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Functional treatment of airway obstruction and feeding problems in infants with Robin sequence

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ABSTRACT

Background Robin sequence (RS), characterised by micrognathia/retrognathia and glossoptosis with or without cleft palate, presents with intermittent upper airway obstruction and feeding difficulties. Active intervention is required to reduce the risk of brain damage or sudden death. Most treatment options are poorly studied and/or invasive. Our group developed a functional approach including early feeding training and the pre-epiglottic baton plate (PEBP), an orthodontic appliance with a velar extension shifting the base of the tongue forward.

Patients and methods We evaluated the effect of this approach on sleep study results and early weight gain by searching our electronic patient database for infants with isolated RS, born at or referred to our department between 1 January 2003 and 31 December 2012 and treated with the PEBP.

Results Of 122 patients identified, 360 overnight sleep study results, obtained at admission, prior to hospital discharge and 3 months postdischarge, were available (117 infants had complete data). These showed a decrease in the mixed-obstructive apnoea index from (median; IQR) 8.8 (2.1–19.7) to 1.8 (0.6–5.4); p<0.001 and 0.2 (0–1.3); p<0.001, respectively. Z-scores for weight improved from −0.7 (−1.39 to −0.24) upon admission to −0.5 (−0.90 to +0.02) at follow-up (p=0.02), accompanied by a decrease in the proportion of infants requiring nasogastric tube feeding from 66% to 8%. No infant required craniofacial surgery or tracheostomy.

Conclusions These longitudinal cohort data suggest that this functional approach may be an option to treat both, upper airway obstruction and feeding problems, in infants with isolated RS.

What is already known on this topic?

- Robin sequence is associated with recurrent upper airway obstruction and feeding problems.
- Treatment options vary; most are considerably invasive or poorly evaluated.

What this study adds?

- The functional treatment approach audited here was associated with improved sleep study results in the supine position and normal weight gain with oral feeding.
- Collecting objective data like the mixed-obstructive apnoea index and Z-scores for weight appears important to examine treatment approaches for this rare condition.

INTRODUCTION

Robin sequence (RS), characterised by micrognathia, retrognathia and glossoptosis with or without cleft palate, presents clinically with intermittent upper airway obstruction (UAO) and feeding difficulties, which are most severe during the first postnatal months.[1–3] This can lead to hypoxaemia, hypercapnia, cor pulmonale, failure to thrive, neurodevelopmental delay and even sudden death.[4 5] The incidence of RS is between 1:8500 and 1:14 000.[6–8] It is associated with other malformations in about half the cases.[5]

Isolated RS does not appear directly to affect neurodevelopment. Active intervention is therefore required to reduce the risk of brain damage or sudden death resulting from UAO and intermittent hypoxaemia. Endoscopic studies showed that the airway obstruction in RS results from the reposition of the dorsum of the tongue and/or an inward movement of the lateral pharyngeal walls.[3] Thus, treatment of UAO should aim to stabilise the pharyngeal wall and widen the pharyngeal space by shifting the tongue forward.

Most current treatment options for RS are considerably invasive; none has been subjected to a controlled study design. Prone positioning, which is reported effective for many RS infants, has never been investigated objectively, that is, based on sleep study results. A functional treatment option is based on an intra-oral orthodontic appliance with a velar extension.[9] Our group has further developed this appliance, which now has a long velar extension shifting the dorsum of the tongue forward, thereby widening the pharyngeal space (pre-epiglottic baton plate (PEBP); figures 1 and 2).[10] Having this device tested in a controlled study design,[10] we now performed a clinical audit of its effectiveness regarding growth and UAO in infants with isolated RS.

PATIENTS AND METHODS

We conducted a retrospective audit including all patients with RS admitted to our department between January 2003 and December 2012. This is a national referral centre for RS to which infants usually are only referred by other hospitals after a trial of prone positioning has failed. Clinical data were extracted from the department's electronic

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Figure 1 Palatal plate with velar extension (pre-epiglottic baton plate).

patient database. Treatment always followed the same sequence. At first, infants had a maxillary cast taken and underwent an 8-channel cardiorespiratory sleep study (polygraphy). Using the cast as a model, palatal plates were made from compound soft and hard acrylic (Forestacryl-Strong-S, Foerster, Pforzheim, Germany), covering both the palate (including the cleft) and the alveolar ridges. The palatal plate has a baton reaching 2–3 cm into the pharynx[10] (figure 1). It is held in situ by suction and adhesion. If necessary, a fixative cream (Corega Super-Haftcreme; Procter & Gamble, Cincinnati, OH, USA) is used to improve retention. In severe cases, extraoral wire bows are added to the PEBP and secured on the infant's face using adhesive tape (Steri-Strip and Cavilon-No Sting Barrier Film, Steri-Strip Compound Benzoin Tincture, 3M Health Care, St Paul, MN, USA). The correct length and angle of the baton was controlled endoscopically,[11] and its effectiveness in relieving UAO confirmed by a second sleep study. Infants received each appliance for at least 36 hours before this control sleep study was performed. Treatment was supplemented by stimulation of the oral musculature, based on the Castillo-Morales approach,[12] and feeding training (initially via finger feeding, subsequently by a nurser that allows to control the ease of milk flow during sucking (Playtex Drop-Ins, Playtex Products, Edgewell, North Bergen, NY, USA). A third sleep study was performed 3 months after hospital discharge.

Sleep studies

Sleep studies were performed using a computerised system (Embla N 7000, MedCare, Reykjavik, Iceland). The study montage comprised the following channels and sensors: chest and abdominal wall movements (respiratory inductive plethysmography, MedCare, Reykjavik, Iceland), nasal pressure and linearised nasal airflow (nasal prongs and built-in pressure transducer (MedCare), pulse oximeter saturation (SpO_2) and pulse waveform (Radical Masimo, Irvine, CA, USA), ECG (MedCare), transcutaneous partial pressure of carbon dioxide (Microgas 7650, Linde, Basel, Switzerland) and digital video via infrared camera (Panasonic, Tokyo, Japan). Recordings commenced in the evening and lasted for at least 8 hours; all infants were studied in the supine position.

Recordings were manually analysed, blinded to their timing (before/after treatment), for the presence of respiratory events using standard criteria.[13] In brief, total sleep time (TST) was determined from the first 10 min epoch without movement, artefact or a distorted pulse waveform to the last such 10 min epoch; recordings comprising <3 hours of TST were repeated during the following night. An apnoea was scored if (1) the amplitude of the nasal airflow fell to <20% of the average amplitude of the two preceding breaths, (2) no airflow was detected at the mouth, and (3) the event comprised at least two breath cycles (ie, approximately 4 s). An obstructive apnoea was scored if (1) the above criteria for apnoea were fulfilled and (2) out-of-phase movements of the chest and abdomen were present. A central apnoea was scored if (1) criteria for apnoea were fulfilled and (2) no chest and abdominal wall movements were present. Mixed apnoeas were defined as apnoeas with both central and obstructive components, each lasting at least two breath cycles.

A mixed obstructive apnoea index (MOAI) was calculated as the sum of mixed and obstructive apnoeas per hour of TST. Based upon standard criteria,[13] severity of obstructive sleep apnoea (OSA) was classified as mild (MOAI 1–5), moderate (MOAI 5–10) or severe (MOAI >10).[13 14]

Desaturation events were visually confirmed to exclude spuriously low values. Events with a distorted pulse waveform signal within 7 seconds prior to their onset were considered artifactual and excluded. The number of desaturation events to ≤80% pulse oximeter saturation (SpO_2) was counted and expressed as indices, defined as events per hour of TST (DI80).

Statistical analyses

Descriptive statistics were used to summarise patient characteristics and sleep study results. Data are presented as median (IQR). Comparisons between data obtained at admission, prior to discharge and 3 months later were performed using the Wilcoxon/Kruskal-Wallis test. A p value <0.05 was considered to be statistically significant. All analyses were done with statistical software (Statistical Package for the Social Science, release V.18.0.1 for Windows, SPSS, Chicago, IL, USA).

RESULTS

Over the 11-year period, 207 infants with RS were admitted to our department. Of these, 122 (59%) had isolated and 85 (41%) syndromic RS. The demographic and clinical characteristics of the former group are summarised in table 1.

All infants had at least two interpretable sleep studies recorded, one prior to and one following treatment, thus no infant had to be excluded; also, no infant needed mechanical ventilation or required a tracheostomy. Regarding initial OSA severity, this was classified as mild in 30 (25%), moderate in 19 (15%) and severe in 55 infants (45%) (table 2); 18 infants (15%) had no OSA, but received the PEBP to induce mandibular catch-up growth and to correct glossoptosis. All infants tolerated the therapeutic procedures well. Severe adverse events like bleedings, systemic infections or aspiration were not observed. The most frequent side effect was the occurrence of tender spots on the hard or soft palate. These, however, improved in all affected infants after manually reshaping the plate.

In all infants, the MOAI decreased with PEBP treatment. The Kruskal-Wallis test (H-test) for paired data revealed a statistically significant decrease ($p<0.001$) in the MOAI in all OSA severity groups between admission, discharge and follow-up. At discharge, 10 infants (8% of n=122) still received nasogastric tube feeding and 44 infants (36% of n=122) a hypercaloric diet. Weight gain improved during PEBP treatment (Z-score for weight −0.7 (−1.39 to −0.24) at admission versus −0.5 (−0.90 to +0.02) 3 months after discharge ($p=0.021$).

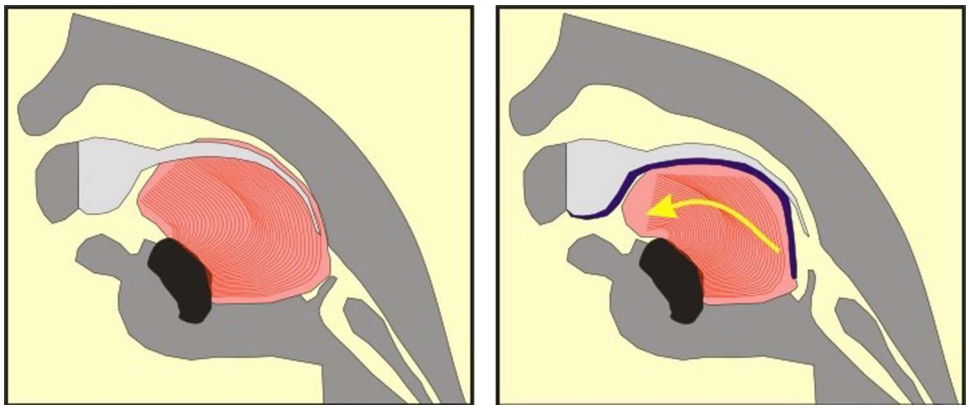

Figure 2 Schematic drawing of the Robin sequence anatomy without and with (right) the pre-epiglottic baton plate (blue line).

Table 1 Patient characteristics

Characteristics	Results
Gender (male/female)	51/71
Gestational age at birth (weeks)	$39^{4/7}$ ($30^{0/7}$–$41^{6/7}$)
Birth weight (g)	3200 (2640–3480)
5 min Apgar score	9 (8–10)
Feeding difficulties (NGT) n (%)	81 (66%)
Age at admission (days)	12.5 (4–42)
Duration of hospital stay (days)	19 (14–27)
MOAI at admission (events per hour)	8.8 (2.1–19.7)

Values are given as median (IQR).
MOAI, mixed-obstructive apnoea index; NGT nasogastric tube.

Table 2 Longitudinal changes in MOAI and DI80 during treatment

Variables	Admission	Prior to discharge	3 months follow-up
Mild UAO (n=30)			
MOAI	2.6 (1.9–4)	0.6 (0–1.3)**	0.2 (0–0.5)**
DI80	0 (0–0.1)	0 (0–0)*	0 (0–0)*
Moderate UAO (n=19)			
MOAI	7.6 (6.6–9.1)	1.2 (0.3–1.8)**	0.1 (0–1.8)**
DI80	0 (0–1.4)	0 (0–0.1)	0 (0–0)
Severe UAO (n=55)			
MOAI	29.0 (14.9–40.6)	1.9 (0.6–5.4)**	0.2 (0–1.3)**
DI80	0.5 (0–2.8)	0 (0–0.2)**	0 (0–0)**

**p<0.001, *p=0.02.
MOAI, mixed-obstructive apnoea index; UAO, upper airway obstruction.

DISCUSSION

In this single-centre cohort of infants referred for RS, we found that an orthodontic appliance, developed by our group, in conjunction with orofacial stimulation and feeding training, significantly reduced the frequency of mixed and obstructive apnoeas during sleep and improved feeding problems and failure to thrive, that is, the leading symptoms in RS.[15]

Oral appliances have been used for over 40 years in RS to facilitate bottle feeding and to keep the tongue out of the cleft.[9] Within a median hospital stay of 19 days, the proportion of infants needing nasogastric tube feeding could be reduced from 66% upon admission to 8% at discharge, suggesting that PEBP treatment may indeed facilitate oral feeding. In addition, the PEBP aims to push the base of the tongue forward to widen the hypopharynx and promote mandibular catch-up growth. While the latter yet awaits objective testing, its effect on sleep-related airway obstruction appeared promising in our longitudinal analyses.

We only analysed our data on infants with isolated RS, yet in about half the cases RS is associated with other malformations. We refrained from studying the latter infants here because of the heterogeneous pathogenesis of their UAO.

Sleep studies were performed in the supine position. This prevented us from demonstrating that positional treatment alone was insufficient in treating UAO, although being a national referral centre, it is our experience that most infants are only referred for PEBP treatment after a trial of positioning has failed in the referring hospital. Although positional treatment has been reported as successful in 40%–70% of RS infants with UAO,[5 16] it rarely proved to be an adequate long-term treatment,[3] has never been investigated using sleep study results and is associated with a 10-fold increase in the risk of sudden infant death syndrome.[15] In addition, it was our aim that PEBP treatment resolved UAO in the prone and also in the supine position, as this is the recommended sleep position for infants.

Infants with RS are traditionally described as developing airway obstruction soon after birth,[2] but its onset may also be delayed.[17] In a recent study of 10 patients with RS-related UAO, 7 only presented between 24 and 51 days of age.[18] This may explain why some patients in our cohort were already >4 weeks old at referral and is also the reason why we applied our treatment approach also in RS infants with a normal sleep study result at admission.

Several infants showed a complete recovery from severe apneic episodes after a comparatively short trial of PEBP treatment. Infants with RS have a decreased retropharyngeal space due to tongue retrusion. Thus, interventions that do not modify the position of the tongue may be more likely to have a high failure rate. The concept to progressively elongate the mandible to correct tongue ptosis, increase pharyngeal airway size and correct micrognathia is also used with mandibular distraction osteogenesis, which may also lead to complete resolution of UAO.[19–21] This intervention, however, is considerably invasive and not without side effects (eg, infection, facial scarring, damage to the inferior alveolar nerve, injury to the tooth buds, mucosal perforation, bone formation defects and possible disturbance of intrinsic mandibular growth).[22 23]

We have documented the persistence of normal sleep study results up to 3 months after hospital discharge. We consider this relatively long follow-up period, including an ascertainment of objective data (ie, sleep study results, standard deviation score for weight), a major strength of our study.

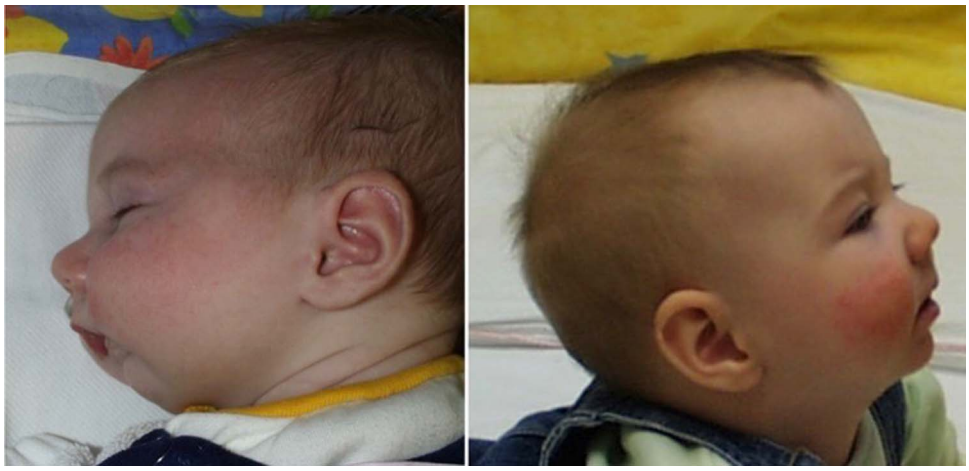

Figure 3 Lateral views of an infant with Robin sequence upon admission at age 1 month (left) and 3 months after discharge (right) following pre-epiglottic baton plate treatment. Published with parental permission.

UAO and feeding problems related to glossoptosis are the most likely reasons for reduced weight gain in RS infants.[14] At least one-third of RS patients require short-term or long-term supportive treatment with nasogastric tube feeding, even after successful airway treatment.[7 24 25] RS patients with feeding difficulties are often identified on the basis of their inability to maintain normal growth or require prolonged feeding times (>30 min).[26] In our study, 66% of infants were initially tube fed, but 92% were fully orally fed at discharge and all but one at the 3-month follow-up visit. This encouraging result may reflect the importance of stimulating the tongue and encourage sucking early on to improve neuromuscular coordination.

Median length of hospitalisation was 19 days (IQR 14–27 days), which is somewhat below that reported for most other treatment modalities for RS except mandibular distraction osteogenesis.[27–30]

Limitations

Our data were not collected prospectively, introducing a potential for bias. However, we tried to minimise this risk by adhering to a rigorous protocol and by including all infants fulfilling our predefined criteria. Sufficiently large cohorts for prospective studies, which clearly provide a higher level of evidence, are difficult to assemble in rare conditions such as RS. Sleep staging was based on behavioural criteria only, but these have been validated and are commonly used in neonates and infants. No infant required a tracheostomy, a finding contrasting other cohort studies on RS.[5 8] This may be due to our decision to focus only on infants with isolated RS, that is, to exclude those with syndromic RS, but may also reflect the effectiveness of our treatment approach. At the other end of the spectrum, we did not test whether OSA would have resolved in some patients just by prone positioning, as we do not consider this a safe alternative for the reasons outlined above.

Some infants (15%) were treated with the PEBP despite a normal initial sleep study result. This was done because an initially normal sleep study does not rule out the later development of obstructive sleep apnoea syndrome in some RS infants.[18] We speculate that the constant gentle pressure the PEBP exerts on the base of the tongue promotes mandibular catch-up growth, a hypothesis that yet awaits objective testing.

In conclusion, the treatment approach reported here in infants with isolated RS may offer a solution to the underlying anatomic dysfunction; whether it also inaugurates mandibular catch-up growth (figure 3) has yet to be proven. It appears to be a safe and effective way to avoid tracheostomy placement and other surgical interventions.

Contributors WB wrote the first draft of the manuscript and critically revised it; SW analysed the data and revised the manuscript; MB, SM-H and JA were involved in data collection and critically revised the manuscript and CFP initiated and supervised this study and critically revised the manuscript.

Competing interests None declared.

Provenance and peer review Not commissioned; externally peer reviewed.

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