REVIEW SERIES

Sleep · 8: Paediatric obstructive sleep apnoea

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In the past 25 years there has been increasing recognition of obstructive sleep apnoea (OSA) as a common condition of childhood. Morbidity includes impairment of growth, cardiovascular complications, learning impairment, and behavioural problems. Diagnosis and treatment of this condition in children differs in many respects from that in adults. We review here the key features of paediatric OSA, highlighting differences from adult OSA, and suggest future directions for research.

In 1889 Hill described snoring and restlessness at night as a cause of ''backwardness and stupidity in children'',[1] but nearly 100 years passed before the first case series of children with obstructive sleep apnoea (OSA) was published.[2] Since that time it has been recognised that OSA is one of the most common respiratory disorders of childhood, affecting an estimated 1–2% of normal children.[3–6] In 1982 Brouillette *et al*[7] published a case series of 22 infants and children with severe complications of OSA. In recent years research in this condition has mushroomed, bringing increasing recognition that OSA may have significant adverse consequences even in milder cases.[4 8–11]

The features of OSA in childhood have been covered in several recent comprehensive reviews.[12–14] Much has been learnt in the quarter century since Guilleminault's original case series,[2] but much remains unknown. We will review paediatric OSA, point out salient differences between OSA in adults and children, and highlight future directions for research in this emerging field.

CLINICAL FEATURES OF OSA IN CHILDHOOD

Children with OSA are as likely to be girls as boys,[8 15] and usually present with snoring, restless sleep and, at times, observed apnoeas during sleep. Traditionally, the prevalence of paediatric OSA is thought to peak in the preschool years due to adenotonsillar hypertrophy.[3 5 8] However, the increasing prevalence of obesity may be leading to the emergence of a new at-risk population in middle childhood and adolescence.[15]

While otherwise normal children with adenotonsillar hypertrophy form the biggest group of children with OSA, other high risk groups have been identified. These include children with craniofacial malformations and anatomical narrowing of the upper airway, children with neuromuscular disease and reduced upper airway tone, obese children, and premature infants. In some of these cases significant OSA may begin in the neonatal period. Studies examining the prevalence of OSA in specific high risk groups have found very high rates of OSA in children with Down's syndrome,[16] achondroplasia,[17] mucopolysaccharoidosis,[18] and spina bifida.[19]

Snoring is less common in children than in adults, with approximately 6–12% of children having habitual snoring, depending on age.[3 4 20] Whether snoring can be regarded as truly benign, without consequences on sleep quality or daytime functioning, has been challenged.[21] However, by current measurements and definitions,[22] only a subgroup of snoring children (approximately 1% of the total population[3–6]) have OSA requiring treatment. Several symptoms are particularly suggestive of OSA in snoring children: frequent daytime mouth breathing, snoring most nights, observed cyanosis or apnoea during sleep, difficulty breathing during sleep, and parental concern about the child's breathing (watches child because afraid of breathing or shakes child to make him/her breathe during sleep).[23] Unfortunately, clinical history is not sufficiently reliable to distinguish OSA from primary snoring,[23] and thus evaluation of breathing during sleep is required to make the diagnosis of OSA.[24]

The original descriptions of children with OSA found high rates of failure to thrive.[2 7] In recent times this finding is unusual.[8 15 25] However, several studies have demonstrated accelerated growth after adenotonsillectomy,[11 25 26] indicating that impairment of growth may occur in many cases even though a child's growth parameters remain in the normal range. Several possible factors have been postulated to underlie this growth impairment, including reduced caloric intake due to adentotonsillar enlargement, increased caloric expenditure due to respiratory effort during sleep, reduced growth hormone release due to sleep disturbance, and peripheral resistance to growth factors. Studies to date, however, have failed to demonstrate changes in caloric intake before and after adenotonsillectomy, and only minimal differences in energy expenditure.[26] Children with OSA were found in one study to have reduced levels of insulin like growth factor binding protein 3 which reflects diurnal growth hormone secretion.[25] It seems paradoxical, however, that growth hormone secretion should be affected when children with OSA have normal amounts of slow wave sleep (the sleep stage in which this hormone is secreted[27 28]) and episodes of airway obstruction are usually predominantly in rapid eye movement sleep.[29] Thus, the underlying cause of

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growth impairment in children with OSA requires further elucidation.

Excessive daytime sleepiness is a cardinal feature of the obstructive sleep apnoea syndrome in adults,[30 31] but only a minority of parents of children with OSA describe their child as sleepy.[3 23 32] There is some evidence that affected children are more sleepy by objective measures,[32 33] but they are more likely to manifest problems with learning, attention, and behaviour.[4 10 34] One large study in the USA demonstrated OSA in 18% of children performing in the lowest 10% of the first grade (aged approximately 6 years); significant improvement in performance was seen after adenotonsillectomy.[10] Others have demonstrated specific cognitive deficits in learning and mental processing in children with OSA.[32 35 36] Up to 25% of parents of children with OSA describe hyperactivity and behaviour problems;[4 37] conversely, high rates of sleep disordered breathing have been demonstrated in children with behavioural problems.[38–40] Improvements in daytime behaviour have been found in children who have had adenotonsillectomy for OSA.[9 37 41] The severity of OSA at which such problems with learning and behaviour become more common has not been established.

Key outstanding questions

The neurocognitive morbidity of OSA in 2–5 year old children has been ignored because of the difficulty in testing children in this age group. Further investigation of the effects of OSA on preschool children will help determine treatment priority for this group. At what level of severity of OSA do adverse consequences become manifest, and therefore which children are most likely to benefit from treatment? Some normative data are available,[42 43] and it is clear that some children with severe OSA are markedly improved by treatment, but the severity level at which the benefits of treatment (essentially adenotonsillectomy) outweigh the risks is not clear. A randomised controlled trial of adenotonsillectomy for mild OSA will be required to establish a treatment threshold.

RELATIONSHIP WITH ADULT OSA

Few studies have assessed the long term outcome of children with OSA. While an increased prevalence has been described in family members of adults with OSA,[44 45] this has not been specifically studied in children and most children with OSA do not have a positive family history. Increased collapsibility of the upper airway in children with OSA[46] may contribute to an increased risk of recurrence of OSA in adulthood, but only one small longitudinal study has addressed this, finding recurrence of OSA in three of 28 adolescents after successful treatment of OSA in the prepubertal period.[47] In all likelihood the cause of OSA in childhood is complex, with contributions from the bony skeleton and soft tissues of the upper airway, the size of lymphoid structures in relation to the airway, neural factors in the upper airway including airway collapsibility and sensation, arousal threshold, and obesity. Each of these factors may be at least partly genetically determined. However, a focus on modifiable risk factors—analogous to the recent emphasis in sudden infant death syndrome research[48]—is more likely to lead to clinically useful information—for example, the contribution of allergy and infection to enlargement of the tonsils and adenoids, and prevention and treatment of childhood obesity. The extent to which both genetic and modifiable factors contribute to OSA in a given individual is likely to affect the risk of recurrence of OSA in adulthood.

Both clinical studies and large population studies of OSA in adults suggest that OSA severity tends to increase progressively over time if untreated.[49–52] To date, studies in childhood would suggest that benign snoring does not progress to OSA with increasing age,[53 54] although small numbers, short follow up time, heterogeneous populations (especially in terms of age), and incomplete follow up make firm conclusions difficult. However, untreated OSA in childhood may lead to right ventricular hypertrophy, cor pulmonale, and systemic hypertension.[7 55 56] One study found a reduced right ventricular ejection fraction (<35%) in 37% of children aged under 7 years with clinically diagnosed OSA, 80% of whom had no clinical evidence of pulmonary hypertension.[57] Other studies have found increased left and right ventricular mass[58] and elevated diastolic blood pressure[56] in children with OSA. OSA in adults has medium to long term adverse cardiovascular effects such as hypertension, myocardial infarction, and stroke,[49 59] and it is therefore possible that this ''adult OSA'' may begin in childhood or adolescence. Early recognition of OSA in childhood and provision of appropriate treatment may not only treat or prevent medium term complications such as learning difficulties, but may potentially prevent serious long term cardiovascular complications.

Key outstanding questions

Are children with OSA treated by adenotonsillectomy at higher risk than the general population of developing OSA in adulthood? What is the natural history of untreated snoring or mild OSA in childhood? What surveillance mechanisms are appropriate for this population? Will the increasing prevalence of obesity in childhood lead to earlier onset of ''adult OSA''?

PATHOPHYSIOLOGY

Upper airway resistance increases during sleep,[60 61] with airway narrowing due to a reduction in tonic activity of the pharyngeal dilator muscles.[62–64] Negative pressure is generated in the upper airway during inspiration, but under normal conditions this negative pressure is balanced by the activity of the pharyngeal dilator muscles and does not lead to collapse of the upper airway.[65] However, in situations of increased upstream resistance such as that caused by enlargement of the upper airway lymphoid tissues in many children with OSA, collapse may occur.[46] The adenoids, situated on the roof of the nasopharynx, enlarge from infancy through adolescence in normal children and then decrease in size during adult life.[66–68] They may grow downward into the nasopharyngeal lumen,[69] forward through the posterior choanae,[70] or inferiorly, overlapping with the level of oropharyngeal obstruction by the tonsils.[71] The tonsils also begin to enlarge in early childhood. Upper airway soft tissues, including the tonsils and adenoids, grow more rapidly than the bony structure of the nasopharynx from 3 to 5 years of age, with a consequent decrease in size of the airway during this period.[72] Studies using magnetic resonance imaging of the upper airway have shown that children with OSA have larger adenoids and tonsils than control subjects of the same age.[69 71 73] However, there is not a linear relationship between clinical assessment of adenoid and tonsillar size and severity of OSA.[69 73 74] Many children have adenotonsillar enlargement, but relatively few have OSA. This may be partly explained by increased upper airway collapsibility in children with OSA, in whom the critical pressure at which the upper airway collapses (Pcrit) is positive (mean (SD) 1 (3) cm H_2O) compared with a markedly negative Pcrit (−20 (9) cm H_2O) in children with primary snoring.[46] The pathophysiology of OSA in childhood is therefore likely to be a complex interaction between physiological factors such as ventilatory drive and neuromuscular control, and anatomical factors such as airway structure and adenotonsillar enlargement.

Key outstanding questions

What makes the adenoidal and tonsillar tissue of some children grow to such an extent that they impair breathing?

DEFINITIONS

Standardised definitions of apnoea and hypopnoea have been proposed for adults,[30 31] although significant variation in both definitions and methods of measurement continues to exist between sleep laboratories. Application of these adult definitions to studies in children leads to under-recognition of OSA.[75] Children with upper airway obstruction often have more hypopnoeas (reduction in airflow) than full apnoeas, and thus a definition based on the number of apnoeas per hour of sleep may miss significant OSA.[75] In some cases partial upper airway obstruction may continue for several minutes (obstructive hypoventilation), and thus the definition of OSA in children should include criteria for hypercapnia.[42 76] In addition, due to the higher respiratory rate in children, it has been proposed that apnoeas of any length be counted rather than using a 10 second limit as in adult studies.[31]

Normal ranges for breathing parameters during sleep have yet to be defined in children. Less than one apnoea per hour of sleep is generally considered statistically normal,[42] and hypopnoeas in normal children are probably also rare.[43] The level of the apnoea/hypopnoea index associated with adverse outcomes has also not been determined in children. In adults, even mild OSA with sleep disturbance is associated with impairments in daytime functioning[77] and an increased risk of the development of hypertension.[59] It is possible that abnormal breathing during sleep has even more impact in young children who are undergoing rapid neural development.

Key outstanding questions

A consensus definition of hypopnoea has not been established in children, making comparison of research results from different centres problematic. A detailed definition of hypopnoea and the obstructive sleep apnoea syndrome in children is needed, at least for research purposes. This should include the technology used to define a reduction in airflow (see below), and whether desaturation, hypercapnia and/or arousal is required.

EFFECTS ON SLEEP QUALITY

Children with OSA have more arousals from sleep than normal children,[78] but the proportion of time spent in the different stages of sleep is usually preserved[27 28 79 80] compared with adults in whom the sleep structure is frequently severely abnormal. In children, airway obstruction is often limited to (or predominant in) rapid eye movement (REM) sleep, owing to the loss of upper airway and intercostal muscle tone that is most marked in this sleep state.[29] Despite this, REM sleep continues to be present in normal amounts in children with OSA, although microdisruption of REM sleep may be present.[41 81]

In adults, obstructive apnoeas are terminated by an arousal, with upper airway muscle activation and restoration of upper airway patency.[82] Arousals in the context of sleep disordered breathing are thus beneficial in that ventilation is restored, but the adverse consequences of frequent arousals include sleep disturbance and deficits in daytime functioning.[83–85] The role of arousals in the termination of respiratory events in children is not entirely clear, and probably depends on age as well as individual arousal threshold.[81] Mograss *et al*[41] found that movement arousals terminated nearly all obstructive apnoeas and hypopnoeas in children, whereas McNamara *et al*[81] described EEG arousals after only 39.3% of respiratory events in quiet sleep and 37.8% of events in active sleep in children. These different conclusions probably stem from differences in the definition of arousals, with one group including subcortical arousals (that is, without EEG changes) and the other confined to EEG arousal.

Key outstanding questions

More research is needed to clarify the role of cortical and subcortical arousal in the recovery from respiratory events in children. As yet there is no consensus on the importance of sleep disruption. For instance, can a child be considered to have OSA if the polysomnogram is abnormal and sleep is disrupted but there are no demonstrable abnormalities of growth, cardiovascular function, or neurobehavioural functioning? The association between arousal frequency and the daytime consequences of OSA in children requires further elucidation.

POLYSOMNOGRAPHY IN CHILDREN

Polysomnography in children involves the simultaneous recording of sleep state (EEG, EOG and chin EMG), respiration (movements and airflow), ECG, muscle activity (anterior tibial region), gas exchange (Sa_{O_2} and P_{CO_2}), and snoring.[24] This should be carried out ''in a manner that is minimally invasive or disruptive to the child's usual sleep patterns'',[24] and therefore involves a parent staying with the child throughout the night and staff experienced and skilled in the care of children. Due to the tendency of children to move a lot during sleep and the inability of young children to understand the nature and purpose of the test, close observation is required by trained technicians to ensure that good quality recordings are achieved. This process is more labour intensive in children than in adults, in many cases requiring one-on-one supervision by a sleep laboratory technologist.

In most technical respects, polysomnography in children is similar to that in adults. Age is an important factor in the EEG determination of sleep state, with the proportion of time spent in the various sleep states changing with age, and typical features of some sleep states not present until late in the first year of life. Polysomnography in children should include assessment of adequacy of ventilation using P_{CO_2} measurements because of the frequent finding of partial airway obstruction and obstructive hypoventilation without apnoeas.[75] Specialist paediatric end-tidal P_{CO_2} equipment is required because of the small tidal volumes and low expiratory flow rates of infants and young children, and use of simultaneous end-tidal and transcutaneous P_{CO_2} recordings during polysomnography increases the proportion of a study with P_{CO_2} measurements available.[76] For the definition of apnoeas and hypopnoeas during sleep, calibrated respiratory inductance plethysmography and nasal pressure recordings have the best relationship with quantitative tidal volume and flow, respectively, in adults.[30] Owing to their ease of use, thermistors (heat sensitive electrodes that provide a qualitative representation of air flow) are widely used in paediatric sleep laboratories, but they are less representative of tidal volume and are also troublesome in small infants where changes in temperature with each breath may be very small relative to environmental conditions. One study has reported the use of nasal pressure recordings in infants and children and found that nasal pressure recordings were more sensitive for detecting episodes of airway obstruction than thermistors, especially for hypopnoeas.[86] However, signal loss was more common due to the catheter becoming dislodged from the nose. Quantitative respiratory inductance plethysmography avoids the use of facial transducers and may therefore be particularly useful and reliable in this age group.[87 88]

An upper airway resistance syndrome, wherein partial airway obstruction leads to arousal from sleep and significant daytime symptoms in the absence of desaturation, has been described in children.[89] Currently, as in adults,[30] definition of this syndrome requires the inclusion of an oesophageal pressure catheter in a sleep study, a technique that is not

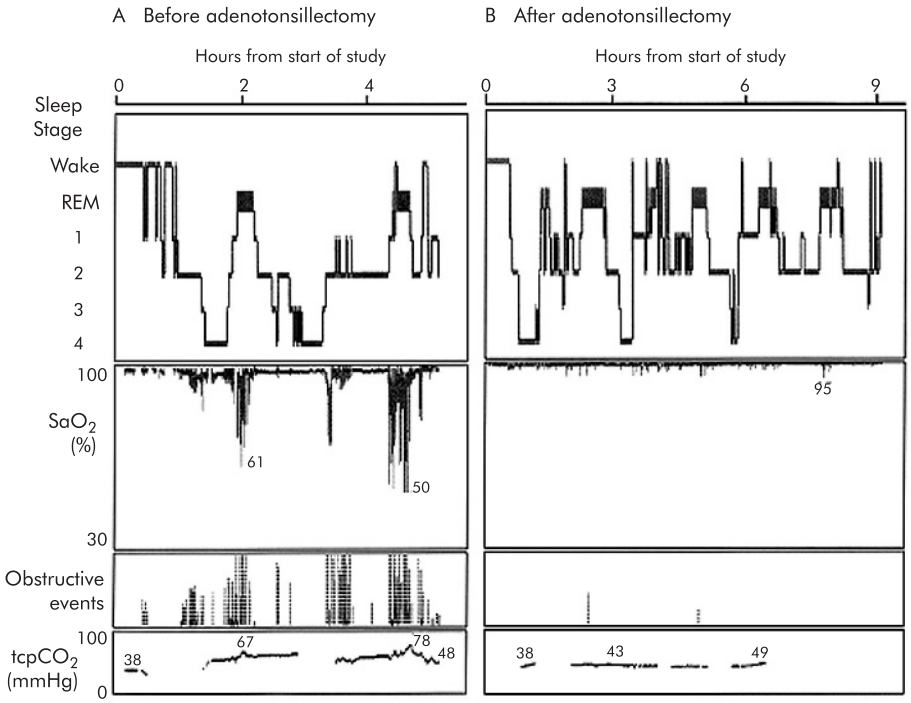

Figure 1 (A) Summary of polysomnographic recording in a three-year-old boy with loud snoring, restless sleep, poor growth, and tonsillar enlargement. The hours from the start of the study are shown at the top; the study was terminated after 5 hours due to severe desaturation (second panel from top). The obstructive events (third panel) predominantly occurred in rapid eye movement sleep (sleep structure summarised in top panel). Hypercapnia developed over the course of the study with acute rises during periods of REM sleep associated obstructed breathing. The apnoea/hypopnoea index was 36 events/hour with a Sa_{O_2} nadir of 42%, a respiratory arousal index of 22/hour, and 89% of the study spent with a P_{CO_2} above 6.6 kPa. (B) Polysomnography results in the same child 1 month after adenotonsillectomy showing complete resolution of OSA. The apnoea/hypopnoea index was 0 events/hour with a Sa_{O_2} nadir of 94% and 0% of the study spent with a P_{CO_2} above 6.6 kPa.

widely practised in paediatric sleep laboratories. New techniques such as pulse transit time may provide a less invasive way of detecting the swings in blood pressure that occur with swings in intrathoracic pressure under conditions of upper airway obstruction, and the abrupt rise in blood pressure that occurs with arousals terminating respiratory events.[90–92]

As polysomnography is not widely available to children, and the measurement techniques themselves may disturb sleep, simpler alternatives have been sought that can be performed in the child's home. Abbreviated studies such as overnight oximetry[93] and daytime nap polysomnography[94] are highly predictive of OSA if positive but have a low sensitivity, so that many children will require polysomnography.[24 95] However, children with a positive overnight oximetry and more severe OSA[93] may avoid waiting for polysomnography and thus receive expedited adenotonsillectomy. Cardiorespiratory studies using calibrated respiratory inductance plethysmography, oxygen saturation, heart rate, ECG and videotaping give a reliable assessment of children with possible OSA, with less sleep disturbance than in-laboratory polysomnography[96] but, to date, such a system is not widely available.

Key outstanding questions

Can subtle upper airway obstruction be quantified reliably without use of an oesophageal catheter? The continuing search for new and improved methods of quantifying airflow and ventilation in small children is crucial to refining polysomnographic techniques. New forms of abbreviated testing suitable for use in the home need to be validated against polysomnography in the paediatric population.

TREATMENT

In most cases of OSA in childhood, adenotonsillectomy is a highly effective treatment leading to resolution of abnormal respiration during sleep and improvements in growth, restless sleep, and daytime behaviour (fig 1).[9 79 80 97] Removal of either the tonsils or the adenoids alone carries a significant risk of persistence or recurrence of OSA,[98] but may be appropriate in some cases. OSA is an increasing indication for adenotonsillectomy, and appropriate perioperative management of such children includes overnight stay in hospital after the procedure due to the risk of postoperative airway compromise. The risk of respiratory morbidity following adenotonsillectomy in a general paediatric population is 1%.[99] A diagnosis of OSA increases the risk to around 20%.[100–102] Within the OSA group, several risk factors are associated with a high risk of postoperative airway compromise: age under 2–3 years, co-morbidity such as Down's syndrome or neuromuscular disease, and severe OSA (variously defined as a Sa_{O_2} nadir of <70 or 80%, or an apnoea/hypopnoea index above 10 or 40 events per hour preoperatively).[100–102] A preoperative overnight Sa_{O_2} nadir below 80% increased the probability of postoperative airway complications from 20% to 50% in our hospital,[102] and overnight oximetry may serve as a practical tool for determining children at highest risk of this complication when polysomnography is not available.

In a small number of children OSA is not resolved following adenotonsillectomy or adenotonsillar hypertrophy is not the major factor leading to airway obstruction. This situation is most commonly encountered in infants (for example, with craniofacial malformations) or older children with co-morbid conditions or obesity. In such children,

continuous positive airway pressure (CPAP) may be indicated. CPAP by nasal or face mask has been successfully used in children as young as newborn infants.[103 104] Advances in patient interface (masks, head gear, etc) and ventilator technology, together with skilled and experienced staff and dedicated parents, can make this a viable alternative for long term home treatment. In cases where non-invasive methods are not tolerated or not sufficient, tracheostomy may be indicated.

Other treatments may be indicated in certain cases. Intranasal corticosteroids have been shown to improve nasal obstruction in atopic individuals[105] and to reduce adenoidal size and obstructive symptoms.[70 106 107] Our recent randomised controlled trial showed improvement in the severity of OSA in children treated with intranasal steroids,[108] but further studies are needed to determine which children are most likely to benefit from this treatment. Infants with craniofacial malformation who have severe OSA may be candidates for craniofacial surgery such as mandibular lengthening by distraction osteogenesis.[109 110]

Key outstanding questions

As polysomnography is currently not widely available to children around the world, how can surgical waiting lists be prioritised and how can perioperative risk be adequately assessed? What is the risk of significant postoperative respiratory compromise in children with mild OSA? Could these children safely undergo adenotonsillectomy as day cases? Which children can safely undergo adenotonsillectomy in a general hospital and which require specialist paediatric perioperative management?

CONCLUSIONS

Obstructive sleep apnoea is a common condition of childhood. It is possible that in some cases it heralds an underlying abnormality of the upper airway that becomes manifest as OSA in later life. Perhaps more importantly, however, OSA in childhood may cause disruptions of developmental processes with lasting effects. Treatment is simple and effective in most cases, and early recognition and treatment of the disorder is likely to reduce the high economic costs of untreated OSA in children[111] and improve health outcomes and quality of life.

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