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Polysomnography in Preterm Infants and Children With Chronic Lung Disease

Sharon A. McGrath-Morrow, MD, MBA*, Timothy Ryan, Brian M. McGinley, MD, Sande O. Okelo, MD, Laura M. Sterni, MD, and J. Michael Collaco, MD, MBA

¹Eudowood Division of Pediatric Respiratory Sciences, Johns Hopkins University School of Medicine, Baltimore, Maryland

Summary

Objective—To determine the utility of overnight polysomnography (PSG) in assessing pulmonary reserve in stable preterm children with chronic lung disease (CLD). Study design: A retrospective review and descriptive study of overnight PSGs and clinic visits of preterm infants/children less than 3 years of age who were diagnosed with bronchopulmonary dysplasia at discharge from the hospital and enrolled in the Johns Hopkins CLD patient registry between 2008 and 2010.

Results—Sixty-two clinically stable patients underwent at least one overnight polysomnogram for clinical indications. The majority of patients were referred for oxygen titration (71%). PSGs from first studies revealed a mean respiratory disturbance index (RDI) of 8.2 ± 10.1 events/hr and a mean O₂ saturation (SaO₂) nadir of $86.2 \pm 5.7\%$. In patients who underwent more than one PSG ($n = 23$), a significant decrease in RDI ($P < 0.001$) was found between the first study (mean age: 8.0 ± 3.3 months) and second study (mean age: 13.4 ± 5.2 months). Outpatient clinical measures of mean room air SaO₂ and respiratory rate were not predictive of PSG measures of RDI and SaO₂ nadir.

Conclusion—Mean RDI was higher in stable preterm infants/children with CLD compared to previously published controls. RDI decreased with age in stable preterm infants/children with CLD suggesting improved pulmonary reserve with age. Outpatient clinical measures (respiratory rate and room air SaO₂) did not correlate with RDI and SaO₂ nadir indicating that overnight PSG is more sensitive in assessing pulmonary reserve than outpatient clinical measures.

Keywords

Polysomnography; prematurity; bronchopulmonary dysplasia

*Correspondence to: Sharon A. McGrath-Morrow, MD, MBA, Eudowood Division of Pediatric Respiratory Sciences, David M. Rubenstein Building, Suite 3075B, 200 North Wolfe Street, Baltimore, MD 21287-2533. smcgrath@jhmi.edu.

Additional Supporting Information may be found in the online version of this article.

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INTRODUCTION

Chronic lung disease (CLD) of prematurity is often manifested by poor alveolar growth and airway inflammation, leading to decreased pulmonary reserve.^{1,2} As a result, many preterm infants with CLD are discharged to home on supplemental oxygen. No general consensus exists regarding the assessment of pulmonary reserve or the optimal timing for weaning home supplemental oxygen in children with CLD.

Preterm children with a history of CLD are at higher risk for respiratory complications and re-hospitalization following discharge to home.³ A more accurate assessment of pulmonary reserve may help detect children who are more likely to have a pulmonary decompensation during a viral illness or an environmental exposure. This in turn, could allow for the earlier initiation of preventative strategies and more aggressive treatment of underlying cardiopulmonary disease. Identifying those who may be at increased risk for pulmonary exacerbations or other complications may also help lessen acute medical care usage and lower the economic cost of this chronic disease.⁴

Oxygen saturations (SaO_2) between 92% and 96% are considered desirable for optimal growth and development of preterm children with CLD who have mature retinal vasculature.^{5,6} However, brief pulse oximetry assessments during outpatient clinic visits may not be accurate enough to evaluate pulmonary reserve or assess supplemental oxygen needs, particularly during periods of stress.⁶ Although intermittent and continuous pulse oximetry at home can be useful, inaccurate measurements are common with continuous monitoring and intermittent spot checks may underestimate oxygen desaturation during feedings, activity, and sleep.^{6,7} Although overnight polysomnography (PSG) has been recommended by some as a more accurate test for assessing pulmonary reserve and for determining the appropriate timing for weaning of supplemental oxygen in preterm children with CLD,⁶ there is little data to support the routine use of PSGs to wean or assess supplemental oxygen needs in this population.

We hypothesized that the use of overnight PSGs in stable preterm infants/children with CLD would be more sensitive in detecting intermittent hypoxia, and hence decreased pulmonary reserve, than the use of pulse oximetry in the outpatient setting. To this end, we reviewed overnight PSGs in a cohort of stable preterm infants/children with CLD who were referred for overnight PSGs to assess supplemental oxygen needs and to evaluate for the presence of sleep-disordered breathing (SDB). We also evaluated differences in PSG measurements by age using cross-sectional and longitudinal PSG data.

METHODS

Study Population

The Institutional Review Board of the Johns Hopkins Medical Institutions approved the patient registry and informed consent was obtained. Inclusion criteria for the registry included (i) a diagnosis of BPD at the time of NICU discharge, (ii) a diagnosis of CLD by the staffing pediatric pulmonologist as defined by the presence of respiratory symptoms (tachypnea or wheezing), the use of chronic respiratory medications (diuretics or inhaled

corticosteroids), and/or the use of home supplemental oxygen at the first clinic visit, (iii) born at 34 weeks of gestation, and (iv) less than 3 years of age at the time of the visit. Of the 194 recruited subjects in the registry, 62 underwent PSG for clinically indicated reasons, between April 2004 and June 2010. Studies were categorized by the primary intended purpose of study as defined by the ordering physician, namely (i) to titrate or wean supplemental oxygen or (ii) to assess for SDB or adequacy of ventilator settings. All patients undergoing an overnight PSG had a stable respiratory status at the time of the study.

Supplemental Oxygen Titration Protocol

Baseline titration goals were to maintain SaO_2 at 94% or greater. If the baseline SaO_2 was greater than 94%, then supplemental oxygen would be weaned. Oxygen was not increased for transient oxygen desaturations unless SaO_2 were 90% and SaO_2 drops occurred 3 times an hour or if SaO_2 drops were severe at <85%. If the patient dropped below an optimal SaO_2 , supplemental oxygen was titrated back up to an optimal SaO_2 , and if the patient had a significant desaturation on a certain level of O_2 , further weaning was not attempted.

Data Collection

A retrospective review of medical records was performed with regard to use of supplemental oxygen, smoke exposure, and daycare attendance. Clinical variables were based on chart review from the pulmonary visit prior to the polysomnographic study; these variables included respiratory rate, SaO_2 based on brief pulse-oximetry performed on room air, and birth weight. The following indices were extracted from overnight PSGs: SaO_2 nadir (SaO_2 nadir), peak end tidal CO_2 (PetCO_2) level, respiratory disturbance index (RDI), obstructive apneas per hour, hypopneas per hour, mixed events per hour, and central apneas per hour. Percent of TST with SaO_2 below 90% was calculated and oxygen desaturation index (ODI) was determined as number of events per hour with oxygen desaturation 3%. These last two measures were only ascertained for individuals who were maintained on room air during the entire study.

Polysomnography

Physiologic signals that were recorded included electroencephalograms (C3-A2, C4-A1, O1-A2), left and right electrooculograms (EOG), submental and tibial electromyograms (EMG), and electrocardiogram (ECG modified V2 lead). Respiratory effort was measured using thoracic and abdominal piezoelectric crystal effort belts (Respironics, Marietta, GA) or inductive plethysmography (Embla, Broomfield, CO). Oxyhemoglobin saturation was measured via pulse oximetry (Novametrics, Marietta, GA) and PetCO_2 was measured at the nose by infrared capnometry (Novametrics). Nasal airflow was acquired with a nasal cannula (Salter Labs, Arvin, CA) connected to a differential pressure transducer (Pro-Tech, Mukilteo, WA), and oronasal airflow was acquired with thermistor. Sleep staging was performed according to standard criteria.⁸ Arousals were identified according to the American Sleep Disorders Association criteria.^{9,10} Recording systems were either Alice 3 (Healthdyne, Marietta, GA) or Somnologica Studio (Medcare Flaga, Reykjavik). Respiratory events were scored in accordance with standard pediatric criteria.¹¹ Obstructive and mixed apneas were scored if they lasted at least two respiratory cycles in duration. The apnea hypopnea index (AHI) was based on the number of obstructive/mixed apneas and

hypopneas that occurred per hour of total sleep time (TST). Hypopneas were defined as a reduction in airflow of at least 50% with an oxygen desaturation of $\geq 3\%$ or an arousal. Central apneas were scored if they were greater than 20 sec or the duration of two missed breaths as determined by baseline breathing pattern and associated with oxygen desaturation of $\geq 3\%$ or an arousal. The mean RDI was defined as the number of obstructive/mixed apneas, hypopneas, and central apneas per hour of TST.

Statistical Analysis

Data are presented as mean $\pm$ standard deviation (SD), unless otherwise indicated. Statistical calculations were performed using STATA 11.0 (College Station, TX). Statistical differences were accepted at $P < 0.05$ and all t -tests were two-tailed.

RESULTS

Patient Demographics

Sixty-two patients <36 months of age underwent overnight PSGs (Table 1). All PSGs were performed in infants/children who had a clinically stable respiratory status. The most common reason for performing the first PSG was to titrate or wean supplemental oxygen via nasal cannula (71%) and the second most common reason was to rule out obstructive sleep apnea (18%).

For the first PSG ($n = 62$), 55 patients (89%) were on room air at the start of the study. Of the 55 patients started on room air, 41 patients remained on room air throughout the study while 14 patients required the initiation of supplemental oxygen. Seven patients were on supplemental oxygen at the start of the study and remained on supplemental oxygen.

The SaO_2 nadir did not differ between studies conducted with and without supplemental oxygen ($P = 0.25$). The majority of patients (77%) who underwent an overnight PSG were on supplemental oxygen at their first clinic visit. The baseline room air SaO_2 in clinic of patients who underwent an overnight PSG was $97.0 \pm 2.5\%$ ($n = 43$).

Sleep Efficiency, Sleep Architecture, and Respiratory Indices From First PSG

The mean TST for the first overnight PSG was 338.6 ± 72.7 min with a mean sleep efficiency of $84.3 \pm 10.2\%$ ($n = 58$). The proportion of TST spent in non-REM sleep was $68.5 \pm 9.5\%$ and the proportion of TST spent in REM sleep was $31.6 \pm 9.5\%$ ($n = 57$). The mean SaO_2 nadir, PetCO_2 , and RDI for the first PSG were $86.2 \pm 5.7\%$, 52.3 ± 6.4 mmHg, and 8.2 ± 10.1 events/hr, respectively (Table 2). The age of infants/children who underwent a PSG but who were not referred for oxygen titration study, was older than those who were referred for an oxygen titration study ($P < 0.008$). However, there were no differences in respiratory measurements or indices between PSGs done for oxygen titration and PSGs done for other reasons. Using linear regression, no associations were found between RDI or SaO_2 nadir from the first PSG and room air SaO_2 or respiratory rate in the outpatient setting.

RDI Decreased and SaO₂ Nadir Increased With Age

Preterm children with CLD often have more respiratory symptoms in the first few years of life compared to term infants.¹² During this time they are also more likely to be re-hospitalized and to have more upper and lower respiratory illnesses than term infants. This may reflect a decrease in pulmonary reserve secondary to their CLD.¹³ Respiratory problems, however tend to improve by 4–5 years of age.¹⁴ To determine if increasing age in preterm children with CLD correlated with improved respiratory measurements by PSG, a crosssectional analysis of PSG measurements by age was done (Table 3). We found that the mean SaO₂ nadir increased from $84.7 \pm 6.1\%$ in infants 12 months of age to $88.1 \pm 4.0\%$ in children 12–18 months of age ($P < 0.01$). RDI decreased from 9.0 ± 9.4 events/hr in infants 12 months of age to 3.4 ± 2.9 events/hr in children 18–36 months of age ($P < 0.01$).

Longitudinal changes were then evaluated among 23 patients who underwent at least two PSGs within the first 3 years of life (Table 4). For the first PSG, 83% of studies were conducted to wean or titrate supplemental oxygen and 17% to evaluate SDB, and for the second PSG, 87% were conducted to wean or titrate supplemental oxygen, and 13% to evaluate SDB. We found that RDI significantly decreased between the first and second PSG ($P < 0.001$). A significant decrease was also found in the number of hypopneas and central apneas per hour as well as a decreasing trend for mixed apneas per hour between the first and second study. Although changes in SaO₂ nadir and number of obstructive apneas per hour were not significant, there was a trend towards a higher mean SaO₂ nadir and a lower frequency of obstructive events in the second study compared to the first ($P < 0.15$ and $P < 0.07$, respectively).

Polysomnographic Indicators of Hypoxia

We next were interested in determining if indices of hypoxia on PSGs were associated with outpatient measures of respiratory rate and SaO₂. Measurements were obtained from PSGs done entirely on room air and included SaO₂ nadir, ODI, % of TST with SaO₂ below 90%, and central apneas associated with desaturation. We found that central apneas with oxygen desaturation were frequent in infant/children with stable CLD. The mean average duration of central apneas was 5.8 ± 2.1 sec, the mean longest duration for central apneas was 8.9 ± 3.0 sec, and there were no central apneas 20 sec or longer in duration. We found no association between SaO₂ nadir, ODI, % of TST with SaO₂ below 90%, central apneas with oxygen desaturation, and respiratory rate and room air SaO₂ in clinic (Table 5).

In 24 studies, we also evaluated the frequency of central apneas associated with an arousal or a bradycardia. We found that few central apneas were associated with arousals. However, there was an association between a higher frequency of central apneas with bradycardia and a higher respiratory rate in clinic (Table 5).

We also examined associations between oxygen ODI and % of TST with SaO₂ below 90% with other PSG values of SDB (Supplemental Table 1). We found that ODI was associated with SaO₂ nadir (R value = 0.62) and RDI (R value = 0.70). Associations were also found between % of TST with SaO₂ below 90% and SaO₂ nadir (R value = 0.77) and RDI (R value = 0.63). Taken together these findings suggest that ODI, % of TST with SaO₂ below

90%, SaO₂ nadir and RDI may be useful markers in assessing gas exchange abnormalities during sleep and may be proxy markers for pulmonary reserve in preterm children with CLD.

DISCUSSION

Maintaining normal SaO₂ in preterm infants and children with CLD can improve growth, attenuate pulmonary hypertension, and decrease the risk for sudden death associated with hypoxemia.¹⁵⁻¹⁷ Assessment of pulmonary reserve in this fragile population can be difficult in an outpatient clinical setting. In this retrospective review, we analyzed overnight PSGs from preterm infants and children with CLD referred for either an oxygen titration study or to assess SDB. The mean room air SaO₂ recorded in clinic for these patients was 97%, a value considered within the normal range for healthy term and preterm infants.¹⁵ In children that underwent an overnight PSG, we found no correlation between mean respiratory rate and room air SaO₂ in the outpatient setting and mean RDI and SaO₂ nadir by overnight PSG. These findings suggest that outpatient assessment of pulmonary status, using respiratory rate and room air SaO₂ as indicators of pulmonary reserve, may not be sensitive enough to detect intermittent hypoxia and decreased pulmonary reserve in preterm infants/children with a history of CLD. Finally, we found that respiratory measurements by PSGs improved with age in preterm infants/children with CLD and that ODIs and time spent below 90% SaO₂ may be useful measurements for assessing pulmonary reserve in these children.

PSGs have been traditionally used for diagnosing SDB and evaluating gas exchange abnormalities during sleep in children and adults.^{18,19} This is done through continuous monitoring of SaO₂, end tidal CO₂, and the assessment of SDB patterns during different stages of sleep. Supporting the utility of PSGs, others have found that short-term awake SaO₂ have not been predictive of oxygen desaturation during sleep or with prolonged monitoring.^{7,17} We also did not find a correlation between respiratory rate and SaO₂ in the outpatient setting and SaO₂ nadir or RDI by overnight PSG. In our study, the preterm infants/children with CLD had higher RDIs and lower SaO₂ nadir compared to published normal values in children who underwent overnight PSGs.²⁰ Traeger et al. reported that normal children, between the ages of 2 and 9 years old, had a mean RDI of 0.4 ± 0.6 events/hr, mean SaO₂ nadir of $92 \pm 3\%$, and mean central apnea indexes of 0.08 ± 0.14 events/hr. In our study, the mean RDI and mean central apnea index were higher in all age groups suggesting decreased pulmonary reserve with CLD. Central apneas in our study were scored if they were greater than 20 sec or the duration of two missed breaths as determined by baseline breathing pattern and associated with oxygen desaturation of $\geq 3\%$ or an arousal. The majority of central apneas in our study were brief and associated with oxygen desaturation, likely reflective of diminished oxygen reserve. Interestingly, we found an association between higher respiratory rate in clinic and an increased frequency of central apneas with bradycardia on the PSG. Although validation is needed, this type of central apnea may indicate more significant pulmonary disease in this population. Causes that may contribute to oxygen desaturation during central apneas during sleep in children with CLD include impaired alveolarization, control of breathing abnormalities, high metabolic rate, increased intrapulmonary shunting, and alterations in pulmonary mechanics.²¹ Preterm

infants have also been shown to have increased chest wall compliance with paradoxical breathing, increased endexpiratory lung volumes above resting lung volumes, decreased lung volumes, and higher respiratory rates.²²⁻²⁷

It has been observed that many infants and children with a history of BPD have clinical improvement with age, however little quantitative data has been published on age-related changes in pulmonary reserve in this population. In our study, we found that the mean RDI decreased with age. This may indicate an improvement in pulmonary reserve, due to postnatal alveolar “catch up growth” and improved lung mechanics.²⁸ Although limited by size, our study provides additional insight into the longitudinal changes in PSG metrics that can occur in stable infants and children with CLD. Since postnatal alveolar growth occurs primarily during the first 2 years of life, PSG may help distinguish between children with CLD who have improved pulmonary reserve (a proxy for alveolar growth) versus those who do not, prompting more aggressive follow-up and intervention for those who may be at increased risk for respiratory morbidity.

Although brief intermittent oxygen desaturations associated with apneas were common in the younger children that we studied, it is unknown whether they adversely affect health outcomes. Older children with hypoxia and SDB have been shown to be at increased risk of neurocognitive morbidity.^{29,30} Studies in rodents have shown that intermittent hypoxia may have a detrimental effect on cognitive function due to increased oxidative stress and inflammation^{31,32} and recent studies in preterm NICU patients have suggested that hypoxemic events or lower oxygen target levels may adversely affect clinical outcomes.^{33,34} Although not addressed in this study, the impact of anemia may also compound the adverse effects of hypoxia. Additional prospective studies are needed to determine if intermittent hypoxic events during sleep can have detrimental effects on health outcomes of preterm children with CLD after discharge from the NICU.

Our study has several limitations. It is retrospective in nature and patients were primarily recruited from an urban setting with a selection bias towards preterm infants and children at high risk for respiratory morbidity. Our study also did not include preterm infants without a history of CLD but who may have decreased pulmonary reserve and be at increased risk for respiratory morbidity when stressed. PSGs were also only performed in patients in which there was a clinical indication, primarily that of weaning or titrating oxygen. Longitudinal studies of preterm infants with and without CLD following discharge from the NICU would help to further address the natural history of pulmonary reserve in these populations. Also, before PSGs can be widely recommended for oxygen weaning in preterm infants with CLD a prospective study is warranted to study the significance of increased RDIs, oxygen desaturations, and other PSG metrics on health outcomes, especially in view of the expense, time required for testing, and the need for an experienced technician and sleep specialist to interpret the data. Nevertheless, while other tests such as continuous pulse oximetry can help with assessing pulmonary reserve, overnight PSGs in a controlled environment can provide critical information on gas exchange, RDI, and SDB during different stages of the sleep cycle in a population at high risk for respiratory morbidity.

In conclusion we found that the use of overnight PSG in preterm children with CLD may be useful in identifying children with decreased pulmonary reserve compared to assessment in the outpatient setting. Furthermore, cross-sectional and longitudinal analyses of PSGs from preterm infants and children with CLD indicated an overall improvement in pulmonary reserve with age. Prospective studies are needed to fully assess longitudinal changes in PSGs with age and to determine if PSG respiratory indices correlate with respiratory health outcomes in infants and children with CLD.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Kallapur SG, Jobe AH. Contribution of inflammation to lung injury and development. *Arch Dis Child Fetal Neonatal Ed.* 2006; 91:F132–F135. [PubMed: 16492951]
2. Jobe AJ. The new BPD: an arrest of lung development. *Pediatr Res.* 1999; 46:641–643. [PubMed: 10590017]
3. Walsh MC, Szeffler S, Davis J, Allen M, Van Marter L, Abman S, Blackmon L, Jobe A. Summary proceedings from the bronchopulmonary dysplasia group. *Pediatrics.* 2006; 117:S52–S56. [PubMed: 16777823]
4. Greenough A, Alexander J, Burgess S, Bytham J, Chetcuti PA, Hagan J, Lenney W, Melville S, Shaw NJ, Boorman J, Coles S, Pang F, Turner J. Preschool healthcare utilisation related to home oxygen status. *Arch Dis Child Fetal Neonatal Ed.* 2006; 91:F337–F341. [PubMed: 16705008]
5. Kotecha S, Allen J. Oxygen therapy for infants with chronic lung disease. *Arch Dis Child Fetal Neonatal Ed.* 2002; 87:F11–F14. [PubMed: 12091281]
6. Fitzgerald DA, Massie RJ, Nixon GM, Jaffe A, Wilson A, Landau LI, Twiss J, Smith G, Wainwright C, Harris M. Infants with chronic neonatal lung disease: recommendations for the use of home oxygen therapy. *Med J Aust.* 2008; 189:578–582. [PubMed: 19012558]
7. Barratt CW, Vyas H, Hayes-Gill BR, Crowe JA, Flatman D. Detection of previously unrecognized daytime desaturation in children with chronic lung disease. *J Med Eng Technol.* 2007; 31:101–108. [PubMed: 17365434]
8. Rechtschaffen, A.; Kales, A. A manual of standardized terminology, techniques and scoring system for sleep stages of human subjects. Los Angeles: Brain Information Services/Brain Research Institute, University of California; 1968.
9. The AASM manual for the scoring of sleep and associated events—rules, terminology and technical specifications. American Academy of Sleep Medicine. 2007
10. EEG arousals: scoring rules and examples: a preliminary report from the Sleep Disorders Atlas Task Force of the American Sleep Disorders Association. *Sleep.* 1992; 15:173–184. [PubMed: 11032543]
11. American Thoracic Society. Standards and indications for cardiopulmonary sleep studies in children. *Am J Respir Crit Care Med.* 1996; 153:866–878. [PubMed: 8564147]
12. Doyle LW, Anderson PJ. Pulmonary and neurological followup of extremely preterm infants. *Neonatology.* 2010; 97:388–394. [PubMed: 20551709]

13. Doyle LW, Ford G, Davis N. Health and hospitalizations after discharge in extremely low birth weight infants. *Semin Neonatol.* 2003; 8:137–145. [PubMed: 15001150]
14. Bhandari A, Panitch HB. Pulmonary outcomes in bronchopulmonary dysplasia. *Semin Perinatol.* 2006; 30:219–226. [PubMed: 16860162]
15. Ellsbury DL, Acarregui MJ, McGuinness GA, Eastman DL, Klein JM. Controversy surrounding the use of home oxygen for premature infants with bronchopulmonary dysplasia. *J Perinatol.* 2004; 24:36–40. [PubMed: 14726936]
16. Fleming PJ, Blair PS. Sudden unexpected deaths after discharge from the neonatal intensive care unit. *Semin Neonatol.* 2003; 8:159–167. [PubMed: 15001152]
17. Moyer-Mileur LJ, Nielson DW, Pfeffer KD, Witte MK, Chapman DL. Eliminating sleep-associated hypoxemia improves growth in infants with bronchopulmonary dysplasia. *Pediatrics.* 1996; 98:779–783. [PubMed: 8885961]
18. Bhattacharjee R, Kheirandish-Gozal L, Spruyt K, Mitchell RB, Promchiarak J, Simakajornboon N, Kaditis AG, Splaingard D, Splaingard M, Brooks LJ, Marcus CL, Sin S, Arens R, Verhulst SL, Gozal D. Adenotonsillectomy outcomes in treatment of obstructive sleep apnea in children: a multicenter retrospective study. *Am J Respir Crit Care Med.* 2010; 182:676–683. [PubMed: 20448096]
19. Barthlen GM. Nocturnal respiratory failure as an indication of noninvasive ventilation in the patient with neuromuscular disease. *Respiration.* 1997; 64(Suppl 1):35–38. [PubMed: 9380959]
20. Traeger N, Schultz B, Pollock AN, Mason T, Marcus CL, Arens R. Polysomnographic values in children 2–9 years old: additional data and review of the literature. *Pediatr Pulmonol.* 2005; 40:22–30. [PubMed: 15858805]
21. Sands SA, Edwards BA, Kelly VJ, Davidson MR, Wilkinson MH, Berger PJ. A model analysis of arterial oxygen desaturation during apnea in preterm infants. *PLoS Comput Biol.* 2009; 5:e1000588. [PubMed: 19997495]
22. Gaultier C. Respiratory adaptation during sleep in infants. *Lung.* 1990; 168(Suppl):905–911. [PubMed: 2117210]
23. Gaultier C. Cardiorespiratory adaptation during sleep in infants and children. *Pediatr Pulmonol.* 1995; 19:105–117. [PubMed: 7659466]
24. Olinsky A, Bryan MH, Bryan AC. Influence of lung inflation on respiratory control in neonates. *J Appl Physiol.* 1974; 36:426–429. [PubMed: 4820324]
25. Agostoni, E.; Mead, J. Statics of the respiratory system. In: Fenn, WO.; Rahn, H., editors. *Handbook of Physiology, Respiration.* Vol. 1. American Physiological Society; Washington, D.C.: 1964. p. 387–409.
26. Numa AH, Newth CJ. Anatomic dead space in infants and children. *J Appl Physiol.* 1996; 80:1485–1489. [PubMed: 8727530]
27. Hjalmarson O, Sandberg KL. Lung function at term reflects severity of bronchopulmonary dysplasia. *J Pediatr.* 2005; 146:86–90. [PubMed: 15644829]
28. Thurlbeck WM. Postnatal human lung growth. *Thorax.* 1982; 37:564–571. [PubMed: 7179184]
29. Halbower AC, Degaonkar M, Barker PB, Earley CJ, Marcus CL, Smith PL, Prahme MC, Mahone EM. Childhood obstructive sleep apnea associates with neuropsychological deficits and neuronal brain injury. *PLoS Med.* 2006; 3:e301. [PubMed: 16933960]
30. Gozal D, Kheirandish-Gozal L. Neurocognitive and behavioral morbidity in children with sleep disorders. *Curr Opin Pulm Med.* 2007; 13:505–509. [PubMed: 17901756]
31. Row BW. Intermittent hypoxia and cognitive function: implications from chronic animal models. *Adv Exp Med Biol.* 2007; 618:51–67. [PubMed: 18269188]
32. McCoy JG, McKenna JT, Connolly NP, Poeta DL, Ling L, McCarley RW, Strecker RE. One week of exposure to intermittent hypoxia impairs attentional set-shifting in rats. *Behav Brain Res.* 2010; 210:123–126. [PubMed: 20122971]
33. Stenson B, Brocklehurst P, Tarnow-Mordi W. Increased 36-week survival with high oxygen saturation target in extremely preterm infants. *N Engl J Med.* 2011; 364:1680–1682. [PubMed: 21524227]
34. Carlo WA, Finer NN, Walsh MC, Rich W, Gantz MG, Laptook AR, Yoder BA, Faix RG, Das A, Poole WK, Schibler K, Newman NS, Ambalavanan N, Frantz ID III, Piazza AJ, Sanchez PJ,

Morris BH, Laroia N, Phelps DL, Poindexter BB, Cotten CM, Van Meurs KP, Duara S, Narendran V, Sood BG, O'Shea TM, Bell EF, Ehrenkranz RA, Watterberg KL, Higgins RD. Target ranges of oxygen saturation in extremely preterm infants. *N Engl J Med*. 2010; 362:1959–1969. [PubMed: 20472937]

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TABLE 1**Study Population Demographics**

	All subjects, mean ($\pm$ SD) [range]
n	62
Sex (% male)	74.2
Race (% White)	32.3
Gestational age (weeks)	25.8 $\pm$ 1.9 [23–34]
Birth weight (g)	812 $\pm$ 333 [469–2324] (n = 57)
Age at discharge (months)	4.7 $\pm$ 3.4 [0.2–24.5] (n = 51)
Age at first clinic visit (months)	7.0 $\pm$ 3.7 [3.4–25.7]
Supplemental oxygen (% on at first clinic visit)	77.4
Respiratory rate in clinic (bpm) ^I	46.3 $\pm$ 14.3 [20–80] (n = 56)
Room air pulse oximetry in clinic (% saturation) ^I	97.0 $\pm$ 2.5 [89–100] (n = 43)
Second-hand smoke (% ever exposed)	24.6 (n = 57)
Daycare (% ever attended)	31.0 (n = 58)

^I At visit just prior to first polysomnography.

TABLE 2

Mean Respiratory Indices From First Polysomnography

Mean ($\pm$ SD) [range]	All first studies	Oxygen titration via nasal cannula	Other sleep-disordered breathing ^I	Unpaired <i>t</i> -test, <i>P</i> -value
n	62	44 (71%)	18 (29%)	—
Age at study (months)	10.2 $\pm$ 5.4 [2.5–31.4]	9.0 $\pm$ 3.2 [3.4–17.5]	13.0 $\pm$ 8.2 [2.5–31.4]	0.008
Studies conducted without supplemental O ₂ (%)	66.1	61.4	77.8	0.22
Oxygen saturation nadir (%)	86.2 $\pm$ 5.7 [64–96]	85.8 $\pm$ 4.90 [64–95]	87.2 $\pm$ 7.3 [70–96]	0.38
Oxygen saturation nadir for studies without supplemental O ₂ (%)	86.8 $\pm$ 5.5 [70–96] (n = 41)	86.6 $\pm$ 3.5 [80–95] (n = 27)	87.0 $\pm$ 8.3 [70–96] (n = 14)	0.84
Peak end-tidal CO ₂ (mmHg)	52.3 $\pm$ 6.3 [42–76] (n = 60)	52.6 $\pm$ 6.4 [42–76]	51.4 $\pm$ 6.3 [42–64] (n = 16)	0.54
RDI (events/hr)	8.2 $\pm$ 10.1 [0–43]	7.8 $\pm$ 8.3 [0–43]	9.0 $\pm$ 13.8 [0–42]	0.66
Obstructive apnea (events/hr)	0.7 $\pm$ 1.6 [0–7.3]	0.6 $\pm$ 1.5 [0–7]	0.8 $\pm$ 1.9 [0–7.3]	0.80
Hypopnea (events/hr)	2.8 $\pm$ 6.1 [0–33]	2.4 $\pm$ 5.2 [0–33]	3.6 $\pm$ 7.9 [0–28.1]	0.50
Mixed apnea (events/hr)	1.1 $\pm$ 2.1 [0–13]	1.2 $\pm$ 2.3 [0–13]	0.6 $\pm$ 1.3 [0–5.6]	0.32
Central apnea (events/hr)	3.6 $\pm$ 4.6 [0–24.4]	3.4 $\pm$ 3.6 [0–16.1]	4.1 $\pm$ 6.5 [0–24.4]	0.63

^I Includes 3 studies for evaluation of apnea of prematurity, 11 studies for obstructive apnea, 1 for oxygen initiation, 1 for titration of oxygen via tracheostomy, and 2 studies for titration of ventilator settings.

TABLE 3 Cross-Sectional Analysis of Respiratory Indices in CLD Patients With Increasing Age^I

Mean (±SD) [range]	0–12 Months	12–18 Months	18–36 Months
n	57	19	15
Age at study (months)	7.9 ± 2.4 [2.5–11.9]	14.1 ± 1.4 ** [12.1–17.5]	25.9 ± 5.8 ** [18.7–35.6]
Oxygen saturation nadir (%)	84.7 ± 6.1 [64–95]	88.1 ± 4.0 ** [78–94]	87.0 ± 4.2 [81–94]
Peak end-tidal CO ₂ (mmHg)	53.2 ± 6.1 [42–76] (n = 56)	51.2 ± 6.0 [43–68] (n = 18)	52.9 ± 3.9 [44–60]
RDI (events/hr)	9.0 ± 9.4 [0.2–43]	5.2 ± 9.6 [0–43]	3.4 ± 2.9 ** [0.2–8.2]
Obstructive apnea (events/hr)	0.7 ± 1.7 [0–7.3]	0.6 ± 1.3 [0–4.7]	0.5 ± 1.3 [0–4.2]
Hypopnea (events/hr)	2.4 ± 4.9 [0–28.1]	2.5 ± 7.5 [0–33]	0.6 ± 1.3 * [0–4.9]
Mixed apnea (events/hr)	1.2 ± 2.3 [0–13]	0.7 ± 1.3 [0–5.5]	0.2 ± 0.4 ** [0–1.6]
Central apnea (events/hr)	4.4 ± 4.7 [0–24.4]	1.4 ± 1.2 ** [0–4]	2.1 ± 2.1 * [0.1–7.4]

^I A total of 98 studies were conducted on the 62 subjects in this study. For this table, 7 studies were dropped, including 3 studies obtained after 36 months, 1 for titration of oxygen via tracheostomy, and 3 studies for titration of ventilator settings.

* Statistically different than 0–12 months group ($P < 0.05$) by regression clustered by individual as an individual may be represented in more than one group.

** Statistically different than 0–12 months group ($P < 0.01$) by regression clustered by individual as an individual may be represented in more than one group.

TABLE 4

Longitudinal Comparison of Respiratory Indices From First and Second Polysomnographies *

	First study, mean ($\pm$ SD) [range]	Second study, mean ($\pm$ SD) [range]	Paired <i>t</i> -test <i>P</i> -value
N	23	23	—
Age at study (months)	8.0 $\pm$ 3.3 [3.3–16.3]	13.4 $\pm$ 5.2 [4.0–24.1]	<0.001
Oxygen saturation nadir (%)	83.6 $\pm$ 5.4 [70–91]	85.7 $\pm$ 6.5 [69–92]	0.15
Peak end-tidal CO ₂ (mmHg)	54.6 $\pm$ 8.4 [42–76] (n = 22)	53.3 $\pm$ 5.4 [43–68] (n = 22)	0.47
RDI (events/hr)	14.5 $\pm$ 13.3 [0.5–43]	5.2 $\pm$ 6.3 [0.2–24.3]	<0.001
Obstructive apnea (events/hr)	1.3 $\pm$ 2.0 [0–7]	0.5 $\pm$ 1.3 [0–4.7]	0.07
Hypopnea (events/hr)	5.5 $\pm$ 9.2 [0–33]	0.9 $\pm$ 2.0 [0–9.5]	0.015
Mixed apnea (events/hr)	2.3 $\pm$ 3.1 [0–13]	0.8 $\pm$ 1.9 [0–8.9]	0.05
Central apnea (events/hr)	5.2 $\pm$ 5.9 [0.2–24.4]	2.8 $\pm$ 2.7 [0–11.8]	0.022

* Twenty-seven subjects had two or more studies. Two subjects with tracheostomies $\pm$ ventilators and two subjects older than 3 years of age at second study were excluded.

TABLE 5

Polysomnographic Indicators of Hypoxemia*

	Mean $\pm$ SD [range]	Associated with respiratory rate in clinic? ¹	Associated with room air oxygen saturation in clinic? ²
Oxygen saturation nadir (%)	86.5 $\pm$ 5.5 [70–95] (n = 39)	No (<i>P</i> = 0.64; n = 36)	No (<i>P</i> = 0.59; n = 31)
Oxygen desaturation index (events/hr)	7.1 $\pm$ 12.5 [0–50.2] (n = 34)	No (<i>P</i> = 0.75; n = 33)	No (<i>P</i> = 0.74; n = 29)
Time spent below 90% (% of total sleep time)	0.63 $\pm$ 1.72 [0–8.9] (n = 27)	No (<i>P</i> = 0.47; n = 25)	No (<i>P</i> = 0.88; n = 22)
Central apnea associated with desaturation (# of events) ²	19.0 $\pm$ 32.3 [0–173] (n = 35)	No (<i>P</i> = 0.62; n = 32)	No (<i>P</i> = 0.99; n = 29)
Central apnea associated with arousal (% of total central apneas)	3.0 $\pm$ 9.1 [0–33.3] (n = 24)	No (<i>P</i> = 0.06; n = 23)	No (<i>P</i> = 0.90; n = 21)
Central apnea associated with bradycardia (% of total central apneas)	7.2 $\pm$ 16.3 [0–66.7] (n = 24)	Yes (<i>P</i> = 0.005; n = 23)	No (<i>P</i> = 0.59; n = 21)

¹ Association was determined by linear regression with polysomnography index as the dependent variable and adjusted for age at time of clinic visit in months. The reported *P*-value is for the regression co-efficient for the independent variable (i.e., respiratory rate or room air oxygen saturation).

² By scoring definition, central apneas were associated with a desaturation of $\geq 3\%$ or were longer than 20 sec. The mean average duration for central apneas was 5.8 $\pm$ 2.1 sec and the mean longest duration for central apneas was 8.9 $\pm$ 3.0 sec. The overall longest central apnea recorded on any of these 35 studies was 14.5 sec, thus all central apneas observed were associated with desaturation.

* All indices in this table were from first studies conducted completely on room air. Two subjects with tracheostomies $\pm$ ventilators were excluded. Although 39 studies met these criteria, data were not available from every study. The bolding of values indicated significant *P* values.