Congenital Disorders Affecting Sleep

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KEYWORDS

• Obstructive sleep apnea • Micrognathia • Craniosynostosis • Pierre Robin sequence
• Achondroplasia • Trisomy 21 • CHARGE syndrome • Mucopolysaccharidoses

KEY POINTS

- Many congenital disorders result in an increased risk for sleep-disordered breathing.
- Genetic syndromes affecting sleep can be classified into 1 of 4 categories: those producing micrognathia, those producing midface hypoplasia, disorders of neuromuscular control, and miscellaneous disorders.
- It is important to have a high index of suspicion for sleep-disordered breathing in these patients; overnight polysomnography is important to diagnose and confirm the severity of the abnormality and track the response to treatment.
- Treatment should be directed at correcting or improving the underlying abnormality.

MICROGNATHIA

Congenital disorders resulting in micrognathia predispose the patient to sleep-disordered breathing, owing to their increased risk of upper airway obstruction (**Table 1**).

Treacher-Collins Syndrome

Treacher-Collins syndrome (TCS) is an autosomal dominant disorder caused by a mutation in the *TCOF1* gene in the region of 5q32-33.2 that codes for a nucleolar phosphoprotein (treacle).[1,2] Mutations in *POLR1D* and *POLR1C* may also contribute to the etiology of this syndrome.[3] Sixty percent of the cases represent new mutations. There is wide variability in expression, but the characteristic findings include mandibular hypoplasia (78% of cases), often with malar hypoplasia (81%), antimongoloid slanting palpebral fissures (89%), malformed auricles (77%), and coloboma of the eyelid. Conductive deafness is present in 40% of patients. Mental deficiency is reported in only 5% of cases.[4]

The small jaw and malar hypoplasia place these patients at risk for obstructive sleep apnea (OSA). The prevalence of OSA in patients with TCS ranges from 46% to 95%. In a cohort study of 35 patients with TCS, 46% (54% of children; 41% of adults) had OSA as determined by ambulatory polysomnography.[5] In a Norwegian study of 19 patients with TCS, OSA was found in 95% of patients who underwent laboratory polysomnography.[6] Symptom scores are not helpful in determining the presence of OSA in patients with TCS.[7] Both the Brouillette score for children and the Epworth Sleepiness Scale (ESS) for adults had low sensitivity, and poor positive and negative predictive values; the investigators suggested that all patients with the syndrome should undergo evaluation by polysomnography.

Mandibular distraction may be very effective in treating OSA in some patients and may prevent the need for tracheostomy.[8,9] Nasal continuous positive airway pressure (CPAP) can also been used as a bridge[10] pending an increase in the posterior airway space with mandibular growth.

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Sleep Med Clin 7 (2012) 689–702
http://dx.doi.org/10.1016/j.jsmc.2012.10.002
1556-407X/12/$ – see front matter Published by Elsevier Inc.

Table 1
Classification of congenital disorders affecting breathing during sleep

Micrognathia	Midface Hypoplasia	Abnormal Respiratory Control	Multifactorial and Miscellaneous Disorders
Pierre Robin sequence	Achondroplasia	Arnold-Chiari malformation	Mucopolysaccharidoses
Treacher-Collins syndrome	Crouzon syndrome	Prader-Willi syndrome	Down syndrome
	Apert syndrome		Sickle cell anemia
	Pfeiffer syndrome		CHARGE syndrome
	Smith-Magenis syndrome		

Pierre Robin Sequence

The Robin sequence, consisting of micrognathia and posterior displacement of the tongue and soft palate, may occur singly or in association with other malformations, such as trisomy 18, Stickler syndrome, velocardiofacial/DiGeorge syndrome, or cerebro-costo-mandibular syndrome.[11] The initiating defect is the presence of micrognathia or retrognathia at the same time that the palatal shelves are fusing, which occurs between 9 and 11 weeks of gestation. This defect prevents the tongue from settling into the oral cavity and away from the base of the skull. As a result, it remains retrodisplaced between the palatal shelves, impairing fusion and resulting in a U-shaped cleft palate. Eighty-three percent of patients have complete or incomplete cleft palate. This posterior displacement of the tongue is not only a risk factor for airway obstruction, but may also impair the action of the genioglossus, an important dilating muscle of the upper airway.[12] Three-fourths of the patients are symptomatic at birth[13]; up to 83% develop significant airway obstruction within 6 weeks, contributing to morbidity as high as 30%.[4]

Significant hypoxemia may be present without clinically apparent symptoms,[6] but oximetry alone does not provide adequate assessment because obstructive episodes without desaturation will not be detected.[14] Therefore, full polysomnography is recommended.[4,14,15] In a retrospective study of 33 infants who were identified as having Robin sequence,[16] 13 underwent polysomnography within the first year of life, 11 of whom (85%) had OSA with a mean Respiratory Disturbance Index (RDI; calculated as the average number of episodes of apnea, hypopnea, and event-related arousals per hour of sleep) of 40.4. Half of the children with an RDI greater than 10 did not snore, suggesting that snoring should not be used as an indicator for the presence or severity of OSA. Fifteen percent of the patients in one series had gastroesophageal reflux contributing to the frequency and severity of respiratory events[14]; esophageal pH monitoring during polysomnography should be considered in any patient with symptoms suggestive of gastroesophageal reflux or who fails to thrive despite apparently appropriate treatment of their airway obstruction. Untreated OSA can exacerbate feeding difficulties, so early identification and airway intervention may also help lower the incidence of failure to thrive in these infants.

Treatment of OSA in patients with Robin sequence depends on the severity of the obstruction and the presence of associated abnormalities. In a study of 74 infants with Robin sequence,[17] 36 were managed with prone positioning alone and 13 with nasopharyngeal intubation. There have been several studies suggesting that CPAP can successfully be used in patients with Robin sequence[18–20] resulting in a significantly decreased work of breathing as measured by breathing patterns, respiratory efforts, and transcutaneous carbon dioxide pressures (**Fig. 1**).

In severe cases or when conservative management fails, surgical intervention may be required to maintain a patent airway. Several cephalometric-based studies have suggested that the hypoplastic mandible fails to "catch up" and overcome the intrinsic disruption.[21–23] Because of its complications and long-term commitment, the goal of management in infants with Pierre Robin sequence is often to avoid tracheostomy; however, it remains the gold standard for bypassing upper airway obstruction. In a retrospective study of 61 infants with Robin sequence,[24] 25 required tracheostomy. At a mean 4-year follow-up, 52% had tracheostomy-specific complications including tracheitis, pneumonia, and wound breakdown and infection. Other complications included developmental delay and organ dysfunction. Several studies have suggested mandibular distraction