Seminars in Fetal and Neonatal Medicine 26 (2021) 101287

Contents lists available at ScienceDirect

Seminars in Fetal and Neonatal Medicine

journal homepage: www.elsevier.com/locate/siny

Quality of life in children undergoing treatment for Robin Sequence in infancy

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Over the last decades, due to improvements in diagnostic techniques, operative and post-operative care, the focus in pediatrics has shifted from mortality as the main outcome to long-term morbidity outcomes relevant to daily life. In children, recovery and morbidity after treatment or an intervention are related to growth and development in the following three domains: physical, mental, and social development [1]. After hospital discharge, recovery in these three domains runs simultaneously, resulting in a 'new normal' for the child and its parents (for readability, the term parents includes both parents and caregivers). This 'new normal' for children and their parents represents the subjective evaluation of physical, mental and social impairments in daily life; covered by the concept of "quality of life". The latter is therefore an important outcome in value-based health care in pediatrics since it evaluates those outcomes that are most relevant for that patient [2].

Quality of life is also an important outcome in the diagnosis and treatment of children with Robin Sequence (RS). The important quality of life outcomes for RS children are related to their main clinical problems regarding upper airway obstruction and feeding problems which are mostly present already early after birth. The treatment options to treat airway obstruction in RS depend on the severity of the airway obstruction and will therefore vary from conservative treatment with prone positioning to surgical treatment such as giving the child a tracheostomy [3]. Decision-making of the treatment schedule is regularly based on the treating center's preference and experience. A review regarding non-surgical and surgical interventions for airway obstruction in RS children found that in the included studies there seemed to have been a stepwise treatment approach, in which the indication for a certain treatment is the failure of another [3]. At present, it remains uncertain which treatment is best, however, all treatments will have different effects on the quality of life of RS children and their parents.

What all treatments have in common is that RS children are admitted to the neonatal or pediatric intensive care unit (NICU or PICU) which is a very stressful experience for both infants and their parents in itself, regardless of the severity of RS in their child [4]. Besides, the choice for treatment has an impact on the length of stay (LOS) of RS children, which will be another factor of stress. Recently, it was shown that LOS predicted worse quality of life 6 months after discharge in a heterogeneous pediatric intensive care population [4]. After NICU/PICU discharge, RS infants and their parents return home where breathing and feeding problems may persist and parents face new challenges. For example, if the infant was sent home with the advice for prone positioning this might cause anxiety in parents due to the association between prone position sleeping and cot death [5]. If the child was sent home with a tracheostomy, parents have the responsibility to provide 24 h per-day care to their child. A prolonged tracheostomy duration was associated with significant parental concern [6]. Another important stress factor might be the definitive diagnosis of the child, whether the child has an associated syndrome or not. Syndromic RS might cause new challenges for parents of RS children because it is associated with worse quality of life both in parents and children compared with isolated RS [7], see Table 1. In all these different situations, parents will experience stress and worries regarding weight gain and the physical development of their RS infant [8,9]. Besides, mental and social development were also reported by parents as important outcomes in RS children: e.g. the child's well-being, parents' grief, family stress, relationships with providers, and psychological development [10].

The reasons to measure quality of life in RS children may vary from individual patient care to scientific research. The first reason is that monitoring important quality of life outcomes in the daily life of RS children and their parents is important for outpatient care after treatment of these children. Quality of life outcomes provide important information for clinicians regarding functioning and problems in daily life which they can discuss with the patient and/or the parent during their outpatient visit as part of value-based health care. A second reason is that quality of life outcomes are essential in evaluating the effect of the interventions, treatment, and/or management on the daily life of RS children within the center they are treated (before and after treatment). These population-based outcomes might provide reference scores to put the individual patient score assessed during outpatient clinic visits in perspective with that of their peers with the same treatment history. Hong et al. found that mandibular distraction osteogenesis (MDO) in RS infants improved their quality of life [11] measured with the Glasgow Children's Benefit Inventory, see Table 1. There were no differences between isolated and syndromic RS children. Therefore, quality of life

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https://doi.org/10.1016/j.siny.2021.101287

Available online 17 September 2021

outcomes are also essential to evaluate and improve the provided care. A third reason to assess quality of life outcomes is that they are also important in comparing different management strategies in groups of RS children between hospitals and/or countries. Logjes et al. found that MDO and tongue-lip adhesion both resulted in an overall benefit in health-related quality of life outcomes before and after treatment in a small sample of RS children who were treated in two different clinical centers [7]. Since randomized controlled trials (RCTs) are lacking in this field, quality registers and benchmarking between hospitals and countries might provide important insights into the association between certain management strategies and implications for daily life, such as quality of life, of RS children and their parents [12].

All reasons mentioned above require standardized, internationally validated quality of life measurements with reference data from the general population or RS population. There is a difference between generic and disease-specific quality of life questionnaires. Generic measurements assess the subjective evaluation of physical, emotional, and social development in children that are generic for both, the general and the pediatric population. The advantage is that outcomes can be compared across different pediatric populations. The disadvantage is that a generic questionnaire might not be sensitive enough to detect differences or changes within a specific pediatric population. Disease-specific measurements assess those outcomes that are sensitive in that specific pediatric population. In RS research both generic quality of life as well as disease-specific quality of life measurements are used. Basart et al. found that generic assessed quality of life outcomes were similar to Dutch norm scores in a cross-sectional study in older children [13]. There were no differences between isolated and syndromic RS children. In the study of Dulfer et al. a disease-specific quality of life instrument regarding obstructive sleep apnea (OSA) was used in a cross-sectional study in children of various ages [14]. They found that disease-specific quality of life in RS children was worse compared with reference data. Besides, parents' scores of OSA-related quality of life were associated with the presence of OSA/respiratory support in their child. On the other hand, children themselves reported better quality of life scores in some domains compared with children from the general population.

The finding that parents may report different quality of life outcomes in their child than the children themselves is known as the proxy problem [15]. In general, there is a larger agreement between parent and child for observable outcomes (e.g. physical quality of life) than for non-observable outcomes (e.g. emotional and social quality of life) [16]. This parent-child disagreement is affected by the child's age, the domains that are assessed (higher agreement for younger age on physical health, compared to a higher agreement for older age on psychosocial aspects of health), and the parents' own quality of life [17]. Remarkably, the agreement is better between parents and chronically ill children than between parents and their healthy children [16]. For clinical implications, both child reports and parent reports are valuable sources for the impact of the disease and/or treatment on development and functioning in daily life.

Concluding, various treatment strategies are used to treat respiratory and feeding problems in RS children, but it remains unclear which treatment has the best outcomes in the short and long term. As to clinical implications, there is a need for uniform RS management guidelines including not only medical outcomes but also quality of life outcomes in both, children and their parents. These guidelines need to summarize the current evidence-based medical knowledge regarding the various, multidisciplinary aspects of RS, providing recommendations to improve health and quality of life outcomes in RS children and their parents. Quality of life is a very important outcome throughout the diagnosis and management of children with RS. Parents should be seen as important

Table 1
Studies regarding quality of life (QoL) outcomes in RS children.

Authors	Treatment/intervention	Age at surgery (range)	Sample size: # included/total comorbidities	Study design	Follow-up	quality of life reported by the parent/child	Main results
Logjes et al. [7]	Mandibular distraction osteogenesis (MDO) or tongue-lip adhesion (TLA)	24 days (5–131)	N = 22/31 (12 MDO, 10 TLA) N = 13 syndromic	Retrospective, 2 center study	5.9 years (range, 1.3–10.5 years)	Parent: Glasgow Children's Benefit Inventory	QoL benefit after MDO (Mdn = 21.9) and TLA (Mdn = 26.0) are similar. No differences between syndromic/isolated
Hong et al. [11]	Mandibular distraction osteogenesis (MDO)	54 days (21–112)	N = 21/25 MDO N = 14 cleft palate N = 6 syndromic N = 5 tracheostomy prior to MDO	Retrospective, 1 center study	Not mentioned	Parent: Glasgow Children's Benefit Inventory	QoL benefit after MDO (Mean = 54) No differences between syndromic/isolated. No differences between tracheostomy yes/no
Basart et al. [13]	Prone positioning (PP), nasopharyngeal airway (NPA), tongue-lip adhesion (TLA), mandibular distraction osteogenesis (MDO), and tracheotomy (TS)	Not mentioned	N = 102/165 (52 PP, 11 NPA, 17 TLA, 15 MDO, 7 TS) N = 56 syndromic	Cross-sectional, 3 center study	Mean age children: 8.75 years	Parent: TAPQoL (≤5y) DT-P Parent/child: PedSQL (6–18) RS-specific Child: SWA (8–18)	RS children and parents scored similarly to Dutch norm scores. Except for the age group 0–5 who reported more lung, sleep, and motor functioning problems. No differences between syndromic/isolated on child quality of life, but parents of syndromic RS reported more distress than isolated.
Dulfer et al. [14]	Prone positioning (PP) or Respiratory treatment: non-surgical (NST) or Surgical (ST)	Not mentioned	N = 53/111 (27 PP, 18 NST, 8 ST). N = 15 anomalies N = 6 syndromic N = 49 cleft palate	Cross-sectional, 1 center study	Median age child: 8.9 [IQR 5.1–12.7]	Parent: OSA-18 VAS Child: OSA-12 VAS	RS parents, worse scores OSA-18 scores and VAS scores compared with the norm. Parents of RS children with OSA or airway support reported worse OSA-18 scores compared with PP children or no-OSA respiratory support children.

DTP = distress thermometer for parents; PedSQL = pediatric quality of life inventory; RS-specific = newly developed RS-specific quality of life questionnaire; TAPQoL = TNO-AZL preschool quality of life; OSA-12 = child perceptions of the impact of obstructive sleep apnea on them; OSA-18 = parental perceptions of the impact of obstructive sleep apnea on RS child; VAS = visual analoge scale regarding quality of life.

stakeholders in the management of their child with RS [6]. Their quality of life assessments may provide valuable information regarding the child's functioning and may contain a predictive value for the child's development.

As to future research, the scarce studies on quality of life in RS children included small samples of RS children with one or more treatment strategies. RCTs are lacking and are difficult to perform since the treatment strategy is often a center preferred decision. Benchmarking research between hospitals and countries and quality registers might provide important insights into treatment strategies outcomes and implications for daily life, such as quality of life, of RS children and their parents.

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