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Sleep frequently asked questions: Question 1: What abnormalities do babies with cleft lip and/or palate have on polysomnography?

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INTRODUCTION

Cleft lip and/or palate (CL/P) is one of the most common congenital malformations with an estimated birth prevalence world wide of 12.44 (95% CI 9.72–15.93) per 10,000 births for naturally conceived singleton births; prevalence is higher in infants conceived using assisted reproductive technologies [1]. CL/P can occur in isolation or with other anomalies or chromosomal variations and are classified as non-syndromic and syndromic CL/P based on the absence or presence of other congenital anomalies [2]; approximately 2/3rd of CL/P occurs in isolation or as non-syndromic CL/P and 1/3rd as syndromic [3]. CL/P includes a spectrum of clefts of the primary palate (cleft lip and alveolus) and secondary palate (hard and soft palate) and can be incomplete or complete as well as unilateral or bilateral, and subclinical [4]. Palatal clefts also differ in shape with a characteristic U-shaped cleft associated with Robin sequence in contrast to a typical V-shaped in non-syndromic CL/P. The prevalence, type, and severity of CL/P differ by ethnicity, country, regions, and sex with both genetic and environment factors implicated in the aetiology of CL/P [1,2,4]. Associated anomalies as well as cleft type determine the overall presentation of an infant with CL/P including associated respiratory impairments.

Respiratory impairments, including both obstructive and central sleep apnoea, are more prevalent not only in Robin sequence but across the spectrum of CL/P commensurate with the degree of airway disruption. Infants, children, and adults with CL/P have a smaller airway when compared to non-CL/P peers even after lip and palate repair [3]. Micrognathia, most often associated with Robin sequence, occurs across the spectrum of CL/P and will further compromise airway calibre [5]. Nasal airway calibre is disrupted by cleft lip and oropharyngeal musculature is disrupted by cleft palate. These anatomical and functional changes in the upper airway predispose to airway obstruction in addition to challenges with feeding and upper airway clearance. Given the broad spectrum of CL/P and associated anomalies, it can be difficult to determine the risk of respiratory impairments in a specific infant based on a diagnosis of CL/P alone.

ROLE OF POLYSOMNOGRAPHY IN THE ASSESSMENT OF INFANTS WITH CL/P

Polysomnography is the accepted standard for the assessment of breathing during sleep in infants and children; despite its limitations, other methods, including home sleep apnoea testing [6], have not yet proven to be highly predictive of polysomnography results nor cost effective in this young age group. Polysomnography has been used to assess breathing during sleep for infants with Robin sequence since the 1980s with increased recognition of sleep related respiratory disturbance across the CL/P spectrum beginning in the last decade. Polysomnography, which includes measurements of sleep physiology, allows for detailed characterization of respiratory events and patterns, assessment of gas exchange, in addition to examining sleep features, the impact of respiratory disturbances on sleep, and the efficacy of treatment.

Unfortunately, polysomnography is not available in all centres and is often used selectively in the assessment of infants with CL/P, including in those with Robin sequence, in those where it is available. A case series of 7 infants with Robin sequence who represented in the first 2 months of life after being assessed by experienced paediatricians or neonatologists to not have airway obstruction [7] suggests that even expert clinical assessment of the absence of airway obstruction may be inaccurate. On the other side, clinical assessment can falsely identify obstructive sleep apnoea where polysomnography results are negative [8,9]. Polysomnography provides both more objective assessment of breathing during sleep and quantification of airway obstruction.

ABNORMALITIES ON POLYSOMNOGRAPHY IN INFANTS WITH CLEFT LIP AND/OR PALATE

Few studies have examined polysomnography results in infants across the spectrum of infants with CL/P and only two have included prospectively recruited consecutive infants across CL/P

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Table 1
Polysomnography results in prospectively recruited infants with CL/P prior to palate surgery. Comparisons are limited by differences in groups and event types.

Reference	N	Variables	Groups [mean ± SD, median (range)]		
MacLean et al. 2012 [11]	50		ICL/P	Syndromic	RS
		n	35	7	8
		Age (months)	2.7 ± 2.3		
		AHI (events/h)	16.1 ± 1.9	30.9 ± 7.1	45.2 ± 8.6
		OMAHI (events/h)	7.6 ± 1.2	15.6 ± 5.7	34.3 ± 5.1
		Mean S_pO_2 (%)	97.5 ± 0.4	95.9 ± 0.6	96.1 ± 1.4
		Lowest S_pO_2 (%)	83.2 ± 1.1	78.4 ± 2.2	83.0 ± 1.9
		Mean T_cCO_2 (mmHg)	42.1 ± 1.3	44.5 ± 4.4	45.1 ± 2.5
		Max T_cCO_2 (mmHg)	54.7 ± 1.5	65.7 ± 9.9	60.2 ± 8.8
		Period breathing time (% sleep time)	2.0 ± 0.5	1.5 ± 0.5	1.4 ± 1.8
Cielo et al. 2016 [10]	42		Control	ICP	Micrognathia
		n	8	15	19
		Age (months)	3.7 ± 0.09	3.6 ± 1.4	1.7 ± 1.9
		OAHI (events/h)	2.9 (0.5, 5.5)	3.2 (0.3, 30.7)	20.1 (0.8, 54.7)
		Central apnoea index	2.5 (0.1, 0.1)	2.1 (0.3, 7.5)	1.1 (0, 11.1)
		Mean S_pO_2 (%)	99 (97, 100)	98 (96, 99)	96 (92, 99)
		Nadir S_pO_2 (%)	91 (86, 98)	89 (72, 95)	82 (60, 93)
		Sleep time with S_pO_2 <90% (%)	0 (0, 1)	0 (0, 2)	2.2 (0, 34.6)
		Sleep time with S_pO_2 <95% (%)	0.4 (0, 2)	1.5 (0, 31.7)	38 (87.1)
		Mean T_cCO_2 (mmHg)	39.1 ± 5.9	44 ± 4.6	54.4 ± 9.0
		Peak $P_{ET}CO_2$ (mmHg)	45.9 ± 2.7	49.4 ± 2.6	55.0 ± 8.3
		Sleep time with $P_{ET}CO_2$ >50 torr (%)	0 (0, 0)	0 (0, 1.6)	1.6 (0, 51.9)
		Sleep time with $P_{ET}CO_2$ >45 torr (%)	0 (0, 1.2)	2.4 (0, 30.6)	25.8 (0, 90)

AHI, apnoea-hypopnoea index; HI, hypopnea index; ICL/P, isolated cleft lip and/or palate; ICP, isolated cleft palate; OAI, obstructive apnoea index; OAHI, obstructive AHI; OMAHI, obstructive mixed AHI; RS, Robin sequence; SD, standard deviation; S_pO_2, pulse oxygen saturation; T_cCO_2, transcutaneous carbon dioxide.

types (Table 1). Comparison between these studies is limited by differences in the data presented but both show higher levels of airway obstruction in infants with Robin sequence or micrognathia compared to other CL/P groups, and mean as well as lowest oxygen saturations within an appropriate range for age. Oxygen and carbon dioxide parameters measured by percentage below or above specific values (i.e. <90% or 95% for oxygen, >50 torr or 45 torr for carbon dioxide) appear to differentiate groups with and without airway obstruction better than mean, minimum or, maximum values. Sleep parameters do not differ between groups [10] suggesting sleep is preserved at this age even in the face of significant airway obstruction. Obstructive-mixed apnoea-hyponoea index (OMAHI) correlated with direct measurements of total mandibular length in the first cohort [11] while no relationship was seen between apnoea-hypopnoea (AHI) and radiographically measured mandibular length in the second [10]. Follow-up polysomnography showed that AHI decreased in both cleft groups with oxygen and CO_2 parameters improving in the micrognathic group at 6 months of age in one cohort [10] and improvements in AHI, OMAHI, central apnoea-hypopnoea index and oxygen desaturation index at 3 years of age in the other cohort. Neurodevelopmental scores in infants with CL/P did not differ from controls at 6 months of age [10] but were lower in those with CL/P compared to controls for receptive and expressive language at 3 years of age in another cohort [12]. Outcomes at 3 years of age were associated with polysomnographic measures from infancy; more active/rapid eye movement sleep in infancy was associated with better cognition at 3 years of age, higher OMAHI in infancy was associated with more problem behavior at 3 years of age, and lower AHI in infancy was associated with lower weight at 3 years of age [12]. With this small body of work, there is a need for larger, longitudinal studies to better understand the spectrum of breathing concerns in infants with CL/P and how these relate to later outcomes.

ABNORMALITIES ON POLYSOMNOGRAPHY IN INFANTS WITH ROBIN SEQUENCE

Infants with Robin sequence, defined by micrognathia, glossoptosis, and airway obstruction, often receive care with infants with CL/P as the majority of infants with Robin sequence have a palatal cleft. The literature on polysomnography for infants with Robin sequence is much more extensive than that of the broader group of CL/P. The majority of studies focus on treatment and report polysomnography results as summaries (eg. 4 of 4 showed obstruction) or descriptions (e.g. all decreased AHI after surgery) rather than discreet data. Four studies reported polysomnography results from retrospective cohorts of infants with Robin sequence (Table 2); 3 showed substantive elevation in mean measures of airway obstruction and decreases in oxygen parameters [13–15]

Table 2
Polysomnography results in retrospective cohorts of infants with Robin sequence. Comparisons are limited by differences in age, event types, and event definitions.

Reference	*N*	Variables	Result [mean/range, mean ± SD, median (interquartile range)]
Anderson et al. 2011 [13]	13	Age at PSG	1.6 months
		OAHI (events/h)	33.5
		OAI (events/h)	25.2
		HI (events/h)	8.3
		Nadir S_pO_2 (%)	80.2
		Peak T_cCO_2 (mmHg)	58.8
Daniel et al. 2013 [14]	39	Age at PSG	5–141 days
		AHI (events/h)	35.9
		OAHI (events/h)	28.2
		REM OAHI (events/h)	43.7
		Nadir S_pO_2 (%)	79.1
		Peak T_cCO_2 (mmHg)	57.9
Costa et al. 2014 [15]	74	Age at palatoplasty	18 ± 10.5 months
		AHI before palaotplasty (events/h)	3.7 ± 3.5
Khayat et al. 2017 [16]	46	Age at PSG	0.8 ± 0.3 years
		OAHI (events/h)	1.91 (0.4–5.9)
		CI (events/h)	1.5 (0.6–3.0)
		Mean S_pO_2 (%)	98 (96–99)
		Nadir S_pO_2 (%)	82 (77–86)
		Peak T_cCO_2 (mmHg)	49 (44–55)

AHI, apnoea-hypopnoea index; CI, central index; HI, hypopnea index; OAI, obstructive apnoea index; OAHI, obstructive AHI; OMAHI, obstructive mixed AHI; REM, rapid eye movement sleep; SD, standard deviation; S_pO_2, pulse oxygen saturation; T_cCO_2, transcutaneous carbon dioxide.

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