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Review

Obstructive sleep apnoea in children with craniofacial syndromes

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EDUCATIONAL AIMS

- To understand how obstructive sleep apnoea syndrome (OSAS) affects children with different craniofacial conditions
- To become familiar with treatment options available to children with craniofacial conditions who have OSAS
- To identify limitations in available data and the areas that require additional research

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SUMMARY

Obstructive sleep apnoea syndrome (OSAS) is common in children. Craniofacial anomalies such as cleft palate are among the most common congenital conditions. Children with a variety of craniofacial conditions, including cleft palate, micrognathia, craniosynostosis, and midface hypoplasia are at increased risk for OSAS. Available evidence, which is largely limited to surgical case series and retrospective studies, suggests that OSAS can be successfully managed in these children through both surgical and non-surgical techniques. Prospective studies using larger cohorts of patients and including polysomnograms are needed to better understand the risk factors for this patient population and the efficacy of treatment options for OSAS and their underlying conditions.

INTRODUCTION

Obstructive sleep apnoea syndrome (OSAS) is defined in children as a 'disorder of breathing during sleep characterized by prolonged partial upper airway obstruction and/or intermittent complete obstruction. . .that disrupts normal ventilation during sleep and normal sleep patterns.' [1] OSAS is common in children, with the prevalence ranging between 1.2 and 5.8% of the general paediatric population, depending on the criteria used to define OSAS. Most otherwise-healthy children with OSAS have adeno-tonsillar hypertrophy and/or obesity as risk factors. However, specific paediatric populations with underlying diseases are also at risk for OSAS. These include children with a history of prematurity, asthma, Down syndrome, sickle cell disease, achondroplasia, neuromuscular disease and craniofacial anomalies, among others. Children with craniofacial conditions are generally at increased risk for development of OSAS [2] but this population is complex because of its heterogeneity. Thus, individual conditions must be considered in the diagnosis and treatment. OSAS is important to identify in children, as untreated OSAS can result in significant sequelae, including cognitive and behavioral deficits, cardiac ventricular remodeling and hypertension, and inflammation [2].

TYPES OF CRANIOFACIAL CONDITIONS

Craniofacial conditions are highly variable, and may occur in isolation or as part of a syndrome. The Whitaker classification separates craniofacial anomalies into four groups, including clefts, craniosynostoses, hypoplasia, and neoplasia [3], but there is no comprehensive system to classify all craniofacial conditions.

Craniofacial clefts may include a cleft lip, cleft palate or both cleft lip and palate (CLP). Over 200 syndromes include cleft lip and/or palate as a feature, but approximately 85% of clefts occur in isolation [4]. Orofacial clefts are one of the most common congenital conditions, with approximately one in 700 live births being affected. Cleft palate may be unilateral or bilateral, affecting either the soft palate alone or both the hard and soft palate. There are many genetic mutations that cause cleft palate and although some clefts occur as a result of familial inheritance, most are the result of a *de novo* mutation. Syndromes that commonly include cleft palate include

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Pierre Robin sequence, Stickler syndrome, Treacher Collins syndrome, Goldenhar syndrome, and Nager syndrome.

Craniosynostoses are congenital conditions that include premature fusion of one or more of the cranial sutures, resulting in abnormal growth of the skull in the direction parallel to the fused suture. Craniosynostoses affect approximately one in 2500 live births and can be either syndromic or nonsyndromic. Common syndromes that include craniosynostosis include Apert, Cruzon, Pfeiffer, Nuenke, and Saerthe-Chozen syndromes.

Complications of craniofacial conditions

The burden of disease in children with craniofacial conditions is highly variable, but can be substantial. These children are often followed by multidisciplinary teams that include speech therapists, otolaryngologists, audiologists, plastic surgeons, and orthodontists, among others. Children with CLP and Pierre Robin sequence may have cognitive impairment across a range of domains, including both verbal and non-verbal domains. The etiology of cognitive delay is likely multifactorial, and may include hearing dysfunction and frequent hospitalizations. Children with craniosynostosis are also at risk for intellectual disability, with one recent study finding that school age children with syndromic craniosynostosis have an increased risk for having cognitive, motor, and language delays [5]. Cognitive impairment is also seen in children with significant OSAS, but the link between reduced performance and OSAS in the craniofacial population has not been established. In children with syndromic craniosynostosis, OSAS has been shown to be related to poorer quality of life [6].

One of the most common impairments in children with craniofacial conditions is feeding. The causes can be variable depending on the patient's underlying condition, but usually result in an uncoordinated suck-swallow-breathe pattern or an inability to maintain a good seal during sucking. This usually results in longer feeding times, and can cause a host of other medical problems, including dehydration and laryngeal penetration or aspiration. In some children with Pierre Robin sequence, early airway surgery to relieve upper airway obstruction is associated with less need for a feeding tube [7]. Infants with craniofacial conditions are at risk for poor growth, especially early in life [8].

Otitis media with effusion is nearly universal in infants born with cleft palate, and without intervention, can result in a conductive hearing loss that can affect language development. In many of the craniosynostoses, mutations in fibroblast growth factor receptor genes affect inner ear morphogenesis, causing hearing loss [9].

OSAS IN CRANIOFACIAL CONDITIONS

Children with a variety of craniofacial conditions have been shown to be at increased risk for upper airway obstruction, but the lack of prospective studies makes the prevalence of OSAS and the causes of OSAS in this population difficult to determine.

Screening for OSAS in children with craniofacial conditions can be challenging for a number of reasons. Screening tools for OSAS are unreliable in otherwise healthy children and have not been validated in other populations that may have cognitive and hearing deficits that would alter the results of screening tools [10]. One study of children with Treacher Collins syndrome found that the Brouillette questionnaire correlated poorly with polysomnographic findings [11]. Another study found that the Pediatric Sleep Questionnaire was a poor predictor of OSAS in a general craniofacial population [12].

OSAS is the result of both structural factors that reduce the size of the airway as well as neuromotor deficits that impair the ability of the patient to maintain airway patency during sleep. Imaging has been shown to be a powerful tool to assess the structural differences in children with a variety of craniofacial conditions. In children with micrognathia, those who go on to experience clinical episodes of apnoea have been shown to have smaller airway measures on cephalometry than those who remain asymptomatic. [13] Early reports of mandibular distraction osteogenesis (MDO) used cephalometric imaging to demonstrate improvement in glossoptosis and more recent studies have used computed tomography to demonstrate increased oropharyngeal airway volume following distraction. [14]

Table 1
mechanisms of OSAS in children with select craniofacial conditions

Condition	Potential causes of OSAS
Craniofacial cleft	Short mandible, retrognathia ± nasal deformity
Syndromic micrognathia (i.e. Pierre Robin Sequence, Stickler syndrome, etc)	Micrognathia, glossoptosis, ± midface hypoplasia
Craniosynostosis	Midface hypoplasia
Down syndrome	Relative macroglossia, midface hypoplasia, reduced muscle tone
Achondroplasia	Midface hypoplasia, retrognathia

In addition to the structural features that predispose children with craniofacial conditions to OSAS, there is evidence that neuromotor differences also contribute. Craniofacial conditions such as cleft palate and micrognathia cause oropharyngeal muscular dysfunction, which affects swallowing, speech, and breathing. In studies of upper airway muscle function, EMG response during swallowing is reduced in children with cleft palate compared to controls. [15] In other children, micrognathia changes the normal length-tension relationship of upper airway muscles, possibly preventing them from working efficiently. In children with syndromic micrognathia, the upper airway may have increased collapsibility secondary to upper airway muscle fatigue, as a result of the upper airway muscles constantly working against an increased mechanical load with each breath. This is consistent with data from adults, showing that upper airway muscles work near their maximal range during wakefulness in patients with OSAS (Table 1). [16]

Cleft lip/ palate

In children with cleft palate, OSAS is thought to develop from morphologic changes that result in a small midface and retruded mandible. Children with CLP often also have nasal deformities as well, but how these affect upper airway obstruction is not clear (Figure 1). Retrospective studies have shown high rates of OSAS in a referred population with CLP, but these studies are limited by selection bias [17]. A recent prospective study of 50 infants found a mean apnoea hypopnoea index (AHI) of 7.6/hour in those with non-syndromic CLP [18]. Prospective studies of larger cohorts are needed to determine the true prevalence of OSAS in this population and to better understand how risk factors differ from the general pediatric population. One of the difficulties in understanding the prevalence of and risk factors for OSAS in the CLP population is the heterogeneity of the phenotype, with a range from unilateral cleft lip to a cleft that extends through both the soft and hard palate.

In developed countries, children with cleft palate are treated with primary palatoplasty before or around the child's first birthday. The effect of primary palatoplasty on upper airway obstruction has not been well studied, but there is some evidence that children who have OSAS pre-operatively are at risk for developing perioperative airway complications [19].

As many as 13% of children with cleft palate develop velopharyngeal insufficiency as a result of primary palatoplasty,