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Obstructive sleep apnoea in children

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Competing interests
None declared.

Educational aims

- To understand the aetiology and pathophysiology of obstructive sleep apnoea in childhood.
- To recognise sleep apnoea-related morbidity from the cardiovascular and central nervous systems.
- To get familiar with treatment indications and available therapeutic modalities for obstructive sleep apnoea in childhood.

Summary

Adenotonsillar hypertrophy, obesity, craniofacial anomalies and abnormal neuromotor tone are the main conditions predisposing to obstructive sleep apnoea (OSA) in childhood. Overnight polysomnography is the gold standard for diagnosis of the disorder. Sleep apnoeic children experience increased prevalence of enuresis, elevated blood pressure, excessive daytime sleepiness, hyperactivity, learning problems and neurocognitive dysfunction. Successful treatment of paediatric OSA requires a multifaceted approach which will address all the different conditions related to dysfunctional upper airway during sleep.

Definition, aetiology and pathophysiology

Obstructive sleep apnoea (OSA) is a respiratory disorder characterised by intermittent partial and/or complete upper airway obstruction during sleep (hypopnoea or obstructive apnoea, respectively) that may impair normal ventilation and sleep pattern. Snoring, witnessed apnoeas, laboured breathing and restless sleep are the most common clinical manifestations. Reduction or cessation of airflow are frequently accompanied by episodic hypoxia, hypercapnia, arousal from sleep and exaggerated intrathoracic pressure swings.

Children with OSA suffer from functional impairment of the upper airway while asleep, which results from the presence of several different disease entities or conditions: 1) adenotonsillar hypertrophy; 2) obesity; 3) subtle craniofacial abnormalities or profound craniofacial anomalies; 4) abnormal neuromotor tone and/or abnormal control of breathing; and 5) combinations of the previous disorders or conditions (table 1).

In particular, patency of the upper airway during sleep results from complex interactions between upper airway resistance, pharyngeal collapsibility and tone of the pharyngeal dilator muscles and negative intraluminal pressure generated by the inspiratory muscles. In some children, this fine balance of mechanical forces is disturbed. For example, enlarged tonsils and adenoid or obesity may increase resistance to airflow and the tendency of the pharynx to collapse during inspiration (pharyngeal collapsibility).

It has been speculated that inspiratory intraluminal pressure becomes more negative than usual to compensate for increased upper airway resistance and to maintain normal airflow and alveolar ventilation. However,

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Table 1. Characteristic examples of disorders or conditions predisposing to obstructive sleep apnoea in children

Adenotosillar hypertrophy
Obesity
Subtle craniofacial abnormalities or profound craniofacial anomalies
Mild mandibular retrognathia
Marked midfacial hypoplasia (*e.g.* Apert syndrome, Crouzon syndrome)
Marked mandibular hypoplasia (*e.g.* Pierre Robin sequence, Treacher Collins syndrome, Stickler syndrome)
Mucopolysacharidoses
Abnormal neuromotor tone and/or control of breathing
Cerebral palsy
Duchenne muscular dystrophy
Combinations of the above disorders or conditions
Down's syndrome
Achondroplasia
Prader-Willi syndrome

during sleep, when the neuromotor tone of the pharyngeal dilator muscles decreases, negative intraluminal pressure cannot be balanced, leading to intermittent partial or complete pharyngeal airway collapse. Studies in children with OSA have confirmed a higher tendency of the upper airway to collapse compared to age-matched controls [1, 2]. This tendency is complicated by the fact that sleep apnoeic children are less likely to arouse in response to upper airway obstruction or to the apnoea-associated hypercapnia [2, 3].

Epidemiology

Nocturnal polysomnography is the gold standard for the diagnosis of upper airway obstruction during sleep and the mean number of apnoeas and hypopnoeas per hour of sleep time (apnoea–hypopnea index (AHI)) is the most frequently used index of OSA severity [4]. Two population-based studies from the USA (TuCASA and Penn State University Study) have determined OSA prevalence in childhood by overnight polysomnography [5, 6]. Approximately 25% and 1% of 5–12 yr-old children were found to have AHI >1 episode·h^{-1} and >5 episodes·h^{-1}, respectively [5, 6].

Other studies of children recruited from the general population have estimated the frequency of OSA symptoms, and their results have been summarised in a recent review article [7]. The calculated prevalence of snoring by parental report is 7.45% (95% CI: 5.75–9.61) and that of parent-witnessed apnoeas ranges 0.2–4% [7]. In general, parental report of OSA symptoms underestimates the problem. In the Pennsylvania State University (PA, USA) study, presence of snoring was recalled by parents in 14.9% of children but the frequency of the same symptom was identified by polysomnography in 26.1% of subjects [8].

Diagnosis

Most frequent nocturnal symptoms associated with OSA include snoring and difficult breathing during sleep. Other commonly reported nocturnal symptoms include chest retractions, restless sleep, nocturnal sweating, nocturnal enuresis and a higher frequency of various parasomnias. Typical daytime symptoms are usually related to the presence of adenotonsillar hypertrophy and include frequent upper respiratory tract infections, chronic mouth breathing, hearing and eating problems. The classical daytime symptom of OSA in adults, excessive daytime sleepiness, is less commonly reported in children. Many sleep-apnoeic children can present with behavioral and neurocognitive symptoms including hyperactivity, aggressive behavior and poor school performance.

Physical examination of the child with suspected OSA should include visual assessment of the upper airway patency using scoring systems like the Brodsky and Mallampati [9]. Other upper airway-related signs that need to be documented are adenoidal facies, mouth breathing, nasal voice tone, retrognathia, micrognathia or midfacial hypoplasia. Furthermore, the nose and palate also need to be assessed. A neurological examination is also necessary to identify any neurological impairment, since abnormal neuromotor tone contributes to upper airway dysfunction during sleep. Blood pressure measurement should also be performed. Finally, since paediatric OSA can be either a cause of growth delay or it can be related to obesity, it is important to document the growth pattern in children with suspected sleep apnoea.

Polysomnography remains the gold standard in the diagnosis of paediatric OSA. Although it is an expensive and time-consuming diagnostic tool, no other study has been shown to be sensitive and specific enough to diagnose OSA in children. It is important to note that scoring of respiratory events during sleep in children differs from definitions used in adults. For a detailed overview of these definitions and technical prerequisites, we refer to the recently published guidelines of the American Academy of Sleep Medicine [4]. These guidelines can be used to

score respiratory events for adolescents up to the age of 18 yrs. However, an individual sleep specialist can choose to score polysomnography recordings from children ⩾13 yrs of age using the adult criteria.

Thresholds of polysomnography indices for the diagnosis of OSA in childhood are based on normative polysomnographic values derived from healthy children [5, 10–13]. However, it is important to note that these studies differ in terms of subjects' recruitment criteria and in some cases they have used slightly different definitions for the various respiratory events during sleep. In spite of these methodological differences, it is clear that obstructive events in normal children are rare. Moreover, the distribution of respiratory events seems not to be influenced by Tanner stage [14]. Therefore, OSA in children is commonly diagnosed with an apnoea-hypopnoea index ⩾1 episode·h^{-1} [15]. Finally, several studies have shown that a single-night polysomnography is sufficient to diagnose sleep apnoea in children. However, in a child with a normal sleep study but with a very suggestive history and physical examination, a second night might be warranted.

OSA-related morbidity

The main consequence of repetitive apnoeas and hypopnoeas during sleep is intermittent hypoxia, which is a potent trigger of oxidative stress and inflammation [16]. Indeed, several studies have documented increased markers of oxidative stress and inflammation in children who exhibit sleep apnoea [17–20]. Other mechanisms by which OSA may cause complications include increased sympathetic activity [21, 22], increased serum cortisol [23], and hormonal changes resulting from hypoxia, arousal from sleep and secondary sleep debt [24–26].

Neurocognitive and behavioural complications

In spite of major differences in study design, population sample and definitions of OSA and outcome measures, most studies have described an increase in subjective sleepiness, mood disturbance, behaviour problems and deficits in attention, memory and executive functions [27]. Other studies have also demonstrated an association between OSA and lower academic achievement which might persist into adolescence [28, 29]. Halbower *et al*. [30] have reported signs of neuronal damage in children with OSA. Since this is a cross-sectional study, it is not clear whether the neuronal injury would be fully reversible after appropriate treatment.

Another interesting fact is that the prevalence of snoring and OSA is significantly increased in children with attention deficit hyperactivity disorder, and that a clear improvement is seen after adenotonsillectomy [31]. Not all studies have reported a dose-response relationship between severity of OSA and neurobehavioural morbidity. Additional factors such as genetic susceptibility, exposure to passive smoking, obesity, short sleep duration and other sleep disorders may also affect neurocognitive outcomes [27].

Cardiovascular complications

Cardiovascular complications of OSA might be of particular clinical importance to obese children and teenagers because it could augment the many obesity-related cardiovascular consequences. Cross-sectional studies indicate that increasing severity of OSA in obese children and adolescents is associated with increasing risk for the metabolic syndrome [32, 33]. Moreover, several studies reveal a positive correlation between sleep apnoea and insulin resistance and dyslipidaemia in children [25, 26, 34, 35]. However, it must be noted that other studies have failed to find a similar relationship [36–38], possibly due to variations in the magnitude of obesity and the ages of study subjects, reflecting varying severity and/or duration of disease and pubertal status. Cross-sectional studies of patients prior to and following treatment have yielded conflicting results [39–41]. Overall, OSA appears to have modest effects on metabolic function in children, and the long-term consequences of childhood sleep apnoea on metabolic morbidity in early adulthood remain to be demonstrated in longitudinal investigations. Nevertheless, it should also be noted that OSA in childhood is associated with cardiovascular complications, including increase in diastolic blood pressure, blunting of the nocturnal fall in blood pressure [42, 43] and increase in left ventricular mass and reduction in systolic and diastolic cardiac function [44–46].

Effects on growth

Although obesity becomes more and more an important risk factor of childhood OSA, early studies reported growth failure in children with sleep apnoea [47, 48]. Although full-blown failure to thrive is nowadays rarely seen, it is

well known that most children gain weight after adenotonsillectomy [49, 50]. Possible mechanisms for growth impairment include increased energy expenditure during sleep, altered production of growth hormone and increased peripheral resistance to growth factors [51–53].

Treatment

There are no long-term, follow-up studies clarifying whether OSA symptoms, abnormal polysomnography findings, OSA-related morbidity or any of their potential combinations are indications for treatment. For many years, AHI >5 episodes·h^{-1} in children with adenotonsillar hypertrophy has been an indication for adenotonsillectomy [54]. However, recent evidence suggests that even the presence of snoring without apnoeas (AHI <1 episode·h^{-1}) is associated with elevated blood pressure [55]. Even an AHI as low as 1 episode·h^{-1} is related to excessive daytime sleepiness or learning problems [15]. Although sleep apnoea can be accompanied by morbidity, it should be taken under consideration that OSA resolves spontaneously in many children; 70% of pre-adolescent subjects with AHI ⩾1 episode·h^{-1} will have an AHI<1 episode·h^{-1} in adolescence [56].

Despite the absence of controlled trials on the value of OSA treatment, some indications for therapeutic intervention can be summarised as follows:

1) Children with OSA of moderate or higher severity (AHI>5 episode·h^{-1}) should receive some form of treatment, irrespective to the presence of morbidity.
2) Subjects with AHI 1–5 episodes·h^{-1}, but with OSA-related morbidity (*e.g.* enuresis, inadequate somatic growth, poor academic performance, excessive daytime sleepiness, systolic or diastolic blood pressure >95th, pulmonary hypertension) are candidates for treatment.
3) Increasing body mass index percentile and male gender are risk factors for persistent OSA and they should be taken under consideration when treatment decisions are made.
4) Subjects with neuromuscular disorders and craniofacial anomalies frequently have moderate-to-severe OSA and they are at risk for development of pulmonary hypertension [57, 58]. Thus, treatment of OSA is indicated and it may reduce pulmonary artery pressure [59].

The available treatment options for OSA include: administration of anti-inflammatory medications, adenotonsillectomy, weight loss, use of orthodontic appliances, nasal continuous positive airway pressure (nCPAP), midface and mandibular distraction osteogenesis and tracheostomy. If it is determined that a child is a candidate for treatment, then the applied therapeutic modalities should address the specific abnormality or abnormalities causing upper airway dysfunction [57, 60]. For example, a child with adenotonsillar hypertrophy and hypoplastic mandible or midfacial hypoplasia should be treated with the combination of adenotonsillectomy and use of an orthodontic appliance or craniofacial surgery [61, 62].

The need for a multifaceted treatment approach is emphasised by the finding that approximately 20% of patients do not achieve AHI<5 episode·h^{-1} with adenotonsillectomy alone [63]. Obesity is a significant predictor for persistence of OSA postoperatively, indicating that supplemental treatment options such as weight loss and nCPAP have to be used [63, 64]. In addition, children with cerebral palsy and OSA can improve with adenotonsillectomy although their main abnormality (abnormal neuromotor tone) may ultimately require use of nCPAP [65].

Successful treatment of OSA is accompanied by improvement in quality of life [66, 67], significant increase in weight and height [47], resolution or decrease in the frequency of enuresis [68–70], reduction in diastolic blood pressure [39, 71] and reversal of cor pulmonale [72]. Furthermore, children have less daytime sleepiness, hyperactivity and aggression [31, 73–75] and less health care utilisation [76], post-treatment.

One randomised controlled trial supports the administration of intranasal corticosteroids for 6 weeks to children with OSA and adenoidal hypertrophy, which results in improvement in polysomnography indices [77]. Similarly, in a non-randomised, open-label study of children with mild OSA who received montelukast for 16 weeks, both AHI and adenoidal tissue size decreased [78]. Of note, no randomised, controlled trials on the efficacy of adenotonsillectomy have been published [79]. In a retrospective, multicentre study, polysomnography indices have been used as primary outcome measures for evaluating the efficacy of adenotonsillectomy [63]. Postoperatively, significant improvements in AHI, respiratory arousal index and oxygen saturation of haemoglobin nadir have been identified.

In a recent nonrandomised investigation, weight loss by ~35% in children with OSA and a mean body mass index z-score of 2.4–2.8 was related to a significant decrease in the severity of intermittent upper airway obstruction during sleep [80]. However, in children with OSA and obesity who do not respond to weight loss, in those with residual disease after adenotonsillectomy or in sleep apnoeic children with neuromuscular disorders or craniofacial abnormalities, nCPAP may be effective in ameliorating apnoeas and hypopneas [81, 82].

A single randomised, controlled investigation has revealed that application of orthodontic appliances in children with dental malocclusion and OSA is associated with reduced AHI and diminished daytime and night-time symptoms [61, 83]. Mandibular distraction osteogenesis can be effective in the relief of upper airway obstruction affecting children with mandibular hypoplasia [84]. Midfacial distraction osteogenesis has been used in cases of midfacial hypoplasia [85].

Conclusion

OSA is a frequent condition in childhood with recognised morbidity from the cardiovascular and central nervous systems. A combination of different treatment modalities is necessary for the successful alleviation of upper airway dysfunction during sleep.

Educational Questions

1. Adenotonsillectomy in children with obstructive sleep apnoea
a) Consistently results in cure of OSA
b) May not have an initial benefit, but results in improvement in OSA over time
c) Is frequently associated with weight gain
d) Is more effective for obese children than for normal weight children.

2. The respiratory events of a sleep study in a 15-year old obese adolescent must be scored
a) By pediatric rules
b) By adult rules
c) By either pediatric or adult definitions.
d) There is no consensus whether it should be scored by pediatric or adult rules

3. The first treatment option for a normal-weight child with moderate-to-severe OSA is
a) Nasal CPAP
b) Intranasal steroids
c) Adenotonsillectomy
d) Orthodontic treatment

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Suggested answers

1. c
2. c
3. c

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