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Review

Craniofacial disorders associated with airway obstruction in the neonate

Christopher M. Cielo [a, *], Fernando M. Montalva [b], Jesse A. Taylor [c]

[a] Perelman School of Medicine at the University of Pennsylvania, Division of Pulmonary Medicine, The Children's Hospital of Philadelphia, Philadelphia, PA, USA
[b] Hospital Angeles Pedregal, Magdalena Contreras, Mexico City, Mexico
[c] Perelman School of Medicine at the University of Pennsylvania, Division of Plastic and Reconstructive Surgery, The Children's Hospital of Philadelphia, Philadelphia, PA, USA

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SUMMARY

In infants with craniofacial disorders, upper airway obstruction is one of the primary causes for morbidity and mortality in the neonatal period. Infants with craniofacial disorders, including Pierre Robin sequence, are at high risk for obstructive sleep apnea syndrome. Because of the complexity of their care, these neonates are usually followed by a multidisciplinary team to ensure timely evaluation and optimal treatment. In addition to history and physical examination, clinical evaluation may include genetic testing, imaging, endoscopy, and polysomnography. There are various treatment options, both surgical and non-surgical, that may be used depending on clinical assessment, underlying condition, and severity of disease. Recent advances have led to better assessment and treatment of these patients, but many questions remain. This review outlines the available literature pertaining to the evaluation and management of upper airway obstruction in the neonate with craniofacial conditions, with a particular focus on Pierre Robin sequence.

1. Introduction

The clinical findings in children with craniofacial disorders are highly variable, but the burden of disease in these patients may be substantial. Along with feeding difficulty, upper airway obstruction is the primary cause for hospitalization in the neonatal period for this population. Because of the complexity of their care, neonates and children with craniofacial disorders are usually followed by multidisciplinary teams that include speech therapists, otolaryngologists, audiologists, plastic surgeons, and orthodontists, among others. Recent advances have led to better assessment and treatment of these patients, but many questions remain. This review outlines the available literature pertaining to the evaluation and management of upper airway obstruction in the neonate with craniofacial conditions, with a particular focus on Pierre Robin sequence (PRS).

2. Types of craniofacial disorder associated with neonatal airway obstruction

2.1. Craniofacial clefts

Craniofacial clefts may include a cleft lip, cleft palate, or both cleft lip and palate (CLP). Whereas >85% of clefts occur in isolation, there are >200 syndromes that include cleft lip and/or palate as a feature [1]. Orofacial clefts are one of the most frequently occurring congenital conditions, affecting about one in 700 live births. Cleft palate may be unilateral or bilateral, and may include both the hard and soft palate or the soft palate alone. There are many genetic mutations that cause cleft palate; although some clefts occur as a result of familial inheritance, most are the result of de-novo mutations.

In children with cleft palate, upper airway obstruction is thought to develop from morphologic changes that result in a small midface and retruded mandible as well as a smaller airway. Children with CLP often also have nasal deformities that may further contribute to obstruction. Retrospective studies have shown high rates of obstructive sleep apnea (OSA) in a referred population with CLP, but these studies may be limited by selection bias [2]. A

* Corresponding author. Address: 9NW50, Main Hospital, The Children's Hospital of Philadelphia, 34th and Civic Center Boulevard, Philadelphia, PA 19104, USA. Tel.: +1 267 426 5842; fax: +1 267 426 9234.
E-mail address: cieloc@email.chop.edu (C.M. Cielo).

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prospective study that included 35 infants with isolated CLP found heavy or loud breathing in two-thirds and 69% who had more than three obstructive events per hour on polysomnography [3]. Whereas normative values for infants have not been well established, an apnea–hypopnea index (AHI) of 2/h is considered elevated in children. Prospective studies of larger cohorts are needed to determine the true prevalence of OSA in this population and to better understand how risk factors differ from the general pediatric population. One of the challenges in understanding the prevalence of and risk factors for OSA 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.

2.2. Pierre Robin sequence and conditions with micrognathia

In the neonatal period, the mandible is relatively flat with a short ramus and poorly defined articulation with the base of the skull. During infancy, the mandible is prone to retroposition (retrognathia). This, combined with conditions that include reduced mandibular size in the sagittal direction (micrognathia), may result in a posterior–inferior position of the tongue base, which is anchored to the mandible. These posterior forces lead to displacement of the tongue into the hypopharynx (glossoptosis). The combination of these factors leads to obstruction at the tongue base (Fig. 1). The etiology of the mandibular deformity seen in PRS is unclear but may be the result of the extreme neck flexion in combination with other factors during the sixth to 12th week of gestation [5]. This triad of micrognathia, glossoptosis, and tongue-based airway obstruction was first described in the 1920s by Pierre Robin [6] and may be seen as isolated findings or as part of an underlying syndrome. Pierre Robin sequence is estimated to occur in about one in 8500 live births [7] and half of patients may carry syndromic diagnoses. Frequently observed syndromes associated with PRS include Stickler syndrome, velocardiofacial syndrome, and Treacher Collins syndrome (Fig. 2).

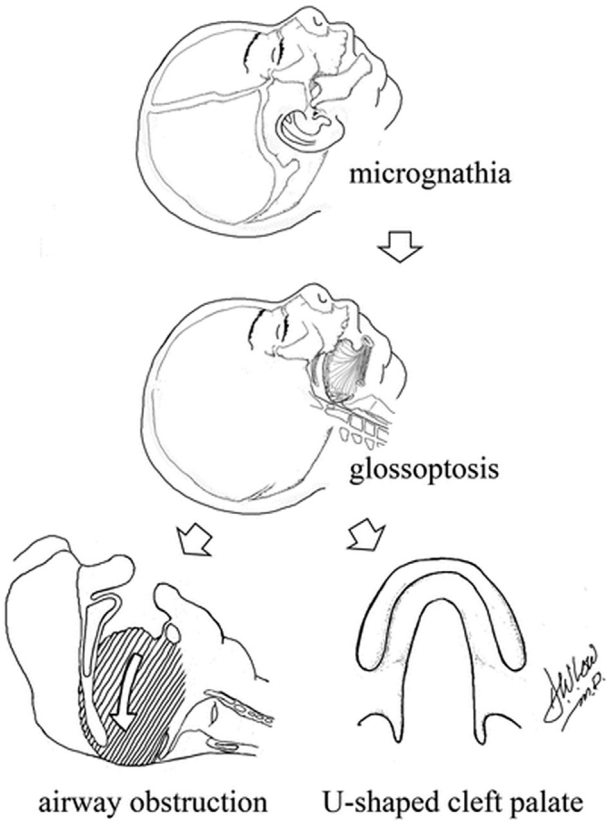

Fig. 1. The "domino effect" of micrognathia and glossoptosis leading to tongue-based airway obstruction in Pierre Robin sequence. (Adapted from Lioy and Sobol [4] with permission.)

Many studies report high rates of OSA in PRS, but most series are limited to patients clinically referred for intervention due to upper airway obstruction [8]. In one recent retrospective study, OSA was identified in 11 of 13 infants with PRS, with a mean AHI of 33.5/h [9]. There was a large amount of variability seen in this series, ranging from 0 to 85.7 obstructions per hour. One prospective study that included nine infants with PRS found that 72% had frequent snoring and that all had significant OSA, with a mean AHI of 45.2/h [3]. The consequences of OSA in these infants are well documented, and include brain injury, failure to thrive, and cor pulmonale [10,11].

Whereas PRS is widely found in isolation, the features may also be seen as part of an identified syndrome (Table 1). Stickler syndrome, Treacher Collins syndrome, and velocardiofacial syndrome are three of the more widely known syndromes that can feature the PRS phenotype with additional characteristic findings discussed below. Hemifacial microsomia also shares some of the same phenotypic features as other conditions with the PRS findings, but the microtia and mandibular hypoplasia are typically unilateral.

2.3. Craniosynostosis

Midface hypoplasia is the main risk factor for OSA in children with syndromic craniosynostosis, but adenotonsillar hypertrophy and choanal atresia may also contribute. Between 40% and 68% of children with syndromic craniosynostosis have OSA but the means of making this diagnosis varies between studies [12,13]. One longitudinal study found that the prevalence of OSA is likely less with advanced age, with children aged <3 years at the highest risk, and that those with midface hypoplasia are more likely to have persistent OSA (Fig. 3) [12].

2.4. Down syndrome

Infants with Down syndrome are susceptible for OSA in part due to midface and mandibular hypoplasia resulting in narrowing of the hypopharynx and relative macroglossia. One recent study of infants with Down syndrome found that 95% of those referred for polysomnograms had OSA, and that 75% had severe OSA. OSA is highly prevalent in children with Down syndrome, with studies showing that as many as 100% of children have sleep-disordered breathing on polysomnograms [14]. In addition to structural abnormalities, low muscle tone also contributes to OSA in this population, with dynamic magnetic resonance imaging demonstrating dynamic upper airway collapse. Higher rates of lingual tonsilar hypertrophy and obesity also contribute to the high prevalence of OSA [15].

2.5. Achondroplasia

Achondroplasia causes craniofacial hypoplasia, including maxillary hypoplasia and depressed nasal bridge. Snoring occurs frequently in children with achondroplasia and studies suggest that the prevalence of OSA is between 10% and 35% [16]. One large series found that nearly half of children referred for polysomnograms had an abnormal finding, but that hypoxemia was the most common abnormality [17]. Compared with children who have OSA due to adenoidal hypertrophy, children with achondroplasia have radiographic evidence of upper airway narrowing and retrognathia. There are neurologic complications associated with achondroplasia, and these patients are also at risk for central sleep apnea.