al*. conducted a double–blind, randomized, placebo-controlled trial in children aged between 2- and 10-years that administration of montelukast improved obstructive apnea index (OAI) and AHI significantly.[74]

Kheirandish-Gozal *et al*. published a double-blind, randomized, placebo-controlled trial on the effect of montelukast on OSA children.[75] The study involved 64 OSA children aged between 2- and 10-years and it showed that AHI of treated children

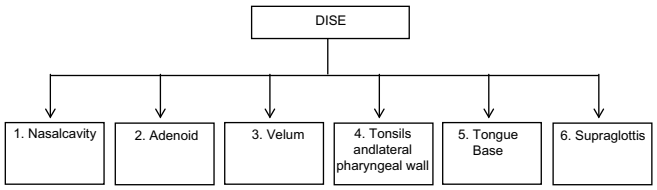

Figure 2: Six important sites recommended for evaluation of obstructive sleep apnea with drug-induced sleep endoscopy.

decreased from 9.2 to 4.2 ($P < 0.0001$) while AHI did not change in those receiving placebo.

A meta-analysis of the above studies was conducted by the authors (DKN, JPN, and SYL) and it showed a reduction of AHI by 2.7 with the use of montelukast [Figure 3].

Combined intranasal corticosteroids and montelukast

Two nonrandomized studies were identified. Kheirandish *et al*. in an open-label control trial (involving 36 children of more than 6 years old) demonstrated that combined use of oral montelukast (4 mg for children <6 years old or 5 mg for children ≥6 years old) and intranasal budesonide (32 mcg/nostril per day) for 12 weeks in postadenotonsillectomy children with residual mild OSA could reduce AHI significantly in treatment group (mean AHI dropped from 3.9 to 0.3) when compared to control group (mean AHI increased from 3.6 to 4.7).[76]

Kheirandish-Gozal *et al*. in a retrospective study showed, involving 836 mild OSA children aged between 2- and 14-years, that the combined use of intranasal corticosteroids and montelukast brought about a significant improvement in AHI.[77]

A meta-analysis of the above studies was conducted by the authors (DKN, JPN, and SYL) and it showed a reduction of AHI by 3.3 with the concurrent use of intranasal corticosteroids and montelukast on OSA children [Figure 4].

Tonsillectomy and Adenoidectomy

Tonsillectomy and adenoidectomy (TandA) is the first-line treatment for children with OSAS with adenotonsillar hypertrophy. The Childhood Adenotonsillectomy Trial (CHAT), a randomized trial of early adenotonsillectomy (eAT) compared to watchful waiting with supportive care (WWSC) for mild-to-moderate childhood OSAS, i.e., AHI ≤5, showed normalization of PSG findings in 79% versus 46% of the respective groups on assessment after 7 months.[78] There were also significantly greater reported reduction in symptoms and improvement in behavior and quality of life in the eAT group than the WWSC group. The significance of the normalization rate of 46% in WWSC group, who nevertheless had worse behavioral performance, warrants further study.[79]

Postoperative complications were reported to be higher in those aged below 3 years, presence of cardiac complications, congenital craniofacial anomalies, neuromuscular disorders, and severe obesity.[80,81] For such high-risk patients, TandA should be performed in facilities with pediatric intensive care

Table 4: The McGill Oximetry Scoring

Score	Comment	Criteria			
		Number of drops in SaO_2 <90%	Number of drops in SaO_2 <85%	Number of drops in SaO_2 <80%	Others
1	Inconclusive for OSA	<3	0	0	Baseline: Stable (<3 clusters of desaturations) and >95%
2	Mild OSA	≥3	≤3	0	3 or more clusters of desaturation events
3	Moderate OSA	≥3	>3	≤3	3 or more clusters of desaturation events
4	Severe OSA	≥3	>3	>3	3 or more clusters of desaturation events

Table 5: Three different intranasal corticosteroids studies in the treatment of obstructive sleep apnea syndrome

Drug	Sample size	Age (year)	Regimen
Mometasone furoate[69]	62	6-18	100 μg/nostril daily for 4 months
Budesonide[70]	62	2-12	32 μg/nostril daily for 6 weeks
Fluticasone propionate[71]	25	1-10	50 μg/nostril twice per day for 1 week, followed by 50 μg/nostril daily for 5 week

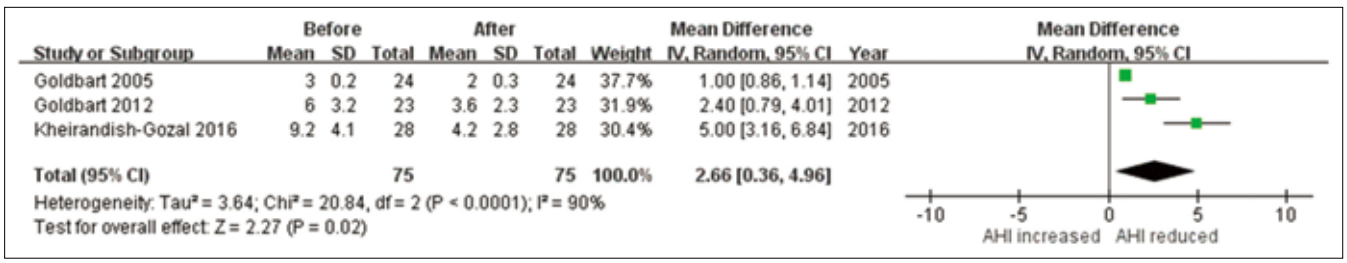

Figure 3: Forest plot for the effects of montelukast on apnea–hypopnea index.

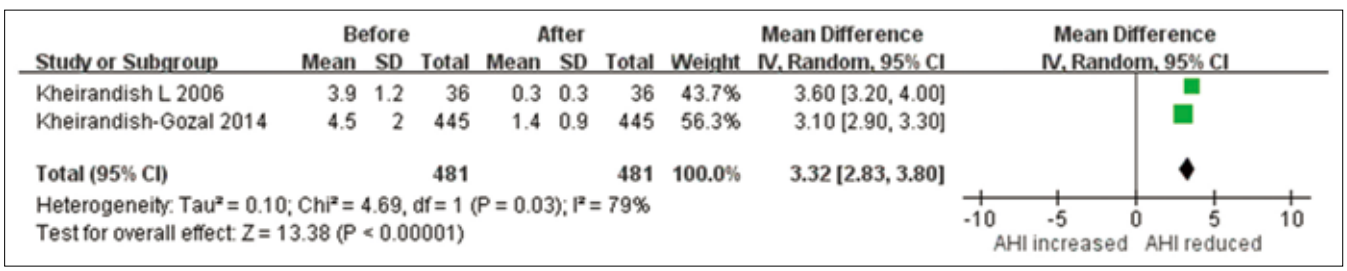

Figure 4: Forest plot for the effects of montelukast combined with intranasal steroids on apnea–hypopnea index.

service. Furthermore, a delay in performing TandA should be considered for patients with recent respiratory infections.

Reevaluation with PSG several months after TandA is recommended to evaluate for residual OSAS. There were no studies evaluating the timing of postoperative PSG evaluation. The recommendation of a few months is to allow healing and resolution of inflammation and swelling of the operative site before reassessment.[80,82-84] If PSG is not available, other options outlined in the "management algorithm of OSAS" may be considered.

The prevalence of residual OSAS after TandA ranged from 34% to 87% in the literature, depending on the characteristics of the study population and AHI definition used for residual OSAS.[85] A meta-analysis of the effect of TandA on AHI was undertaken by the authors (DKN, JPN, and SYL). Databases including PubMed, MEDLINE, EMBASE, and Cochrane Review from 1998 to 2015 were searched. The keywords used included tonsillectomy, adenoidectomy, OSA, sleep apnea, sleep apnea syndrome, and children. Success as defined by postoperative AHI <5 for all children and obese children was 80% and 55%, respectively [Figures 5 and 6], and it decreased to 55% and 30%, respectively, if success was defined as AHI <1–2 [Figures 7 and 8].[79,80,82-84,86-117]

The risk factors for residual OSAS after TandA are severe OSA at baseline, asthma, obesity, or weight gain after TandA, trisomy 21, cerebral palsy, craniofacial abnormalities, upper/lower airway abnormalities, for example, laryngomalacia.[86,93-96,100,105,107,110,114,118-120]

Growth data from the CHAT showed that TandA for OSAS in children resulted in significantly greater than expected weight

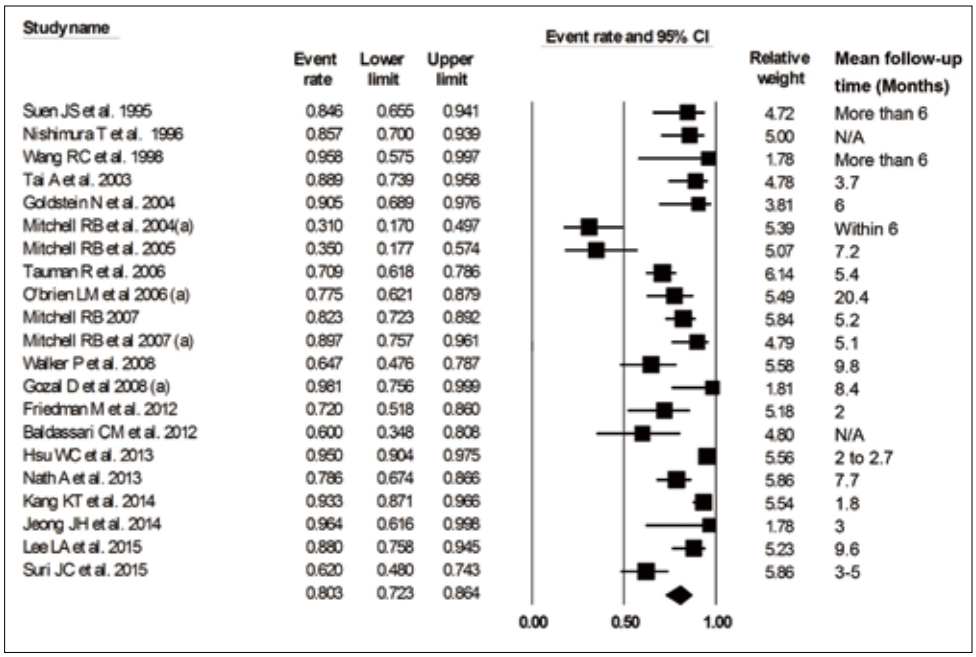

Figure 5: Forest plot for success in achieving an apnea–hypopnea index <5 postoperatively in children (not classified by body mass index). There was significant heterogeneity among these studies ($I^2 = 82.53$). Data were analyzed with random-effects model estimate.

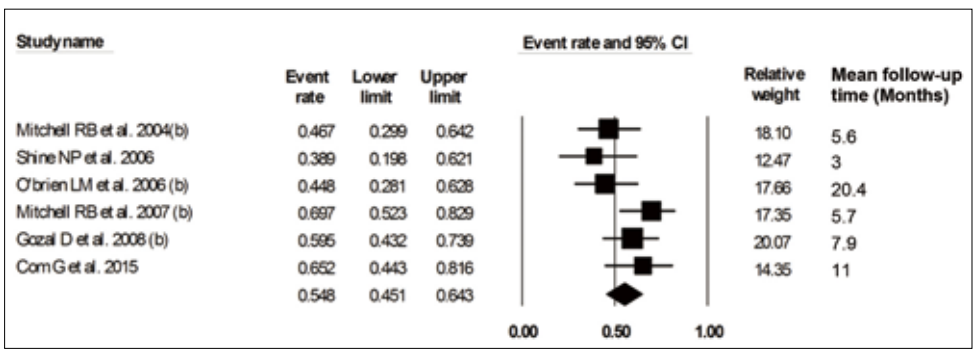

Figure 6: Forest plot for success in achieving an apnea–hypopnea index <5 postoperatively in obese children. There was significant heterogeneity among these studies ($I^2 = 36.62$). Data were analyzed with random-effects model estimate. Obese was defined as Z-score from >1.2, ≥2 to ≥2.33 or body mass index ≥95th percentile.

gain from baseline, even in initially overweight children.[121] This puts overweight children at greater risk of residual or recurrent OSAS after TandA.[120]

The management of residual OSAS after TandA is dependent on the severity of the residual OSAS. Further diagnostic tests (e.g., drug-induced sleep endoscopy [DISE], cine magnetic resonance imaging) to evaluate the level of obstruction may be useful.[63,117,119,121]

Huang *et al*. demonstrated that 53% of children had an AHI >1 at 6-month follow-up after TandA, it increased to 68% at the end of the 36-month follow-up. Risk factors for recurrence of OSAS such as severe OSAS, obesity, and a large increase in body mass index after TandA, allergic rhinitis, enuresis, and older age were identified.[115] Biggs *et al*. performed a 4-year follow-up study for school-aged children (12–16 years old). Improvement in SDB was associated with improvements in some aspects of neurocognition but not behavior among the children. Therefore, it was suggested that a longer period of follow-up was required to observe the neurocognitive changes.[122] The treatment options for persistent or recurrent OSAS after TandA are listed in Table 6.

Orthodontic Treatment

Orthodontic treatment (e.g., rapid maxillary expansion [RME], mandibular advancement devices [MAD]) may be an effective treatment option for childhood OSAS in a selected group of patients. There are, however, limited studies on orthodontic treatment for pediatric OSA, with the majority of studies being nonrandomized clinical trials.

RME is an orthodontic treatment which increases the transverse diameter of the hard palate by reopening the mid-palatal suture with an expandable dental appliance inserted into the

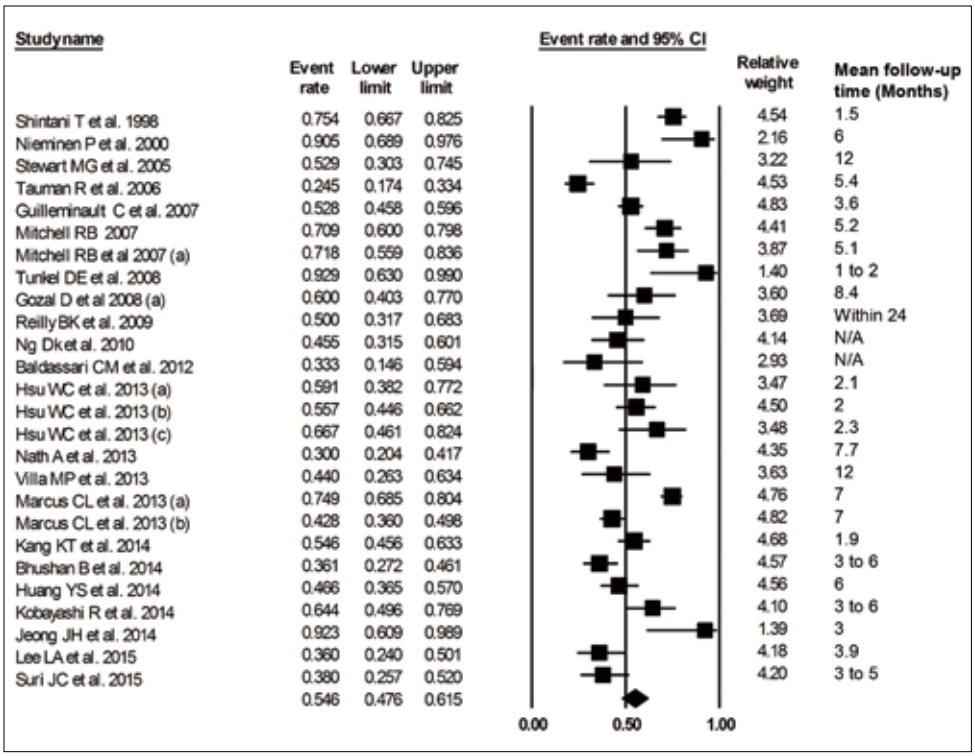

Figure 7: Forest plot for success in achieving an apnea–hypopnea index <1–2 postoperatively in normal children (those have not been classified by body mass index). There was significant heterogeneity among these studies ($I^2 = 85.77$). Data were analyzed with random-effects model estimate.

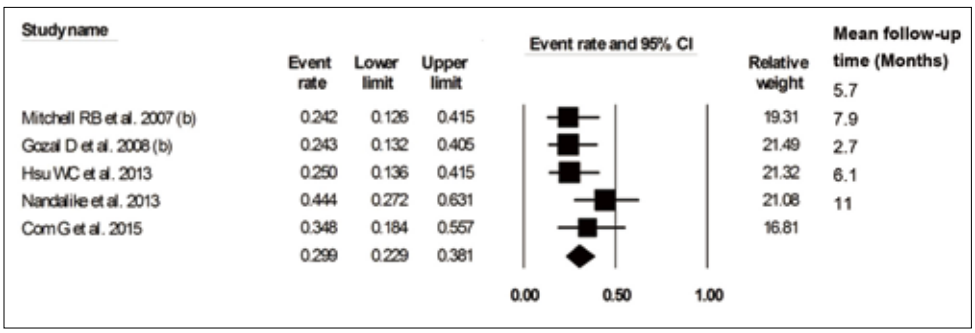

Figure 8: Forest plot for success in achieving an apnea–hypopnea index <1–2 postoperatively in obese children. There was significant heterogeneity among these studies ($I^2 = 8.11$). Data were analyzed with random-effects model estimate. Obese was defined as Z-score from 1.2 to ≥2.33 or body mass index ≥95th percentile.

mouth close to the hard palate. It also has a secondary impact on placement of the mandible. It may be an option in the management of OSA in children with maxillary contraction, with long-term treatment effect shown in follow-up studies.[113,124-128] A meta-analysis of RME was undertaken by Huynh *et al*. who reported that the AHI decreased by 6.2 after using RME from four studies.[129]

MADs increase the upper airway size by positioning the mandible and tongue forward.[130] In the same review by Huynh *et al*., a meta-analysis of MADs on two studies was undertaken.[129,131,132] With MAD, the AHI decreased by 5.1.

The authors (DKN, JPN, and SYL) updated the meta-analysis by searching databases including PubMed, MEDLINE, EMBASE, and Cochrane Review from 2001 to 2015. The keywords used included sleep apnea, OSA, sleep apnea syndrome, MAD, and children. RevMan (version 5.2, The Cochrane Collaborations, London, UK) was used for the meta-analysis. AHI was found to be decreased by 6.5 with MAD treatment [Figure 9] from three studies.[131-133]

Nasal Expiratory Positive Airway Pressure Valve

This device comprises two small adhesive disposable valves applied to both nares. The valves have negligible resistance during inspiration, but generate resistance during expiration, creating a positive end-expiratory pressure from 4 to 17 cmH_2O.[134] Initial studies showed reduction in AHI and symptoms in adults with OSA, but subsequent studies did

Table 6: Treatment options for persistent obstructive sleep apnea syndrome after tonsillectomy and adenoidectomy

Treatments	Comments
Watchful waiting	Generally for mild OSAS, AHI <5, with few or no symptoms and no complications of OSAS
Medical treatment	Nasal corticosteroids and/or leukotriene receptor antagonist[76]
Weight loss	Weight loss is a treatment option for OSAS in overweight/obese children[123]
Positive airway pressure	For moderate/severe OSAS, AHI ≥5
Orthodontic treatment	For mild-to-moderate OSAS
Orofacial myofunctional therapy	For mild-to-moderate OSAS
Other surgical options	Other surgical procedures are considered in a small subset of children with OSAS, after careful evaluation of the upper airway in children with moderate/severe OSAS. Options include tongue surgery, for example, midline glossectomy, genioglossus advancement, maxillo and/or mandibular distraction osteogenesis or tracheostomy[98,113]

OSAS: Obstructive sleep apnea syndrome, AHI: Apnea-hypopnea index

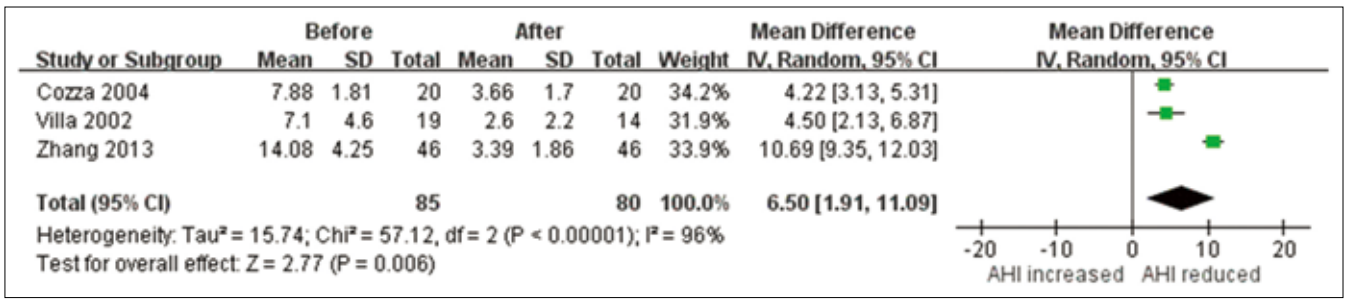

Figure 9: Forest plot for the effects of mandibular advancement device on apnea–hypopnea index.

not show benefit in adults with moderate-to-severe OSA.[135,136] A recent randomized, double-blind, placebo-controlled, crossover pilot study of nasal expiratory positive airway pressure (NEPAP) device on 14 CPAP candidates aged 8–16 years showed significant improvement in OAI with NEPAP in some patients but deterioration in a few patients, suggesting that it must only be prescribed under PSG monitoring.[137]

Positive Airway Pressure

The basic mechanism of positive airway pressure (PAP) is to overcome dynamic upper airway obstruction by stenting the airway open by pneumatic pressure. PAP therapy has been found to be effective in improving polysomnographic parameters in pediatric patients with OSAS.[138-143] In addition, there were also improvements in subjective parental assessment of sleepiness, snoring, and difficulty in breathing during sleep.[138] Significant improvement in neurobehavioral function in children after 3 months of PAP therapy was demonstrated, even in developmentally delayed children.[142]

PAP therapy should be considered in children who are not surgical candidates or have contraindications for TandA and those who continue to have moderate/severe OSAS after TandA.[143-145] PAP may also be considered for children with severe preoperative OSAS, co-existing morbidities such as cor pulmonale, morbid obesity, neuromuscular disorders, and craniofacial abnormalities.[87,96]

There are two modes of PAP – continuous positive airway pressure (CPAP) and bi-level positive airway pressure (BPAP). There is no difference in adherence between CPAP and BPAP.[146] The optimal setting should ideally be adjusted under PSG.[147] The maximum CPAP is 15 cmH_2O for <12-year-old children and 20 cmH_2O for ≥12-year-old children. CPAP should be switched to BPAP if the patient demonstrates persistence of OSA despite maximum CPAP. For BPAP, the inspiratory positive airway pressure should be started at 4 cm above the expiratory positive airway pressure (EPAP), and the EPAP pressure set at the level eliminates OSA. Long-term follow-up is needed since the required PAP setting may change over time for growing children with change in airway size and structure, as well as body weight.

If PSG titration is not available, the use of auto-titrating PAP devices for titrating pressures can be considered in patients down to 8 months of age without significant comorbidities although the body weight for auto-titrating PAP is usually above 30 kg.[148] PAP also can be titrated under DISE in selected centers with expertise.

In areas where none of the above are available, one may offer CPAP with pressure around 6–8 cmH2O for nonobese nonsyndromic OSAS and 8–10 cm for obese nonsyndromic children and to monitor for clinical response.[139] Data downloaded from PAP machines are useful in monitoring treatment adherence as parental reports are often not reliable.[146]

Adherence is the major barrier to PAP as an effective therapy for childhood OSAS.[146,149,150] Behavioral intervention, education, training, and close follow-up were shown to improve PAP adherence.[151]

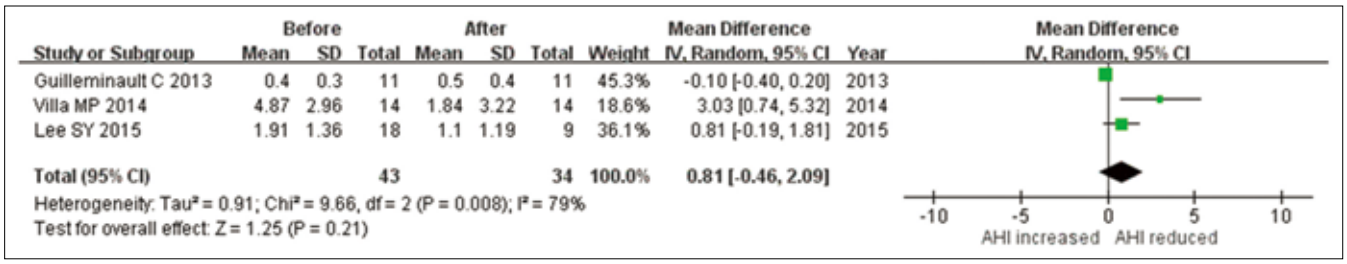

Figure 10: Forest plot for the effects of myofunctional therapy on apnea–hypopnea index.

A proper interface is crucial for the successful administration of PAP. The ideal interface should ensure comfort and fit, while minimizing leak.[152] Excessive leak can impact on sleep quality, patient–ventilator synchrony, and the amount of effective ventilation delivered to the patient.[153] If a child mouth breathes significantly, a chin strap should be used.

PAP should be provided with a heated humidifier because of the high flow of dry room air that would overwhelm the capacity of the nose to humidify and warm the incoming air. Notwithstanding the above measure, some patients would still have prominent nasal symptoms that would benefit from intranasal steroids. Skin irritation and ulceration can occur from a tight-fitting mask or from accumulation of skin oils and debris from poor mask maintenance.[154-157] Mid-facial hypoplasia was reported with long-term use of nasal CPAP.[158] A study showed that nasal PAP compliant individuals experienced a retrusion of the mid-face after a few years.[159] Use of nasal mask and nasal pillow on alternate nights might be tried to avoid the pressure effect on mid-face. Facial profile should be assessed every year for adverse impact on growth. For children requiring chin strap, the effect on the mandibular condyle should also be assessed yearly.

Orofacial Myofunctional Therapy

Orofacial myofunctional therapy (OMT) is potentially an option for the treatment of OSAS. It is defined as the treatment for the muscles of the face and mouth, which is crucial for the maintenance of the craniofacial integrity to achieve normal nasal breathing.[160] OMT reeducation trains a normal and strong sucking, a good mastication employing both sides of jaw, normal swallowing, normal tongue position, and nasal breathing with lips in good contact at rest.[13] Nasal breathing during wake and sleep is the demonstration of normal respiratory functioning, and persistence of mouth breathing is an indicator of an abnormal respiratory function.[161]

Guilleminault *et al*. reported a retrospective study of 11 children who received OMT.[162] The exercise group was followed up for the first 6 months. Exercise was repeated several times daily in the first 6 months. At 4-year follow-up, the exercise group remained cured of OSA (AHI 0.5 ± 0.4/h) compared to the control group which had a recurrence of OSA (AHI 5.3 ± 1.5/h).

In a prospective, randomized controlled study done by Villa *et al*., 27 post-TandA children were randomized to either OMT or control group.[163] Children were required to perform exercises every day at home, at least three times a day, 10–20 repetitions each time. Both groups performed nasal washing twice a day. The treatment group consisted of 14 patients and their pre- and post-exercise AHI was evaluated after 2 months of OMT. The AHI decreased from 4.9 to 1.8 ($P = 0.004$) while the control group had minimal change in AHI (4.6–4.1).

In a retrospective case series study done by Lee *et al*., 26 children out of 64 children had persistent SDB after TandA and 35 of the 64 children showed a pattern of mouth breathing.[161] Eighteen children of the mouth breathing group were followed up for a year with OMT offered. However, only nine of them underwent 6 months of OMT three times a week. The non-OMT group showed a significant worse AHI, 2.9, when compared to the exercise group, 1.1.

A forest plot was constructed with RevMan (version 5.2, The Cochrane Collaborations, London, UK) for the studies of Villa *et al*., Guilleminault *et al*., and Lee *et al*. by the authors (DKN, JPN, and SYL, respectively). The overall AHI was reduced by 0.81 with 95% confidence interval crossing zero [Figure 10]. Hence, further studies are warranted for OMT in childhood OSAS.

Conclusion

This is the first position statement on the management of childhood OSA in Asia, which would serve as a guideline for doctors in this area so that a more uniform approach can be adopted for this disease. While there are still considerable knowledge gap in this area, this statement provides the foundation for future studies.

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Conflicts of interest

There are no conflicts of interest.

References

1. Marcus CL, Brooks LJ, Draper KA, Gozal D, Halbower AC, Jones J, *et al.* Diagnosis and management of childhood obstructive sleep apnea syndrome. Pediatrics 2012;130:576-84.

2. Li AM, So HK, Au CT, Ho C, Lau J, Ng SK, *et al.* Epidemiology of obstructive sleep apnoea syndrome in Chinese children: A two-phase community study. Thorax 2010;65:991-7.
3. Marcus CL, Brooks LJ, Draper KA, Gozal D, Halbower AC, Jones J, *et al*. Diagnosis and management of childhood obstructive sleep apnea syndrome. Pediatrics 2012;130:576-84.
4. Kaditis AG, Alonso Alvarez ML, Boudewyns A, Alexopoulos EI, Ersu R, Joosten K, *et al.* Obstructive sleep disordered breathing in 2- to 18-year-old children: Diagnosis and management. Eur Respir J 2016;47:69-94.
5. Ng DK, Chan CH. A review of normal values of infant sleep polysomnography. Pediatr Neonatol 2013;54:82-7.
6. Wise MS, Nichols CD, Grigg-Damberger MM, Marcus CL, Witmans MB, Kirk VG, *et al.* Executive summary of respiratory indications for polysomnography in children: An evidence-based review. Sleep 2011;34:389-98AW.
7. Schwab RJ, Kim C, Bagchi S, Keenan BT, Comyn FL, Wang S, *et al.* Understanding the anatomic basis for obstructive sleep apnea syndrome in adolescents. Am J Respir Crit Care Med 2015;191:1295-309.
8. Wilhelm CP, deShazo RD, Tamanna S, Ullah MI, Skipworth LB. The nose, upper airway, and obstructive sleep apnea. Ann Allergy Asthma Immunol 2015;115:96-102.
9. Ng DK, Chan CH, Hwang GY, Chow PY, Kwok KL. A review of the roles of allergic rhinitis in childhood obstructive sleep apnea syndrome. Allergy Asthma Proc 2006;27:240-2.
10. Wing YK, Hui SH, Pak WM, Ho CK, Cheung A, Li AM, *et al.* A controlled study of sleep related disordered breathing in obese children. Arch Dis Child 2003;88:1043-7.
11. Lam YY, Chan EY, Ng DK, Chan CH, Cheung JM, Leung SY, *et al.* The correlation among obesity, apnea-hypopnea index, and tonsil size in children. Chest 2006;130:1751-6.
12. Xu Z, Jiaqing A, Yuchuan L, Shen K. A case-control study of obstructive sleep apnea-hypopnea syndrome in obese and nonobese Chinese children. Chest 2008;133:684-9.
13. Guilleminault C, Akhtar F. Pediatric sleep-disordered breathing: New evidence on its development. Sleep Med Rev 2015;24:46-56.
14. Dyken ME, Lin-Dyken DC, Poulton S, Zimmerman MB, Sedars E. Prospective polysomnographic analysis of obstructive sleep apnea in Down syndrome. Arch Pediatr Adolesc Med 2003;157:655-60.
15. Williams K, Scheimann A, Sutton V, Hayslett E, Glaze DG. Sleepiness and sleep disordered breathing in Prader-Willi syndrome: Relationship to genotype, growth hormone therapy, and body composition. J Clin Sleep Med 2008;4:111-8.
16. Huang YS, Guilleminault C. Pediatric obstructive sleep apnea and the critical role of oral-facial growth: Evidences. Front Neurol 2013;3:184.
17. Huang YS, Quo S, Berkowski JA, Guilleminault C. Short lingual frenulum and obstructive sleep apnea in children. Int J Pediatr Res 2015;1:1-4.
18. Huang YS, Hwang FM, Lin CH, Lee LA, Huang PY, Chiu ST. Clinical manifestations of pediatric obstructive sleep apnea syndrome: Clinical utility of the Chinese-version Obstructive Sleep Apnea Questionaire-18. Psychiatry Clin Neurosci 2015;69:752-62.
19. Suresh S, Wales P, Dakin C, Harris MA, Cooper DG. Sleep-related breathing disorder in Duchenne muscular dystrophy: Disease spectrum in the paediatric population. J Paediatr Child Health 2005;41:500-3.
20. Dauvilliers Y, Stal V, Abril B, Coubes P, Bobin S, Touchon J, *et al.* Chiari malformation and sleep related breathing disorders. J Neurol Neurosurg Psychiatry 2007;78:1344-8.
21. Hibbs AM, Johnson NL, Rosen CL, Kirchner HL, Martin R, Storfer-Isser A, *et al.* Prenatal and neonatal risk factors for sleep disordered breathing in school-aged children born preterm. J Pediatr 2008;153:176-82.
22. Weinstock TG, Rosen CL, Marcus CL, Garetz S, Mitchell RB, Amin R, *et al.* Predictors of obstructive sleep apnea severity in adenotonsillectomy candidates. Sleep 2014;37:261-9.
23. Zhu Y, Au CT, Leung TF, Wing YK, Lam CW, Li AM. Effects of passive smoking on snoring in preschool children. J Pediatr 2013;163:1158-62.e4.
24. Spruyt K, Gozal D. A mediation model linking body weight, cognition, and sleep-disordered breathing. Am J Respir Crit Care Med 2012;185:199-205.
25. Hogan AM, Hill CM, Harrison D, Kirkham FJ. Cerebral blood flow velocity and cognition in children before and after adenotonsillectomy. Pediatrics 2008;122:75-82.
26. Biggs SN, Walter LM, Jackman AR, Nisbet LC, Weichard AJ, Hollis SL, *et al.* Long-term cognitive and behavioral outcomes following resolution of sleep disordered breathing in preschool children. PLoS One 2015;10:e0139142.
27. Quan SF, Archbold K, Gevins AS, Goodwin JL. Long-term neurophysiologic impact of childhood sleep disordered breathing on neurocognitive performance. Southwest J Pulm Crit Care 2013;7:165-75.
28. Chan JY, Li AM, Au CT, Lo AF, Ng SK, Abdullah VJ, *et al.* Cardiac remodelling and dysfunction in children with obstructive sleep apnoea: A community based study. Thorax 2009;64:233-9.
29. Li AM, Au CT, Sung RY, Ho C, Ng PC, Fok TF, *et al.* Ambulatory blood pressure in children with obstructive sleep apnoea: A community based study. Thorax 2008;63:803-9.
30. Mulvaney SA, Goodwin JL, Morgan WJ, Rosen GR, Quan SF, Kaemingk KL. Behavior problems associated with sleep disordered breathing in school-aged children – The Tucson children's assessment of sleep apnea study. J Pediatr Psychol 2006;31:322-30.
31. Chervin RD, Archbold KH. Hyperactivity and polysomnographic findings in children evaluated for sleep-disordered breathing. Sleep 2001;24:313-20.
32. Song SA, Tolisano AM, Cable BB, Camacho M. Neurocognitive outcomes after pediatric adenotonsillectomy for obstructive sleep apnea: A systematic review and meta-analysis. Int J Pediatr Otorhinolaryngol 2016;83:205-10.
33. Chan KC, Shi L, So HK, Wang D, Liew AW, Rasalkar DD, *et al.* Neurocognitive dysfunction and grey matter density deficit in children with obstructive sleep apnoea. Sleep Med 2014;15:1055-61.
34. Cortese S, Faraone SV, Konofal E, Lecendreux M. Sleep in children with attention-deficit/hyperactivity disorder: Meta-analysis of subjective and objective studies. J Am Acad Child Adolesc Psychiatry 2009;48:894-908.
35. Guilleminault C, Lee JH, Chan A, Lopes MC, Huang YS, da Rosa A. Non-REM-sleep instability in recurrent sleepwalking in pre-pubertal children. Sleep Med 2005;6:515-21.
36. Carotenuto M, Esposito M, Parisi L, Gallai B, Marotta R, Pascotto A, *et al.* Depressive symptoms and childhood sleep apnea syndrome. Neuropsychiatr Dis Treat 2012;8:369-73.
37. Kukwa W, Kukwa A, Galazka A, Grochowski T, Krzeski A, Gronkiewicz Z, *et al.* Snoring but not BMI influences aggressive behavior and concentration problems in children. Otolaryngol Pol 2015;69:22-9.
38. Yue W, Hao W, Liu P, Liu T, Ni M, Guo Q. A case-control study on psychological symptoms in sleep apnea-hypopnea syndrome. Can J Psychiatry 2003;48:318-23.
39. Brooks LJ, Topol HI. Enuresis in children with sleep apnea. J Pediatr 2003;142:515-8.
40. Khositseth A, Chokechuleekorn J, Kuptanon T, Leejakpai A. Rhythm disturbances in childhood obstructive sleep apnea during apnea-hypopnea episodes. Ann Pediatr Cardiol 2013;6:39-42.
41. Constantin E, McGregor CD, Cote V, Brouillette RT. Pulse rate and pulse rate variability decrease after adenotonsillectomy for obstructive sleep apnea. Pediatr Pulmonol 2008;43:498-504.
42. O'Brien LM, Gozal D. Autonomic dysfunction in children with sleep-disordered breathing. Sleep 2005;28:747-52.
43. Kwok KL, Ng DK, Cheung YF. BP and arterial distensibility in children with primary snoring. Chest 2003;123:1561-6.
44. Hakim F, Gozal D, Kheirandish-Gozal L. Sympathetic and catecholaminergic alterations in sleep apnea with particular emphasis on children. Front Neurol 2012;3:7.
45. Chaicharn J, Lin Z, Chen ML, Ward SL, Keens T, Khoo MC. Model-based assessment of cardiovascular autonomic control in children with obstructive sleep apnea. Sleep 2009;32:927-38.
46. Chan KC, Au CT, Chook P, Lee DL, Lam HS, Wing YK, *et al.* Endothelial function in children with OSA and the effects of adenotonsillectomy. Chest 2015;147:132-9.

47. Nieminen P, Löppönen T, Tolonen U, Lanning P, Knip M, Löppönen H. Growth and biochemical markers of growth in children with snoring and obstructive sleep apnea. Pediatrics 2002;109:e55.
48. Marcus CL, Carroll JL, Koerner CB, Hamer A, Lutz J, Loughlin GM. Determinants of growth in children with the obstructive sleep apnea syndrome. J Pediatr 1994;125:556-62.
49. Schnall RP, Shlitner A, Sheffy J, Kedar R, Lavie P. Periodic, profound peripheral vasoconstriction – A new marker of obstructive sleep apnea. Sleep 1999;22:939-46.
50. O'Brien LM, Gozal D. Potential usefulness of noninvasive autonomic monitoring in recognition of arousals in normal healthy children. J Clin Sleep Med 2007;3:41-7.
51. Brouillette RT, Morielli A, Leimanis A, Waters KA, Luciano R, Ducharme FM. Nocturnal pulse oximetry as an abbreviated testing modality for pediatric obstructive sleep apnea. Pediatrics 2000;105:405-12.
52. Nixon GM, Kermack AS, Davis GM, Manoukian JJ, Brown KA, Brouillette RT. Planning adenotonsillectomy in children with obstructive sleep apnea: The role of overnight oximetry. Pediatrics 2004;113(1 Pt 1):e19-25.
53. Pavone M, Cutrera R, Verrillo E, Salerno T, Soldini S, Brouillette RT. Night-to-night consistency of at-home nocturnal pulse oximetry testing for obstructive sleep apnea in children. Pediatr Pulmonol 2013;48:754-60.
54. Sher AE, Shprintzen RJ, Thorpy MJ. Endoscopic observations of obstructive sleep apnea in children with anomalous upper airways: Predictive and therapeutic value. Int J Pediatr Otorhinolaryngol 1986;11:135-46.
55. Croft CB, Thomson HG, Samuels MP, Southall DP. Endoscopic evaluation and treatment of sleep-associated upper airway obstruction in infants and young children. Clin Otolaryngol Allied Sci 1990;15:209-16.
56. Contencin P, Nottet JB, Yacoubian K, Soussi T, Nivoche Y, Narcy P. Pharyngolaryngeal fibroscopy under general anesthesia in children. Technique and indications in sleep apnea and hypopnea. Ann Otolaryngol Chir Cervicofac 1991;108:373-7.
57. Myatt HM, Beckenham EJ. The use of diagnostic sleep nasendoscopy in the management of children with complex upper airway obstruction. Clin Otolaryngol Allied Sci 2000;25:200-8.
58. Goldberg S, Shatz A, Picard E, Wexler I, Schwartz S, Swed E, *et al.* Endoscopic findings in children with obstructive sleep apnea: Effects of age and hypotonia. Pediatr Pulmonol 2005;40:205-10.
59. Thevasagayam M, Rodger K, Cave D, Witmans M, El-Hakim H. Prevalence of laryngomalacia in children presenting with sleep-disordered breathing. Laryngoscope 2010;120:1662-6.
60. Fung E, Witmans M, Ghosh M, Cave D, El-Hakim H. Upper airway findings in children with Down syndrome on sleep nasopharyngoscopy: Case-control study. J Otolaryngol Head Neck Surg 2012;41:138-44.
61. Koo SK, Choi JW, Myung NS, Lee HJ, Kim YJ, Kim YJ. Analysis of obstruction site in obstructive sleep apnea syndrome patients by drug induced sleep endoscopy. Am J Otolaryngol 2013;34:626-30.
62. Truong MT, Woo VG, Koltai PJ. Sleep endoscopy as a diagnostic tool in pediatric obstructive sleep apnea. Int J Pediatr Otorhinolaryngol 2012;76:722-7.
63. Durr ML, Meyer AK, Kezirian EJ, Rosbe KW. Drug-induced sleep endoscopy in persistent pediatric sleep-disordered breathing after adenotonsillectomy. Arch Otolaryngol Head Neck Surg 2012;138:638-43.
64. Ulualp SO, Szmuk P. Drug-induced sleep endoscopy for upper airway evaluation in children with obstructive sleep apnea. Laryngoscope 2013;123:292-7.
65. Psaltis AJ, Li G, Vaezeafshar R, Cho KS, Hwang PH. Modification of the Lund-Kennedy endoscopic scoring system improves its reliability and correlation with patient-reported outcome measures. Laryngoscope 2014;124:2216-23.
66. Chan DK, Liming BJ, Horn DL, Parikh SR. A new scoring system for upper airway pediatric sleep endoscopy. JAMA Otolaryngol Head Neck Surg 2014;140:595-602.
67. Konermann M, Radü HJ, Teschler H, Rawert B, Heimbucher J, Sanner BM. Interaction of sleep disturbances and gastroesophageal reflux in chronic laryngitis. Am J Otolaryngol 2002;23:20-6.
68. Alexopoulos EI, Kaditis AG, Kalampouka E, Kostadima E, Angelopoulos NV, Mikraki V, *et al.* Nasal corticosteroids for children with snoring. Pediatr Pulmonol 2004;38:161-7.
69. Chan CC, Au CT, Lam HS, Lee DL, Wing YK, Li AM. Intranasal corticosteroids for mild childhood obstructive sleep apnea – A randomized, placebo-controlled study. Sleep Med 2015;16:358-63.
70. Kheirandish-Gozal L, Gozal D. Intranasal budesonide treatment for children with mild obstructive sleep apnea syndrome. Pediatrics 2008;122:e149-55.
71. Brouillette RT, Manoukian JJ, Ducharme FM, Oudjhane K, Earle LG, Ladan S, *et al.* Efficacy of fluticasone nasal spray for pediatric obstructive sleep apnea. J Pediatr 2001;138:838-44.
72. Liu HT, Lin YC, Kuan YC, Huang YH, Hou WH, Liou TH, *et al.* Intranasal corticosteroid therapy in the treatment of obstructive sleep apnea: A meta-analysis of randomized controlled trials. Am J Rhinol Allergy 2016;30:215-21.
73. Goldbart AD, Goldman JL, Veling MC, Gozal D. Leukotriene modifier therapy for mild sleep-disordered breathing in children. Am J Respir Crit Care Med 2005;172:364-70.
74. Goldbart AD, Greenberg-Dotan S, Tal A. Montelukast for children with obstructive sleep apnea: A double-blind, placebo-controlled study. Pediatrics 2012;130:e575-80.
75. Kheirandish-Gozal L, Bandla HP, Gozal D. Montelukast for children with obstructive sleep apnea: Results of a double-blind, randomized, placebo-controlled trial. Ann Am Thorac Soc 2016;13:1736-41.
76. Kheirandish L, Goldbart AD, Gozal D. Intranasal steroids and oral leukotriene modifier therapy in residual sleep-disordered breathing after tonsillectomy and adenoidectomy in children. Pediatrics 2006;117:e61-6.
77. Kheirandish-Gozal L, Bhattacharjee R, Bandla HP, Gozal D. Antiinflammatory therapy outcomes for mild OSA in children. Chest 2014;146:88-95.
78. Redline S, Amin R, Beebe D, Chervin RD, Garetz SL, Giordani B, *et al.* The Childhood Adenotonsillectomy Trial (CHAT): Rationale, design, and challenges of a randomized controlled trial evaluating a standard surgical procedure in a pediatric population. Sleep 2011;34:1509-17.
79. Marcus CL, Moore RH, Rosen CL, Giordani B, Garetz SL, Taylor HG, *et al.* A randomized trial of adenotonsillectomy for childhood sleep apnea. N Engl J Med 2013;368:2366-76.
80. Mitchell RB, Kelly J. Outcome of adenotonsillectomy for obstructive sleep apnea in children under 3 years. Otolaryngol Head Neck Surg 2005;132:681-4.
81. Ma AL, Lam YY, Wong SF, Ng DK, Chan CH. Risk factors for post-operative complications in Chinese children with tonsillectomy and adenoidectomy for obstructive sleep apnea syndrome. Sleep Breath 2012;16:909-11.
82. Mitchell RB, Kelly J. Outcome of adenotonsillectomy for severe obstructive sleep apnea in children. Int J Pediatr Otorhinolaryngol 2004;68:1375-9.
83. Walker P, Whitehead B, Gulliver T. Polysomnographic outcome of adenotonsillectomy for obstructive sleep apnea in children under 5 years old. Otolaryngol Head Neck Surg 2008;139:83-6.
84. Ng DK, Wong JC, Chan CH, Leung LC, Leung SY. Ambulatory blood pressure before and after adenotonsillectomy in children with obstructive sleep apnea. Sleep Med 2010;11:721-5.
85. Lee CH, Hsu WC, Chang WH, Lin MT, Kang KT. Polysomnographic findings after adenotonsillectomy for obstructive sleep apnoea in obese and non-obese children: A systematic review and meta-analysis. Clin Otolaryngol 2016;41:498-510.
86. Nath A, Emani J, Suskind DL, Baroody FM. Predictors of persistent sleep apnea after surgery in children younger than 3 years. JAMA Otolaryngol Head Neck Surg 2013;139:1002-8.
87. Suen JS, Arnold JE, Brooks LJ. Adenotonsillectomy for treatment of obstructive sleep apnea in children. Arch Otolaryngol Head Neck Surg 1995;121:525-30.
88. Nishimura T, Morishima N, Hasegawa S, Shibata N, Iwanaga K, Yagisawa M. Effect of surgery on obstructive sleep apnea. Acta Otolaryngol Suppl 1996;523:231-3.
89. Wang RC, Elkins TP, Keech D, Wauquier A, Hubbard D. Accuracy of

clinical evaluation in pediatric obstructive sleep apnea. Otolaryngol Head Neck Surg 1998;118:69-73.
90. Tal A, Bar A, Leiberman A, Tarasiuk A. Sleep characteristics following adenotonsillectomy in children with obstructive sleep apnea syndrome. Chest 2003;124:948-53.
91. Goldstein NA, Pugazhendhi V, Rao SM, Weedon J, Campbell TF, Goldman AC, *et al.* Clinical assessment of pediatric obstructive sleep apnea. Pediatrics 2004;114:33-43.
92. Mitchell RB, Kelly J. Adenotonsillectomy for obstructive sleep apnea in obese children. Otolaryngol Head Neck Surg 2004;131:104-8.
93. Tauman R, Gulliver TE, Krishna J, Montgomery-Downs HE, O'Brien LM, Ivanenko A, *et al.* Persistence of obstructive sleep apnea syndrome in children after adenotonsillectomy. J Pediatr 2006;149:803-8.
94. O'Brien LM, Sitha S, Baur LA, Waters KA. Obesity increases the risk for persisting obstructive sleep apnea after treatment in children. Int J Pediatr Otorhinolaryngol 2006;70:1555-60.
95. Mitchell RB. Adenotonsillectomy for obstructive sleep apnea in children: Outcome evaluated by pre- and postoperative polysomnography. Laryngoscope 2007;117:1844-54.
96. Mitchell RB, Kelly J. Outcome of adenotonsillectomy for obstructive sleep apnea in obese and normal-weight children. Otolaryngol Head Neck Surg 2007;137:43-8.
97. Gozal D, Capdevila OS, Kheirandish-Gozal L. Metabolic alterations and systemic inflammation in obstructive sleep apnea among nonobese and obese prepubertal children. Am J Respir Crit Care Med 2008;177:1142-9.
98. Friedman M, Samuelson CG, Hamilton C, Maley A, Taylor D, Kelley K, *et al.* Modified adenotonsillectomy to improve cure rates for pediatric obstructive sleep apnea: A randomized controlled trial. Otolaryngol Head Neck Surg 2012;147:132-8.
99. Baldassari CM, Kepchar J, Bryant L, Beydoun H, Choi S. Changes in central apnea index following pediatric adenotonsillectomy. Otolaryngol Head Neck Surg 2012;146:487-90.
100. Hsu WC, Kang KT, Weng WC, Lee PL. Impacts of body weight after surgery for obstructive sleep apnea in children. Int J Obes (Lond) 2013;37:527-31.
101. Kang KT, Weng WC, Lee CH, Lee PL, Hsu WC. Discrepancy between objective and subjective outcomes after adenotonsillectomy in children with obstructive sleep apnea syndrome. Otolaryngol Head Neck Surg 2014;151:150-8.
102. Jeong JH, Guilleminault C, Park CS, Son HL, Lee HK, Hwang SH, *et al.* Changes in salivary cortisol levels in pediatric patients with obstructive sleep apnea syndrome after adenotonsillectomy. Sleep Med 2014;15:672-6.
103. Lee LA, Li HY, Lin YS, Fang TJ, Huang YS, Hsu JF, *et al.* Severity of childhood obstructive sleep apnea and hypertension improved after adenotonsillectomy. Otolaryngol Head Neck Surg 2015;152:553-60.
104. Suri JC, Sen MK, Venkatachalam VP, Bhool S, Sharma R, Elias M, *et al.* Outcome of adenotonsillectomy for children with sleep apnea. Sleep Med 2015;16:1181-6.
105. Shine NP, Lannigan FJ, Coates HL, Wilson A. Adenotonsillectomy for obstructive sleep apnea in obese children: Effects on respiratory parameters and clinical outcome. Arch Otolaryngol Head Neck Surg 2006;132:1123-7.
106. Com G, Carroll JL, Tang X, Melguizo MS, Bower C, Jambhekar S. Characteristics and surgical and clinical outcomes of severely obese children with obstructive sleep apnea. J Clin Sleep Med 2015;11:467-74.
107. Shintani T, Asakura K, Kataura A. The effect of adenotonsillectomy in children with OSA. Int J Pediatr Otorhinolaryngol 1998;44:51-8.
108. Nieminen P, Tolonen U, Löppönen H. Snoring and obstructive sleep apnea in children: A 6-month follow-up study. Arch Otolaryngol Head Neck Surg 2000;126:481-6.
109. Stewart MG, Glaze DG, Friedman EM, Smith EO, Bautista M. Quality of life and sleep study findings after adenotonsillectomy in children with obstructive sleep apnea. Arch Otolaryngol Head Neck Surg 2005;131:308-14.
110. Guilleminault C, Huang YS, Glamann C, Li K, Chan A. Adenotonsillectomy and obstructive sleep apnea in children: A prospective survey. Otolaryngol Head Neck Surg 2007;136:169-75.
111. Tunkel DE, Hotchkiss KS, Carson KA, Sterni LM. Efficacy of powered intracapsular tonsillectomy and adenoidectomy. Laryngoscope 2008;118:1295-302.
112. Reilly BK, Levin J, Sheldon S, Harsanyi K, Gerber ME. Efficacy of microdebrider intracapsular adenotonsillectomy as validated by polysomnography. Laryngoscope 2009;119:1391-3.
113. Villa MP, Castaldo R, Miano S, Paolino MC, Vitelli O, Tabarrini A, *et al.* Adenotonsillectomy and orthodontic therapy in pediatric obstructive sleep apnea. Sleep Breath 2014;18:533-9.
114. Bhushan B, Sheldon S, Wang E, Schroeder JW Jr. Clinical indicators that predict the presence of moderate to severe obstructive sleep apnea after adenotonsillectomy in children. Am J Otolaryngol 2014;35:487-95.
115. Huang YS, Guilleminault C, Lee LA, Lin CH, Hwang FM. Treatment outcomes of adenotonsillectomy for children with obstructive sleep apnea: A prospective longitudinal study. Sleep 2014;37:71-6.
116. Kobayashi R, Miyazaki S, Karaki M, Hoshikawa H, Nakata S, Hara H, *et al.* Evaluation of adenotonsillectomy and tonsillectomy for pediatric obstructive sleep apnea by rhinomanometry and the OSA-18 questionnaire. Acta Otolaryngol 2014;134:818-23.
117. Nandalike K, Shifteh K, Sin S, Strauss T, Stakofsky A, Gonik N, *et al.* Adenotonsillectomy in obese children with obstructive sleep apnea syndrome: Magnetic resonance imaging findings and considerations. Sleep 2013;36:841-7.
118. Ye J, Liu H, Zhang GH, Li P, Yang QT, Liu X, *et al.* Outcome of adenotonsillectomy for obstructive sleep apnea syndrome in children. Ann Otol Rhinol Laryngol 2010;119:506-13.
119. Donnelly LF, Shott SR, LaRose CR, Chini BA, Amin RS. Causes of persistent obstructive sleep apnea despite previous tonsillectomy and adenoidectomy in children with down syndrome as depicted on static and dynamic cine MRI. AJR Am J Roentgenol 2004;183:175-81.
120. Bhattacharjee R, Kheirandish-Gozal L, Spruyt K, Mitchell RB, Promchiarak J, Simakajornboon N, *et al.* Adenotonsillectomy outcomes in treatment of obstructive sleep apnea in children: A multicenter retrospective study. Am J Respir Crit Care Med 2010;182:676-83.
121. Katz ES, Moore RH, Rosen CL, Mitchell RB, Amin R, Arens R, *et al.* Growth after adenotonsillectomy for obstructive sleep apnea: An RCT. Pediatrics 2014;134:282-9.
122. Biggs SN, Vlahandonis A, Anderson V, Bourke R, Nixon GM, Davey MJ, *et al.* Long-term changes in neurocognition and behavior following treatment of sleep disordered breathing in school-aged children. Sleep 2014;37:77-84.
123. Verhulst SL, Franckx H, Van Gaal L, De Backer W, Desager K. The effect of weight loss on sleep-disordered breathing in obese teenagers. Obesity (Silver Spring) 2009;17:1178-83.
124. Pirelli P, Saponara M, Guilleminault C. Rapid maxillary expansion in children with obstructive sleep apnea syndrome. Sleep 2004;27:761-6.
125. Pirelli P, Saponara M, Guilleminault C. Rapid maxillary expansion (RME) for pediatric obstructive sleep apnea: A 12-year follow-up. Sleep Med 2015;16:933-5.
126. Villa MP, Malagola C, Pagani J, Montesano M, Rizzoli A, Guilleminault C, *et al.* Rapid maxillary expansion in children with obstructive sleep apnea syndrome: 12-month follow-up. Sleep Med 2007;8:128-34.
127. Villa MP, Rizzoli A, Miano S, Malagola C. Efficacy of rapid maxillary expansion in children with obstructive sleep apnea syndrome: 36 months of follow-up. Sleep Breath 2011;15:179-84.
128. Guilleminault C, Monteyrol PJ, Huynh NT, Pirelli P, Quo S, Li K. Adeno-tonsillectomy and rapid maxillary distraction in pre-pubertal children, a pilot study. Sleep Breath 2011;15:173-7.
129. Huynh NT, Desplats E, Almeida FR. Orthodontics treatments for managing obstructive sleep apnea syndrome in children: A systematic review and meta-analysis. Sleep Med Rev 2016;25:84-94.
130. Ramar K, Dort LC, Katz SG, Lettieri CJ, Harrod CG, Thomas SM, *et al.* Clinical practice guideline for the treatment of obstructive sleep apnea and snoring with oral appliance therapy: An update for 2015. J Clin Sleep Med 2015;11:773-827.
131. Cozza P, Ballanti F, Prete L. A modified monobloc for treatment of young children with obstructive sleep apnea. J Clin Orthod 2004;38:241-7.
132. Villa MP, Bernkopf E, Pagani J, Broia V, Montesano M, Ronchetti R. Randomized controlled study of an oral jaw-positioning appliance for

the treatment of obstructive sleep apnea in children with malocclusion. Am J Respir Crit Care Med 2002;165:123-7.
133. Zhang C, He H, Ngan P. Effects of twin block appliance on obstructive sleep apnea in children: A preliminary study. Sleep Breath 2013;17:1309-14.
134. Braga CW, Chen Q, Burschtin OE, Rapoport DM, Ayappa I. Changes in lung volume and upper airway using MRI during application of nasal expiratory positive airway pressure in patients with sleep-disordered breathing. J Appl Physiol 2011;111:1400-9.
135. Kryger MH, Berry RB, Massie CA. Long-term use of a nasal expiratory positive airway pressure (EPAP) device as a treatment for obstructive sleep apnea (OSA). J Clin Sleep Med 2011;7:449-53B.
136. Rossi VA, Winter B, Rahman NM, Yu LM, Fallon J, Clarenbach CF, *et al.* The effects of Provent on moderate to severe obstructive sleep apnoea during continuous positive airway pressure therapy withdrawal: A randomised controlled trial. Thorax 2013;68:854-9.
137. Kureshi SA, Gallagher PR, McDonough JM, Cornaglia MA, Maggs J, Samuel J, *et al.* Pilot study of nasal expiratory positive airway pressure devices for the treatment of childhood obstructive sleep apnea syndrome. J Clin Sleep Med 2014;10:663-9.
138. Marcus CL, Beck SE, Traylor J, Cornaglia MA, Meltzer LJ, DiFeo N, *et al.* Randomized, double-blind clinical trial of two different modes of positive airway pressure therapy on adherence and efficacy in children. J Clin Sleep Med 2012;8:37-42.
139. Marcus CL, Ward SL, Mallory GB, Rosen CL, Beckerman RC, Weese-Mayer DE, *et al.* Use of nasal continuous positive airway pressure as treatment of childhood obstructive sleep apnea. J Pediatr 1995;127:88-94.
140. Waters KA, Everett FM, Bruderer JW, Sullivan CE. Obstructive sleep apnea: The use of nasal CPAP in 80 children. Am J Respir Crit Care Med 1995;152:780-5.
141. Guilleminault C, Pelayo R, Clerk A, Leger D, Bocian RC. Home nasal continuous positive airway pressure in infants with sleep-disordered breathing. J Pediatr 1995;127:905-12.
142. Marcus CL, Radcliffe J, Konstantinopoulou S, Beck SE, Cornaglia MA, Traylor J, *et al.* Effects of positive airway pressure therapy on neurobehavioral outcomes in children with obstructive sleep apnea. Am J Respir Crit Care Med 2012;185:998-1003.
143. Smith DF, Benke JR, Yaster S, Boss EF, Ishman SL. A pilot staging system to predict persistent obstructive sleep apnea in children following adenotonsillectomy: Predicting persistent pediatric OSA. Laryngoscope 2013;123:1817-22.
144. Marcus CL, Brooks LJ, Draper KA, Gozal D, Halbower AC, Jones J, *et al*. Diagnosis and management of childhood obstructive sleep apnea syndrome. Pediatrics 2012;130:e714-55.
145. Preutthipan A, Sritippayawan S, Kuptanon T. Thai Guideline for Childhood Obstructive Sleep Apnea; 2013. Available from: http://www.thaipedlung.org. [Last accessed on 2016 Mar 23].
146. Marcus CL, Rosen G, Ward SL, Halbower AC, Sterni L, Lutz J, *et al.* Adherence to and effectiveness of positive airway pressure therapy in children with obstructive sleep apnea. Pediatrics 2006;117:e442-51.
147. Kushida CA, Chediak A, Berry RB, Brown LK, Gozal D, Iber C, *et al.* Clinical guidelines for the manual titration of positive airway pressure in patients with obstructive sleep apnea. J Clin Sleep Med 2008;4:157-71.
148. Palombini L, Pelayo R, Guilleminault C. Efficacy of automated continuous positive airway pressure in children with sleep-related breathing disorders in an attended setting. Pediatrics 2004;113:e412-7.
149. Uong EC, Epperson M, Bathon SA, Jeffe DB. Adherence to nasal positive airway pressure therapy among school-aged children and adolescents with obstructive sleep apnea syndrome. Pediatrics 2007;120:e1203-11.
150. O'Donnell AR, Bjornson CL, Bohn SG, Kirk VG. Compliance rates in children using noninvasive continuous positive airway pressure. Sleep 2006;29:651-8.
151. Koontz KL, Slifer KJ, Cataldo MD, Marcus CL. Improving pediatric compliance with positive airway pressure therapy: The impact of behavioral intervention. Sleep 2003;26:1010-5.
152. Pavone M, Verrillo E, Caldarelli V, Ullmann N, Cutrera R. Non-invasive positive pressure ventilation in children. Early Hum Dev 2013;89 Suppl 3:S25-31.
153. Teschler H, Stampa J, Ragette R, Konietzko N, Berthon-Jones M. Effect of mouth leak on effectiveness of nasal bilevel ventilatory assistance and sleep architecture. Eur Respir J 1999;14:1251-7.
154. King MS, Xanthopoulos MS, Marcus CL. Improving positive airway pressure adherence in children. Sleep Med Clin 2014;9:219-34.
155. Pépin JL, Leger P, Veale D, Langevin B, Robert D, Lévy P. Side effects of nasal continuous positive airway pressure in sleep apnea syndrome. Study of 193 patients in two French sleep centers. Chest 1995;107:375-81.
156. Massie CA, Hart RW, Peralez K, Richards GN. Effects of humidification on nasal symptoms and compliance in sleep apnea patients using continuous positive airway pressure. Chest 1999;116:403-8.
157. Kirk VG, O'Donnell AR. Continuous positive airway pressure for children: A discussion on how to maximize compliance. Sleep Med Rev 2006;10:119-27.
158. Li KK, Riley RW, Guilleminault C. An unreported risk in the use of home nasal continuous positive airway pressure and home nasal ventilation in children: Mid-face hypoplasia. Chest 2000;117:916-8.
159. Roberts SD, Kapadia H, Greenlee G, Chen ML. Midfacial and dental changes associated with nasal positive airway pressure in children with obstructive sleep apnea and craniofacial conditions. J Clin Sleep Med 2016;12:469-75.
160. Moeller JL, Paskay LC, Gelb ML. Myofunctional therapy. Sleep Med Clin 2014;9:235-43.
161. Lee SY, Guilleminault C, Chiu HY, Sullivan SS. Mouth breathing, "nasal disuse," and pediatric sleep-disordered breathing. Sleep Breath 2015;19:1257-64.
162. Guilleminault C, Huang YS, Monteyrol PJ, Sato R, Quo S, Lin CH. Critical role of myofascial reeducation in pediatric sleep-disordered breathing. Sleep Med 2013;14:518-25.
163. Villa MP, Brasili L, Ferretti A, Vitelli O, Rabasco J, Mazzotta AR, *et al.* Oropharyngeal exercises to reduce symptoms of OSA after AT. Sleep Breath 2015;19:281-9.