Management of infants with Pierre Robin sequence

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Abstract

Pierre Robin sequence is a congenital disorder classically characterized by retrognathia, glossoptosis and upper airway obstruction with or without cleft palate. This condition affects neonates and can cause serious respiratory and feeding difficulties requiring prompt intervention.

Currently there are no standardized management algorithms for neonates with Pierre Robin sequence and management of the condition remains a challenge. Assuring adequate breathing and feeding should always be the first point of concern.

Early diagnosis, sequential planning of treatment, adequate monitoring and multidisciplinary approach are essential for infants referred with Pierre Robin sequence.

We discuss here the full scope of the disease and the various management options.

Introduction

Pierre Robin sequence (PRS) is a clinical triad first described in 1923 by Pierre Robin and characterized by underdevelopment of the mandible (micro- and/or retrognathia), backwards placement of the tongue (glossoptosis) and respiratory obstruction. The term sequence is used, as each morphological anomaly is believed to arise from a cascade of events, retrognathia being considered as the triggering event. Although the presence of a cleft palate is not essential to the diagnosis, nearly 90% of infants also present with a cleft palate (1). The severity of cleft palate varies from simple bifid uvula, or occult submucosal cleft, to full palatal U-shaped or V-shaped cleft.

PRS has an estimated incidence of about 1 in 8000 newborns with a sex ratio of 1:1.

The condition can be isolated or associated with other malformations or syndromes, the latter being present in about 25-50% of the cases. The cause of this condition is not clearly identified, though different developmental theories coexist.

Prenatal diagnosis is quite challenging and the condition is most often established after birth, when the neonate presents with breathing or feeding difficulties.

Severity of PRS is often assessed by anatomical evaluation, however a functional classification scheme is more adapted for evaluating respiratory and feeding difficulties (2). The spectrum of the clinical presentation ranges from isolated episodes of upper airway obstruction and feeding difficulties to severe obstructive sleep apnea (OSA) and failure to thrive.

There are considerable differences in both definition and management of PRS between care centers and standardized treatment protocols are lacking (3).

Despite the significant initial respiratory and feeding difficulties, the evolution of Pierre Robin sequence is generally positive in isolated forms having benefited from adequate initial management.

Airway obstruction

The diagnosis of PRS is mainly clinical and somewhat subjective. Although retrognathia is defined as a 10-12 mm retraction of the inferior dental arc behind the superior arch, mandibular size is mainly assessed by clinical sight. Its diagnosis and that of glossoptosis remains subjective. *In fine*, the only objective sign in PRS is the respiratory obstruction.

The airway obstruction in infants with PRS is primarily caused by posterior placement of the tongue into the hypopharynx. Polysomnography (PSG) is a noninvasive and objective investigation tool to assess the severity of upper airway obstruction as there is a poor correlation between anatomical features and functional severity (4). PSG allows measurements of obstructive sleep apnea in terms of apnea index but also length and impact of the obstruction on the heart rate and oxygen saturation. PSG is therefore an effective tool to guide decision making for adequate treatment and for quantitatively measuring the efficacy of a given intervention. Controversy around the role of PSG is undoubtedly influenced by access to PSG and home monitoring devices (5).

In Belgium, where PSG is readily available, all infants with PRS should be rapidly assessed by PSG to evaluate the degree of airway obstruction. In our experience, we recommend PSG around the age of 3-4 weeks.

Once the degree of OSA is evaluated, the first priority of treatment is to relieve respiratory difficulties. Treatment of upper airway obstruction differs considerably between countries. Several methods have been used ranging from adapted positioning to invasive surgery (6).

Most physicians agree that prone positioning is the treatment of choice for mild PRS. There is however debate over the management of moderate and severe cases in which prone positioning alone is not sufficient.

There is still debate over the optimal criteria to determine conservative versus surgical management for patients with PRS. Neonates with severe airway obstruction at birth or soon after birth need more interventional treatment although there is a lack of clear-cut OSA criteria to define neonates requiring more than just conservative treatment, hindering development of standardized management guidelines.

Prone sleep positioning in widely used as first-line treatment in PRS and most are successfully managed by positioning alone (7).

Placing the infant in a prone position allows for forward movement of the mandible and the tongue by gravity. The tongue falling forward instead of backward in the pharynx increases the oropharyngeal space and reduces airway obstruction.

Prone sleeping position resolves airway obstruction in 40 to 70% of infants, although there are very few published studies documenting this effect of positioning on upper airway obstruction by PSG (1,8). However, there is great debate over recommending prone position in particular in infants with breathing difficulties as non supine positioning is clearly associated with increased risk of sudden infant death.

Again, in Belgium, we have easy access to home cardiovascular monitoring devices allowing us to benefit from prone positioning without endangering the infant.

Choosing the best intervention for a neonate with PRS should be individually tailored. In our institutional practice we recommend comparative PSG or at least oximetry in different positions to define the best sleep position for each child. We generally associate prone positioning with raised position (reverse Trendelenburg) and elevate shoulders. At discharge, when prone positioning is indicated, we equip the infant with a home monitoring device. When positioning alone is not sufficient, a nasopharyngeal tube is generally our second option (3). This is a flexible rubber tube inserted through the nose and ending at base of tongue to prevent the tongue from covering the epiglottis and therefore helping to keep the airway open.

In a retrospective cohort study from 1997 to 2014 of 172 infants with PRS treated in our center 91% were successfully managed by positioning alone and 9% required nasopharyngeal tube (9).

Conservative management (defined as prone positioning) is considered to be successful if the patients demonstrate stable airway (confirmed by PSG), absence of significant apnea and bradycardia on monitoring device and sustainable weight gain.

When conservative measures fail, there is need to resort to other nonsurgical or surgical practices. Depending on local expertise, the second line of treatment is often using a nasopharyngeal tube. Main difficulties with the nasopharyngeal tube are excessive secretions and obstruction of the tube itself.

A valid alternative is the use of noninvasive ventilation (most commonly continuous positive airway pressure). Nevertheless, this can be challenging in infants with PRS.

Although nonsurgical management is sufficient for many infants with PRS, those who fail will require surgical management.

Surgical options to relieve upper airway obstruction include the following techniques.

Glossopexy, also known as tongue-lip adhesion; in this procedure, the tongue is anchored to the lower lip and mandible, securing the tongue in an anterior lingual position and preventing occlusion of the upper airway (10). This technique has been somewhat abandoned because it prevents the tongue from moving correctly and makes feeding quite a challenge. The success rate is low and the risk of dehiscence not negligible.

Subperiosteal release of the floor of the mouth musculature is another surgical technique to partially relieve the excessive tension creating the glossoptosis theoretically allowing the tongue base to fall down to the floor of the mouth.

Mandibular distraction osteogenesis has been adopted by many centers as the primary surgical intervention for obstruction in PRS patients, though not in very young infants. Lengthening of the mandible addresses both retrognathia and glossoptosis by creating more space for the tongue and bringing the tongue forward through its attachments to the lingual surface of the mandible. The results are evidently not immediate, as the mandible is lengthened by progressive distraction. Complications include scarring, infection, facial nerve damage, dental and orthodontic complications.

Finally, tracheostomy, which was historically the only option for airway stabilization, is a definite and rapid option when upper airway obstruction is severe and requires immediate treatment. This technique can be associated with significant morbidity including delays in language development.

Studies comparing different treatment options are difficult to interpret as the discrepancies in expertise in performing each intervention between centers can impact treatment outcome.

It is important to keep in mind that most of these treatments serve as a temporizing measure while awaiting natural mandibular growth. Although there is controversy on this subject, findings support the hypothesis of (partial) mandibular catch-up growth in the PRS infant (11). Furthermore, infants exhibit improvement in OSA severity on sequentially performed PSG tests with advancing age (12).

The natural history of OSA in Pierre Robin patients treated conservatively shows improvement over the first 6-8 months of life with resolution by the age of 15 months. Factors potentially explaining this progress include craniofacial and airway growth and maturation of respiratory control (12).

Feeding difficulties

Feeding difficulties are very common and should be addressed rapidly to avoid major weight loss during the first days of life and to insure proper growth during the first months. Adequate feeding is essential to growth and to general well-being of the infant and the parent-infant relationship. Feeding and growth issues are generally consequential to multiple factors. They can be due to poor-quality sucking, dysfunctional swallowing, tendency to aspiration or acid gastro-esophageal reflux. They can also be secondary to respiratory problems causing elevated energy requirements or to associated anomalies or underlying syndrome (13).

Breastfeeding *per se* is generally not feasible due to the fact that the cleft palate makes it particularly hard to create a vacuum in the mouth, which is necessary to induce suction. Breastfeeding can be proposed for short periods, as appetizer or desert, to stimulate lactation and maternal contact, while avoiding fatigue. Maternal milk remains highly recommended and should be given with adapted bottle and positioning. When artificial milk is necessary, hypoallergenic milk is recommended as children with cleft palate present a higher rate of allergies, particularly to milk products, because these allergens come in direct contact with nasal mucosa.

Correct positioning during feeding is crucial. The best position for bottle feeding is an upright sitting position to limit milk flowing into the nasal cavity and aspiration. One hand is used to hold the infant's head (neck elongation) and the other to handle the bottle in order to apply pressure if needed to help suction and a finger under the jaw applying an upright movement to help advance the mandible (chin traction).

Use of a specialized cleft palate bottle such as Haberman nipple can help but is generally not necessary. In our center, we use classical disposable bottles (which are slightly suppler) with soft nipples and widened opening. Oro-facial physiotherapy is also used to stimulate the proper movement.

Feedings should be completed in 30 minutes or less, more time suggests the baby is working too hard and spending too much energy. Infants with PRS can benefit from more frequent but shorter feeding sessions to avoid fatigue. Calories might need to be added if volume intake is not optimal. Early intervention by a dietitian is recommended to reduce impacts of feeding difficulties.

Infants with PRS express to some extent glosso-pharyngo-laryngo-esophageal dysmotility. Gastro-esophageal reflux is therefore frequent and should also be taken into consideration and addressed by thickening the milk, offering adequate positioning during and after milk intake and if necessary use of proton pump inhibitors.

If failure to thrive persists despite these measures, feeding through a nasogastric tube (or in fewer cases gastrostomy) might be indicated. Some studies describe up to 40-70% of PRS cases that require nasogastric tube feeding for up to several months and may even require gastrostomy (1). Generally, 70% achieve full oral feeds by one month of age (12). Feeding difficulties correlate with longer length of hospitalization and are more frequent and more severe in patients with associated anomalies or syndromes (13,14). Poor weight gain can also be responsible for delaying surgical correction.

Growth and feeding should be routinely monitored during the first weeks or months of life and diet adapted accordingly. Growing and gaining weight will allow a better growth of the mandible, therefore a better positioning of the tongue, and in turn, less respiratory obstruction.

Malformative assessment

PRS is frequently associated with other anomalies or syndromes. Most studies conclude that 50% are isolated findings while the other 50% are associated with other malformations or genetic syndromes. Routine screening for associated malformations is recommended with cardiac, cerebral and renal ultrasounds.

The two most common syndromes associated with PRS are Stickler syndrome and 22q11 deletion syndrome. A molecular karyotype is performed and a genetic consult offered. An ophthalmological evaluation is recommended around the age of 12 months.

Otitis media is quite often (occurring in over 80% of the time) and is due to inadequate pneumatization of the mastoid cavity and poor middle ear drainage. This can lead to conductive hearing loss. Evoked auditory potentials need to be performed to exclude other causes of hearing loss.

Cleft palate repair

In our center, patients with isolated cleft palate (so without PRS), benefit from early closure of the palate around the age of 3 months. Early reconstruction of the oral cavity allows the tongue to regain a normal position, to restore normal deglutition, to reduce regurgitations and to prevent otological complications. Closure of the cleft palate also plays an important role in speech acquisition.

The limiting factor for early surgery is respiratory obstruction as this can be amplified by closing the palate. Depending on the degree of OSA measured by PSG, surgery might need to be delayed up to 6 months of age or even later in more severe cases of PRS.

Trans-tympanic tubes are placed in practically all children during the closure of the cleft palate to prevent serous otitis media, with the hearing impairment and infectious complications (15).

The mandible does generally not require surgery as its natural course is to grow with age to a normal size.

Multidisciplinary follow-up

Both feeding and airway obstruction are routinely evaluated during the first months of life and improve over time. This is attributable to normal developmental growth allowing craniofacial and airway growth and maturational changes of respiratory control.

The main complications observed in patients after cleft palate repair are ear and hearing complications, speech disorders, swallowing disturbances and infections of the upper respiratory tract. After staphylorraphy, children can present speech disorders with hypernasality generally due to velopharyngeal insufficiency. Speech therapy is often required. Corrective surgery can be offered in cases with poor response to therapy.

Growth and neurocognitive development are closely linked to underlying OSA. Our observations match those of previous publications demonstrating a generally normal long-term development in children with an isolated Pierre Robin sequence (16).

Long term follow-up should be offered by a trained multidisciplinary team including a pediatrician with expertise in developmental and sleep medicine, a plastic surgeon, a maxillo-facial surgeon, an otolaryngologist, a geneticist, a dentist, an orthodontist, an orofacial physiotherapist and speech pathology experts. The purpose of the follow-up is to prevent and correct these complications (15).

Conclusion

In infants referred for PRS, our primary goal is to offer effective and safe treatment until they have grown out of their respiratory and feeding difficulties. Objective assessment of OSA severity is essential.

There is a long list of options for management of airway obstruction in infants with PRS and a lack in standardizing treatment protocols. Rigorously comparing outcomes following a treatment plan remains difficult due to variations in the cohorts, in the severity of the phenotype and the experience of the care giving center.

Nevertheless, choosing the best intervention for a neonate with PRS should be individually tailored as there is great heterogeneity among this group of patients. The primary goal being to choose the less invasive effective treatment to minimize morbidity.

Future prospective work is needed to evaluate long-term neurodevelopmental outcomes in this population.

Conflict of interest

The authors have no conflict of interest to declare.

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