Sleep-Disordered Breathing among Newborns with Myelomeningocele

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In a matched cohort study, we report that the apnea-hypopnea index is significantly higher in neonates with myelomeningocele (34 ± 22) compared with age-matched controls (19 ± 11; $P = .021$). Assessment of newborns with myelomeningocele for sleep-disordered breathing may facilitate early treatment; the impact on long-term neurodevelopment is unknown. *(J Pediatr 2017;■■:■■-■■).*

Spina bifida is the most common permanently disabling birth defect in the US.[1] Myelomeningocele is the most severe form of spina bifida and is usually accompanied by Chiari II malformations. Despite the recent introduction of fetal surgery to close the spinal defect and reduce the need for ventriculoperitoneal shunts related to Chiari II malformations, long-term neuromotor and intellectual disabilities are expected for most children with myelomeningocele.[2]

Obstructive sleep apnea, central sleep apnea, and sleep-related hypoventilation occur in more than one-half of children with repaired myelomeningocele and Chiari II malformations.[3-5] The abnormal sleep physiology is multifactorial, related to the level of spinal defect; presence of congenital and acquired brainstem abnormalities; musculoskeletal factors; and pulmonary abnormalities. Yet, in clinical practice, routine assessment for sleep-disordered breathing (SDB) is not commonplace for children with myelomeningocele.

Sleep apnea and hypoventilation may be highly consequential, and are potentially treatable, for this patient population. SDB is associated with sudden death in adults with myelomeningocele (relative risk 4.6, 95% CI 2.9-7.3).[6] Emerging evidence suggests that for otherwise healthy children, even mild symptoms of SDB during infancy, such as parent-reported snoring, lead to long-term risk for adverse neurobehavioral consequences.[7,8] However, an extensive literature review revealed no published data on the prevalence of SDB in newborns with repaired myelomeningocele.

We hypothesized that for patients with myelomeningocele, SDB could be present as early as the newborn period, despite recent surgical repair. We designed this matched cohort study to assess the frequency and severity of SDB among newborns with myelomeningocele compared with age-matched newborns who required intensive care but did not have congenital anomalies.

Methods

This study was approved by the Institutional Review Board, and a parent of each participant provided written informed consent. Newborns who were admitted to our level IV neonatal intensive care unit (NICU) after myelomeningocele repair from December 2014 to October 2016 were eligible. Inclusion criteria were fetal or postnatal repair of myelomeningocele and gestational age at delivery >33 weeks. Exclusion criteria were additional congenital anomalies that predispose to SDB (eg, severe micrognathia), or prematurity with gestational age of <33 weeks. Control infants were newborns >33 weeks of gestational age who required NICU care but did not have congenital anomalies and had been recruited for separate research studies. The most common primary admission indication was prematurity. Cases and controls were matched individually by postmenstrual age at the time of the polysomnogram recording.

When medically stable, each newborn underwent a 12-hour attended polysomnogram in the NICU. All infants with myelomeningocele had received their surgical repair prior to polysomnography; none were receiving narcotics or other respiratory depressants at the time of polysomnography. An experienced, registered polysomnographic technologist monitored the study at the bedside and recorded behavioral observations. Polysomnograms included a 9-channel neonatal-montage electroencephalogram (EEG), bilateral electrooculogram, chin surface electromyography (EMG), chest and abdominal excursion belts (inductance plethysmography), nasal pressure, nasal/oral airflow (thermocouples), snoring sensor, oxygen saturation, ECG, bilateral anterior tibialis surface EMG, digital video, and transcutaneous CO_2 monitor. Each polysomnogram was scored according to standard neonatal scoring guidelines,[9] and reviewed and interpreted by a pediatrician board-certified in sleep medicine.

AHI	Apnea-hypopnea index
NICU	Neonatal intensive care unit
SDB	Sleep-disordered breathing

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The primary outcome was the apnea-hypopnea index (AHI; number of scored respiratory events per hour of sleep).[10] Additional standard, objective measures were extracted from each polysomnogram. A systematic review of each patient's chart was completed to abstract information regarding the neonatal admission, subsequent subspecialty care, emergency department visits, and hospital admissions. Demographic and clinical data were managed using REDCap electronic data capture tools hosted at Michigan Medicine (Ann Arbor, MI).[11]

Parents completed standardized questionnaires to assess basic measures of development (Ages and Stages)[12] and quality of life (Infant Toddler Quality of Life Questionnaire)[13,14] when the infants reached 6 months.

The data were analyzed using SPSS Statistics 24 (Armonk, New York). Data for each myelomeningocele subject were compared with an individually matched control subject using Mann-Whitney-Wilcoxon tests. In exploratory analyses of categorical variables, Fisher exact and Kruskal-Wallis tests were used. As this was an initial investigation in this area of research, our priority was to maintain sensitivity to potential associations; we did not adjust for multiple comparisons and $P \leq .05$ was considered significant.

One newborn with a postnatally repaired myelomeningocele was older than the rest of the cohort at the time of the polysomnogram ($44^{4/7}$ weeks postmenstrual age) and an age-matched control was not available. This subject was excluded from the matched analysis; however, the individual's data are presented with description of the full myelomeningocele cohort.

Results

Twenty newborns with myelomeningocele were included (5 fetal repair and 15 postnatal repair). The clinical and demographic details of the cases and age-matched controls are presented in **Table I**.

The overall AHI was higher for infants with myelomeningocele than for controls (mean 34.2 ± 21.9 vs 19.3 ± 11.1; $P = .021$; **Figure**; available at www.jpeds.com). AHI was higher for neonates with myelomeningocele during both quiet sleep ($P = .015$) and active sleep ($P = .015$). Similarly, the hypopnea index was higher in the myelomeningocele cohort than the controls ($P = .044$). Most of the respiratory events were hypopneas, and most of the apneas were central (**Table II**).

The duration of admission was significantly longer for neonates with myelomeningocele than for control subjects (**Table I**, 17.3 ± 17.0 vs 7.3 ± 3.9, $P < .001$). Regression analysis did not reveal an association between AHI and length of stay.

The AHI was not different between the 5 infants who underwent fetal myelomeningocele repair (median AHI 29.0; IQR 26.8, 33.0) and the 15 who had postnatal repair (median AHI 29.6; IQR 20.8, 44.6). The AHI did not vary significantly by myelomeningocele level (n = 10 lumbar 24.9 ± 5.5, n = 6 sacral 43.7 ± 10.9, n = 3 thoracic 6.2 ± 9.0, $P = .09$), nor by the presence of a Chiari II malformation (n = 16 with Chiari II 31.4 ± 23.4, n = 4 with no Chiari II 39.3 ± 16.2, $P = .32$). Among the 20 neonates with myelomeningocele, 5 underwent ventriculoperitoneal shunt placement before their neonatal polysomnogram, 7 underwent shunt placement after the polysomnogram, and 8 did not require shunt placement in the first 6 months of life. Of the 5 with fetal repairs, 2 required shunt placement (1 at age 3 months and 1 at 7 months). Both infants received shunts after they presented with brief resolved unresponsive events 4-6 weeks after their neonatal discharge. One had neonatal AHI = 33, and the other had neonatal AHI = 9.9.

Six-month follow-up surveys were returned for 15 myelomeningocele subjects and 11 control subjects. There were no scored delays in any domains for 9 of the 11 control subjects with completed questionnaires. One control infant had delayed problem solving and another had personal-social delay. Four of the 15 infants with myelomeningocele had delays, and in multiple domains including gross motor, fine motor, problem solving, and personal-social. One was delayed in all 5 domains. There was no difference in neonatal AHI among infants with or without developmental delay at age 6 months (36.0 ± 24.4 vs 29.0 ± 13.1. $P = .78$).

On the Infant Toddler Quality of Life Questionnaire, parents of control infants reported their infants' overall health as "fair"

Table I. Characteristics of 19 newborns with myelomeningocele and their age-matched controls

Clinical characteristic	Patients with myelomeningocele (n = 19)	Control patients (n = 19)
Mean gestational age at birth (wk)	36.6 ± 2.1	36.9 ± 2.3
Mean postmenstrual age at time of polysomnogram (wk)	37.5 ± 2.1	37.5 ± 2.2
Mean chronological age at time of polysomnogram (d)	6.2 ± 3.7	4.7 ± 4.6
Female sex (n)	8	9
Mean duration of initial postnatal admission (d)	17.3 ± 17.0	7.3 ± 3.9
Timing of myelomeningocele repair		
Fetal	5	
Postnatal	14	
Myelomeningocele spinal level		
Thoracic	3	
Lumbar	10	
Sacral	6	
Chiari II malformation confirmed at birth	15*	
Ventriculoperitoneal shunt placed prior to polysomnogram	4	
Number of emergency department visits in first 6 mo (median)	0 (range 0-3)	0 (range 0-2)
Number of postneonatal hospital admissions in first 6 mo (median)	1 (range 0-2)	0 (range 0-0)

*Two of 5 newborns with fetal myelomeningocele repair had a Chiari II malformation.

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