Treatment of Upper Airway Obstruction and Feeding Problems in Robin-Like Phenotype

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Robin sequence (RS) was first delineated by Fairbairn in 1846 and Shukowsky in 1911[1,2]; it was more formally investigated by the French stomatologist Pierre Robin in 1934, who later became the source of the eponym for this condition.[3] Robin described it as consisting of a hypoplastic or retropositioned mandible and glossoptosis, resulting in respiratory distress, with or without a cleft palate. It fulfills criteria for a sequence, in which one or all anomalies found are secondary to another anomaly.[4] The incidence varies between one in 8500 and one in 14 000 live births.[5,6]

The main functional problems associated with RS are upper airway obstruction (UAO) and failure to thrive (the latter resulting from feeding problems, UAO alone, or both problems).[6] Feeding problems are often long-lasting, resulting in gastrostomy rates of 50% in large series.[7] Interventions for RS should thus be assessed by their ability to improve polysomnography (PSG) results and weight gain. Although reported as used in infants with RS by 74% of US pediatric otolaryngology fellowship programs in 1994, only 39% believed PSG to be indicated for most patients with this condition, and just one in 5 performed serial PSG to test for treatment effectiveness.[8] However, it is difficult to document the effect of treatments for RS on UAO without performing PSG, especially because anatomy does not correlate well with function.[9]

For this Medical Progress article, we searched PubMed for studies on the effectiveness of interventions suggested to improve UAO and weight gain in infants with RS (Table). It does not cover surgical techniques for which evidence in the literature is extremely scant or objective documentation of their effectiveness lacking.

Procedures Aimed at Widening the Pharyngeal Space

Prone Positioning

Prone positioning is based on the hypothesis originally proposed by Robin[3] that the narrow pharyngeal space in RS can be corrected by the effect of gravity moving the mandible forward in infants sleeping prone. In some case series, 50% to 80% of patients with RS were reported as having been sufficiently treated with positioning only,[10,11] but none of these studies documented its effectiveness objectively. It has been suggested that the main reason why the prone position appears effective is that the visual cues to UAO (paradoxical chest movements or a pectus excavatum) are less visible in this position.[4] Moreover, it is questionable whether prone positioning alone is sufficient to induce mandibular catch-up growth.[12] Most concerning, however, is that the prone sleep position is associated with a more than 10-fold increase in the risk of sudden infant death syndrome, making it questionable whether parents can safely be advised to place their baby with RS prone for sleep.

Tongue-Lip Adhesion or Glossopexy

This idea on how to widen the pharyngeal space was first proposed by Shukowsky[2] and subsequently reported to result in better survival rates.[13] Success rates for this intervention, on the basis of clinical criteria, vary.[11] Except for the aforementioned study in 1946,[13] we found one study of 48 infants with RS that reported a non-significant increase in weight gain in a mean duration of 1.4 years after tongue-lip adhesion (ie, mean weight increased from the 9.7th to the 17.5th percentile).[14] Another study documented significant UAO in PSG in 6 infants with RS and reported that a follow-up study after tongue-lip adhesion, performed in 5 infants before hospital discharge, demonstrated resolution of significant airway obstruction[15]; more detailed data were not provided. A recent case series reported improved PSG results in 5 of 8 patients studied after tongue-lip adhesion (of a total group of 22 patients) and an unspecified degree of catch-up growth in 10 patients.[16]

In another follow-up study, however, 10 of 11 patients with RS required additional interventions for airway or feeding problems subsequent to tongue-lip adhesion.[17] Moreover, complications such as wound infection, adhesion dehiscence, and scar formation have been reported to occur in approximately one in 5 to one in 4 patients.[11,14] We therefore question whether tongue-lip adhesion can be recommended as a "good surgical treatment for most children" with RS.[16]

Mandibular Distraction Osteogenesis

This procedure aims to correct the mandibular hypoplasia in RS by performing a bilateral vertical mandibular osteotomy

AHI	Apnea-hypopnea index
MOAI	Mixed-obstructive apnea index
PEBP	Pre-epiglottic baton plate
PSG	Polysomnography
RS	Robin sequence
UAO	Upper airway obstruction

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and placing pins for a multi-vector external (or internal) distractor.

Beginning a few days after the operation, distraction is usually done at a rate of 1 to 2 mm daily[18] until the patient has a class III occlusion. This over-correction is considered necessary to sustain an adequate airway in case a (partial) relapse occurs after distraction.[19] The devices are usually removed 4 to 8 weeks after the end of the distraction period. Recently, the successful use of an internal single-stage self-resorbable device also has been reported.[20]

Despite many studies reporting clinical success with this technique, few of them reported changes in weight gain. One study of 10 patients reported a decline in growth rate in 7 patients in the first 12 months after mandibular distraction, despite continued tube feeding in 3 patients.[21] This may be related to dysphagia, often seen in RS, not being corrected by the distraction procedure.[22] In contrast, a study in 17 infants reported accomplishment of full oral feeding in all infants by 3.5 months postoperatively, but provided no growth data.[23]

Several case series reported PSG results before and after mandibular distraction.[18,22-26] All noted an improved or normalized apnea-hypopnea index (AHI) or respiratory disturbance index in most patients studied, but only 3 series provided detailed PSG results. One of the latter studies included 7 patients and reported a decrease in AHI from 60 (SD, 7.3) before distraction to 1.6 (SD, 1.6) at the end of the expander activation.[18] No long-term follow-up data were reported. Another study reported a decrease in mean AHI from 10.6 (range, 0-43) to 2.2 (range, 0-12.9) in 13 infants undergoing distraction osteogenesis,[23] and the third and largest study reported a decrease in AHI from a mean of 39.7 (range, 4.5-177.0) to 5.8 (range, 0-34) in a chart review of 28 infants in whom the procedure was performed and its effect documented with PSG.[26] The authors describing the self-resorbable device aforementioned also reported resolution of UAO (ie, an respiratory disturbance index <2.0) in all 9 of their 14 patients who did not undergo tracheostomy and who were stable enough to tolerate a preoperative sleep study.[20]

Complications include scarring (sometimes hypertrophic), pin site infections (18%), device failure (10%), persistent inferior alveolar nerve lesions (6%) and, somewhat more rarely, damage to tooth buds resulting in long-term tooth loss, dentigerous cyst formation, or relapse of UAO symptoms and temporo-mandibular ankylosis.[27] Some of these complications should be preventable with the new internal resorbable devices, but more data are necessary.[20]

Mandibular Traction

This procedure, first described in 1937,[28] involves fixation of a percutaneous parasymphysial circumferential wire to the mandible, with traction being applied with suspension weights (50-200 g) left in place for 4 to 6 weeks. Its effect on UAO is unknown, and it requires long-term immobilization of the patient during a critical developmental period. Also, a long-term follow-up study showed persistence of retrognathia on cephalometric radiography.[29]

Procedures that Bridge the Narrow Upper Airway

Nasopharyngeal Airway

This device, first suggested by a British group,[30] bridges the narrow pharyngeal space by inserting an endotracheal tube in one of the nares so that it ends just superior to the epiglottis (controlled with endoscopy or radiography). Methods of estimating the required length of the tube without endoscopy or radiography and securing it safely to the nose have been described.[31] One study reported on 22 infants with RS (3 syndromic), with 20 being treated with a nasopharyngeal airway and high-calorie nasogastric tube feeding. Infants were gradually weaned from both tubes while being monitored for oxygen saturation. During a mean duration of hospital stay of 60 days (range, 25-162 days), 18 infants were reported to grow along the percentile of their birth weight, but only 3 were fully bottle fed at discharge. Also, only 10 infants maintained their weight percentile until the time of cleft repair. Unfortunately, no oximetry data were provided.[32] Another study reported weight gain in 8 infants with a nasopharyngeal airway (median age, 50 days; range, 15-180 days; 4 also had supplemental oxygen administered). Their weekly weight gain increased from 86 g before to 255 g with the nasopharyngeal airway, but no data on weight gain after hospital discharge or any PSG results were reported.[33]

Complications include blockage of the tube by secretions and aspiration of gastric contents potentially occurring when the airway is too long.[32] Moreover, it provides no stimulus for the mandible to grow or the tongue to assume a more horizontal position. Although certainly valuable as a temporary measure, it does not solve the anatomical problems underlying the UAO and poor weight gain.

Pneumatic Airway Stenting with Nasal Continuous Positive Airway Pressure or Intermittent Positive Pressure Ventilation

There are some case series on the use of nasal continuous positive airway pressure or intermittent positive pressure ventilation in RS.[34,35] In a recent single-center analysis of 81 patients with RS, 7 (9%) had been treated with nasal intermittent positive pressure ventilation, starting at a mean age of 2 months and lasting for a mean of 16.7 months. Reported benefits included a decrease in the proportion of time spent with oxygen saturation <90% from a mean of 14% to 1% (at a mean airway pressure of 8.3 cm H2O) and a decrease in mean transcutaneous carbon dioxide from 57 to 31 mm Hg. All 7 infants were discharged home with the device, which was used at home for an average of >8 hours per day. No facial adverse effects were reported.[35] There is anecdotal evidence, however, that long-term nasal continuous positive airway pressure use in young children may result in mid-face hypoplasia.[36] Although particularly relevant to patients with RS, who may have a hypoplastic maxilla anyway,[37] this potential adverse effect has not been studied systematically.

Tracheostomy

Tracheostomy clearly resolves UAO, but it does not correct the underlying malformation and puts considerable burden on the families, who often require additional nursing staff and expensive supplies.[38] It is also fraught with numerous complications, including granuloma formation, which occurs in most patients and requires intervention with general anesthesia in 10% of cases,[39] bleeding, pneumothorax, tracheal stenosis, tube displacement, impaired speech development, and even sudden death (the latter in 1%-4% of cases).[40] In a survey of parents of 41 pediatric patients with RS who underwent tracheostomy, 60% of children required ≥3 hospitalizations and 23% of children reported airway problems after decannulation.[41]

Although the procedure should be reserved for severe cases, the proportion of patients undergoing tracheostomy is as high as 50% in some case series.[38] Corresponding to this, 52% of respondents in the aforementioned survey considered tracheostomy the treatment of choice in patients who failed observation and positioning.[8] This, however, is in contrast to other centers' experience (see below).

Palatal Plates

These plates have been used in infants with RS since the late 1960s.[42] Their effect is thought to be mediated via an improved tongue function, with the latter stimulating mandibular growth, although data supporting this concept are sparse.[43,44]

In a recent case series involving 188 infants with RS seen in one center, a palatal plate was used in 134, resulting in a resolution of glossoptosis and, thereby, of clinically evident airway obstruction in 122 (91%).[45] Feeding problems, however, were reported to persist in 26% of patients despite palatal plate therapy, and the extent of airway obstruction was not assessed objectively nor were any data provided on weight gain. Only 9% of the 188 patients, however, received invasive treatments (tracheostomy, 2.1%; glossopexy, 6.9%), which is considerably less than in other large case series.[38]

In infants with more severe UAO, a modified acrylic palatal plate in which a velar extension resembling a spur or baton shifts the base of the tongue forward may considerably improve the UAO (Figures 1 and 2).[46] The baton's stability in this so-called pre-epiglottic baton plate (PEBP) is increased by incorporating a wire into the acrylic (Figure 1). The correct length and angle of the baton are controlled endoscopically, and its effectiveness in relieving UAO can be confirmed with PSG. Treatment is supplemented by stimulation of the oral musculature, on the basis of the Castillo-Morales approach[47] and feeding training (initially via finger feeding, subsequently by a nurser which allows to control the ease of milk flow during sucking [Playtex Drop-Ins, Playtex Products, Neenah, Wisconsin]). The treatment aforementioned requires an interdisciplinary team consisting of an orthodontist, a pediatric sleep specialist, a speech therapist familiar with orofacial regulation therapy, and a pediatrician trained in nasopharyngeal endoscopy. An experienced nursing team is also of paramount importance, especially to train parents in handling the PEBP. Starting this treatment as soon as possible after birth seems to reduce the duration of PEBP treatment, because the mandible has its largest growth potential early in life.[44,46]

In a randomized controlled crossover trial, the effectiveness of the PEBP in relieving UAO was tested against a conventional palatal plate, used as a sham procedure, in 11 infants <3 months old with isolated RS and a mixed-

Figure 1. Lateral and dorsal views of the PEBP. Reprinted with permission from Bacher M et al, Laryngo-Rhino-Otologie 2010;89:621-7.

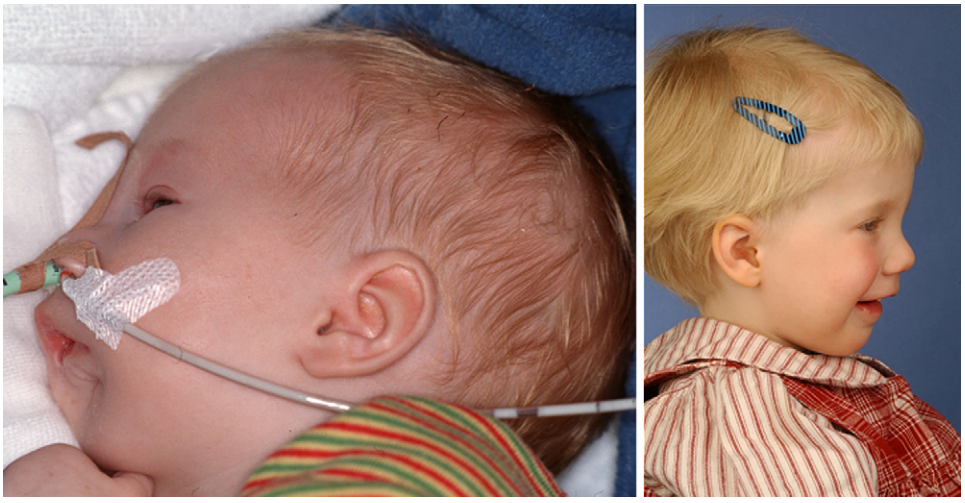

Figure 2. Lateral view of an infant with syndromal RS requiring a naso-pharyngeal airway for airway obstruction. The patient was successfully transitioned to a PEBP, which was used for 3 years with no complications, and had cleft palate repair at 4 years of age. The same patient is shown on the right at 6 years of age. Left panel reprinted from Bacher M. et al., Laryngo-Rhino-Otologie 2010;89:621-7, with permission. Photographs shown with parental permission.

obstructive apnea index (MOAI) >3 while in a supine position. After 48 hours of treatment, median MOAI had fallen from 13.8 to 3.9 with the PEBP ($P < .001$), and it remained unchanged with the sham procedure. In an uncontrolled longitudinal study involving 15 patients (median age at onset of treatment, 5 days), median MOAI fell from 17.2 to 1.2 after 3 months of treatment with the PEBP. All infants had their feeding tubes removed before hospital discharge and continued to gain weight at a mean rate of 24 g/day at discharge and 19 g/day at follow-up. All infants continued to be fully orally fed at this time.[46,48]

Thus, the PEBP is the first intervention applied in RS the effectiveness of which has been tested against a sham procedure in a randomized study design and the long-term effects of which have been shown to address both achievement of appropriate weight gain (without a feeding tube) and resolution of significant UAO (MOAI <3). Variations of the PEBP have been reported, but no studies documented their effect with PSG.[49,50] Because of the lack of comparative long-term studies, it remains unclear whether effective treatment for milder forms of RS-related UAO can also be achieved with a palatal plate without extension, as suggested by Bütow's data.[45]

Table. Treatment approaches used in RS

Approach
1. Widening the pharyngel space
Prone positioning
Tongue-lip adhesion
Mandibular traction
Mandibular distraction osteogenesis
2. Bridging/stenting the obstructed airway
Nasopharyngeal tube
Nasal respiratory support
Tracheostomy
3. Correction of glossoptosis and functional induction of mandibular growth
Palatal plate
PEBP

Cognitive Outcomes in Robin Sequence

Several authors suggested that RS is associated with impaired cognition,[10,51] but it is still unclear whether this is part of this sequence or whether it results from the intermittent hypoxia frequently associated with RS and should thus respond to early treatment of UAO.

In a study of 34 children with non-syndromic RS who had been treated with the PEBP during their first year of life and were compared with a matched control group, cognition was assessed by using the Kaufman Assessment Battery for Children and a self-concept inventory.[52] The cognitive development of the children with RS, although poorer than that of the healthy control subjects by an average of approximately 1 SD, was within the reference range for the inventory in all children, and there was no significant difference compared with control subjects in the distribution of the 3 categories "above average," "average," and "below average," indicating that these infants sustained some, but not substantial, cognitive impairment.[52] These results suggest that the considerable cognitive impairment previously reported in many children with isolated RS may not be directly related to RS, but may rather be mediated via the recurrent hypoxia, sleep disturbance, or both resulting from UAO, which should be preventable with adequate and early treatment.

In conclusion, this review highlights the need to assess any intervention used in RS with objective means (ie, whether it results in adequate weight gain during bottle- or breast-feeding and resolves UAO as documented with PSG). Currently, only few treatments for RS appear to

fulfill these criteria while not impeding facial growth. Because of the lack of clinical studies comparing one treatment modality with another, treatment choices will have to balance data from the studies aforementioned against an institution's experiences with the management strategy used, the support it is able to offer, and the success rate of the management strategy in the center's hands. Further data are necessary to assess the long-term effectiveness of treatments for this rare, but potentially life-threatening condition. ■

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