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Determining Optimal Home Oxygen Flow Rate For Infants With Bronchopulmonary Dysplasia (BPD) Using Near Infrared Spectroscopy

Ahmad A Imran[1], Jagmeet Singh Bajwa[2], Sibasis Daspal[1], Darryl J Adamko[3]

[1]Division of Neonatology, Department of Pediatrics, University of Saskatchewan, Saskatoon, Saskatchewan, Canada; [2]Division of Research, Department of Pediatrics, University of Saskatchewan, Saskatoon, Saskatchewan, Canada; [3]Division of Respirology, Department of Pediatrics, University of Saskatchewan, Saskatoon, Saskatchewan, Canada

Correspondence: Darryl J Adamko, Department of Pediatrics, College of Medicine, 103 hospital Drive, University of Saskatchewan, Saskatoon, SK, S7N 0W8, Canada, Tel +1 306 844-1275, Fax +1 306 844-1210, Email darryl.adamko@usask.ca

Objective: Near-infrared spectroscopy (NIRS) measures cerebral oxygenation and could measure the risk of hypoxia or hyperoxia in infants with bronchopulmonary dysplasia (BPD). We lack normalized data for NIRS values in neonates. We sought normative values of NIRS and proposed that NIRS could better identify a safe oxygen flow rate compared to pulse oximetry (POX).

Methods: This prospective cohort study compared POX and NIRS values in healthy infants in room air (n = 22) with BPD infants (n = 10) on oxygen (0.03, 0.06, 0.12 L/min).

Results: In healthy infants, the average POX value was 97.8%, and NIRS was 78.24%. Time (% time) with hypoxia was similarly low using either POX or NIRS (3.5% and 1.4%). On oxygen, % time with hypoxemia was similarly low with both POX or NIRS (0.03 lpm: 2.35% POX and 0.01% NIRS; 0.06 lpm: 1.43% POX and 0.6% NIRS; 0.12 lpm: 1.46% POX and 0.2% NIRS). In contrast, the potential hyperoxia %time was higher using POX compared to NIRS (96.5% vs 47.9%) in room air healthy infants. Similarly, hyperoxia %time was more common with POX compared to NIRS, but there was no difference with increasing oxygen flow rates (0.03 lpm, 82.13% POX and 41.5% NIRS; 0.06 lpm: 92.49% POX and 34.4% NIRS; 0.12 lpm: 87.00% POX and 34.8% NIRS).

Conclusion: We did not see a dose response correlation between oxygen flow rate and time spent in the hyperoxemic range across different flow rates by POX or cerebral NIRS. We did not see a benefit of NIRS in setting home oxygen flow rates.

Keywords: near infrared spectroscopy, hyperoxia, home oxygen

Introduction

One of the most common co-morbidities that develops from premature birth is bronchopulmonary dysplasia (BPD). BPD is a lung disease that occurs most often in very and extreme preterm infants. It is defined by the infant's need for oxygen therapy for at least 28 days after birth, and then at the time of discharge or corrected gestational age of 36 weeks.[1–3] For preterm infants going home on supplemental oxygen, both hypoxia and hyperoxia can be detrimental.[4,5] A "normal" oxygen saturation level for the preterm infant can be difficult to define. The post hoc analysis of the participants in the COT trial (Canadian Oxygen Trial) showed that intermittent hypoxic events or bradycardia increased the risk of mortality, neurodevelopmental delay, language delay and poor cognitive outcome at a corrected age of 18 months.[6] In contrast, hyperoxemia in the preterm population can lead to free radical production, which is implicated in the pathogenesis of many complications associated within the preterm population.[7,8]

Given the role that hypoxemia and hyperoxemia play in neonatal mortality and morbidity, there is a need for measurement and regulation of oxygen delivery in the NICU.[9] There is limited data in the literature, which addresses the question about the percentage of the time that these preterm infants remain within the targeted oxygen saturation limits. Improved monitoring of brain oxygenation could improve neurodevelopmental outcomes in preterm infants, but there is no consensus on monitoring regional blood flow to the brain.

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Near-infrared spectroscopy (NIRS) is a possible method to indirectly measure brain perfusion, as the presence of thin layers of skin and skull allow good penetration of NIR light into the neonatal brain tissue. Differences in NIR light absorption are used to calculate the concentrations of Oxy (O2Hb) and de-oxy (HHb) hemoglobin concentration using the modified law of Lambert–Beer. NIRS reflects mainly cerebral venous oxygen saturation.[10,11] A recent RCT for the use of NIRS in extreme preterm infants (≤28 weeks gestation) observed that NIRS can be employed for the continuous measurement of cerebral oxygenation.[12] Cerebral oxygenation is used as a substitute for cerebral blood flow, thus NIRS can potentially assess the integrity of cerebral circulation. The reference range for cerebral oxygenation in preterm population has a wide variation. Pellicer et al during the SafeboosC Phase II randomised clinical trial used the range between 55% and 85% in their guideline in the preterm infants in first 3 days of life. The value of <50% was associated with poor neurodevelopmental outcomes.[13] To the best of our knowledge, there are no normalized data for NIRS values in neonate infants going home without oxygen. In our NICU in JPCH we use <60% as abnormal low range (hypoxemia), 60–80% as normal and >80% as high (hyperoxemia) in neonates on oxygen.

While there is discrepancy worldwide for what defines low flow oxygen, given the low minute ventilation of neonates, this definition is critical. While our current practice is to discharge infants with moderate BPD requiring oxygen at a rate of 0.06–0.12 lpm, we do not have data that shows that this flow is adequate, too little, or too high. Many institutions use higher flow rates risking hyperoxia. We hypothesized that combination of NIRS, and pulse oximetry could better identify a safe oxygen flow rate at the time of discharge. To the best of our knowledge, there is a lack of normalized data for NIRS values in neonate infants going home with or without oxygen. As such, we also sought the normative values of NIRS in infants.

Methods

Study Design

This was a prospective cohort study. This study was approved by the Bioethics Board, University of Saskatchewan and complies with the Declaration of Helsinki. After receiving written informed consent from the parents/legal guardians, we enrolled preterm neonates (≤37 weeks, Table 1) admitted to NICU of Jim Pattison Children's Hospital, Saskatoon, SK, Canada. To obtain data for normal baseline NIRS and oximetry values, we recruited a control group of non-BPD preterm infants (n = 22, Table 1) who were being discharged home in room air. For the study group, we enrolled preterm infants with gestational age ≤32 weeks having moderate BPD and going home on oxygen via low flow nasal cannula (n = 10, Table 1). We chose this gestational age as it represents the most vulnerable preterm population from both mortality and morbidity. We excluded all preterm infants with congenital malformations. All infants were ready for discharge without concern for significant morbidities including anemia.

Definitions

Hypoxia was defined as a pulse oximetry (POX) value <90% saturation; hyperoxia as >96% saturation and normal between 90% and 96% for infants on oxygen.[6,14–16] Moderate BPD was defined by an infant's need for supplemental oxygen at 36 weeks' postmenstrual age, or discharge (whichever came first) for babies born <32 weeks. The alarm limits for POX were set according to the NICU policy (low limit of 90% to high limit of 95%) with intention to treat if prolonged hypoxic or hyperoxemic events were observed.[6] NIRS values were stratified in 3 groups as adapted from Pellicer A et al SafeboosC trial: < 60%, 60–80% and >80%. NIRS values of <60% have been reported to suggest hypoxemia in infants with its associated morbidity. NIRS values of >80% are reported to suggest hyperoxemia in neonates on oxygen.[12,13]

Table 1 Subject Characteristics

	Control Group	Study Group
Gender (%male)	56%	
Average Gestational age at birth (range in weeks)	32.7 (26–36)	28.8 (26–30)
Average Gestational Age at Study (range in weeks)	35.6 (32–38)	38.8 (36–43)

Equipment used

NIRS measurements were performed using INVOS TM 5100C Cerebral/Somatic Oximeter and sensors (Medtronic, Brampton, ON, Canada). For pulse oximetry data, we used the Smart monitor (Circadiance, Export, PA, USA) with Massimo oximetry probes (Irvine, CA, USA) and chest leads (Cardinal Health, Waukegan, IL). This monitor displays heart rate, chest excursion, oximetry, and pulse ox waveform using the Synergy-E event software. It is integrated with Massimo technology for accurate oxygen saturation monitoring with an averaging time of 2 seconds.

Methods

We performed 8 hours of measurement using POX and NIRS monitoring in both non-BPD and BPD infants. The data for NIRS and POX study was obtained in room air for non-BPD infants and on the flow rates of 0.03 lpm (1/32), 0.06 lpm (1/16), and 0.12 lpm (1/8) for BPD infants going home on oxygen.

Statistical Analysis

Sample size was chosen for convenience as approximately one patient would fulfill the inclusion criteria every 1–2 months. We employed paired samples *t*-tests to compare the mean values of two key variables, POX and NIRS, across study groups with different oxygen flow rates (0.03 LPM, 0.06 LPM, and 0.12 LPM). Mean and confidence intervals are reported. Cohen's correlation coefficient was calculated to assess the strength of correlation between POX and NIRS. The significance of the correlation was determined using one-sided and two-sided *p*-tests.

Results

Control non-BPD infants on room air: As expected, the average time infants had saturations <90% was quite low at 3.5% (0.73–6.29). As expected, mean time with saturations >90% was 96.5% (93.7–99.3). Similarly, mean time with NIRS value <60 was quite low at 1.4% (−1.36–4.16). In contrast, time at 60–80 was 50.7% (32.7–68.7) and >80% was 47.9% (29.4–66.4). As the control group had no supplemental oxygen given, these values of >80% were unexpected, but determined to be normal and no intervention was taken. The difference of mean saturation between POX and NIRS was 19.557 with the 95% confidence interval of 19.503 to 19.61. This difference of means does correlate with previous studies, which suggested that there is an approximate difference of 20 among the POX and NIRS values with POX being higher that NIRS.

There was no correlation of the POX and NIRS value over short time periods: While the average time data did correlate for NIRS and POX, brief events (<15 seconds) of a desaturation in either NIRS or POX did not demonstrate a correlation. For example, we did not see the NIRS values drop if the POX dropped for a short time (Cohen's correlation coefficient was 0.02).

Study group BPD infants on supplemental O2: For the study group patients, the results were stratified according to oxygen flow rate and oxygen saturation. The average time an infant remained within the set saturation range in a particular flow rate was calculated. At the oxygen flow of 0.03 lpm, the average time the participants remained <90%, 90–96% and >96% were 2.35% (0.32–4.38), 15.52% (−2.11–33.15) and 82.13% (62.87–101.4) of total time respectively. At the oxygen flow of 0.06 lpm, average time <90%, 90–96% and > 96% were 1.43% (0.46–2.41), 9.34% (1.41–17.27) and 89.22% (80.9–97.5) of total time respectively. At the oxygen flow of 0.12 lpm, average time <90%, 90–96% and >96% were 1.59% (0.69–2.49), 12.1% (−3.364–27.56) and 86.3% (70.46–102.2) of total time, respectively.

Similarly, NIRS values were stratified. The average time an infant remained within the set NIRS range with a particular flow rate was calculated. At the oxygen flow of 0.03 lpm, average time the participants remained <60%, 60%–80% and >80% were 0.01% (−0.1–0.03), 58.5% (13.4–103.6) and 41.5% (−3.64–86.6) of total time, respectively. At the oxygen flow of 0.06 lpm, average time the participants remained <60%, 60%–80% and >80% were 0.73% (−0.47–1.94), 68.3% (46.8–89.85) and 30.96% (8.87–53.05) of total time, respectively. At the oxygen flow of 0.12 lpm, average time the participants remained <60%, 60%–80% and >80% were 0.89% (−0.69–2.46), 67.8% (40.47–95.17) and 31.29% (3.46–59.13) of total time, respectively.

Comparison of POX and NIRS data; lack of a dose response to oxygen: The comparison of data between POX and NIRS at different oxygen flow rates was performed (Figure 1). The POX of <90% (hypoxemia) was compared to NIRS

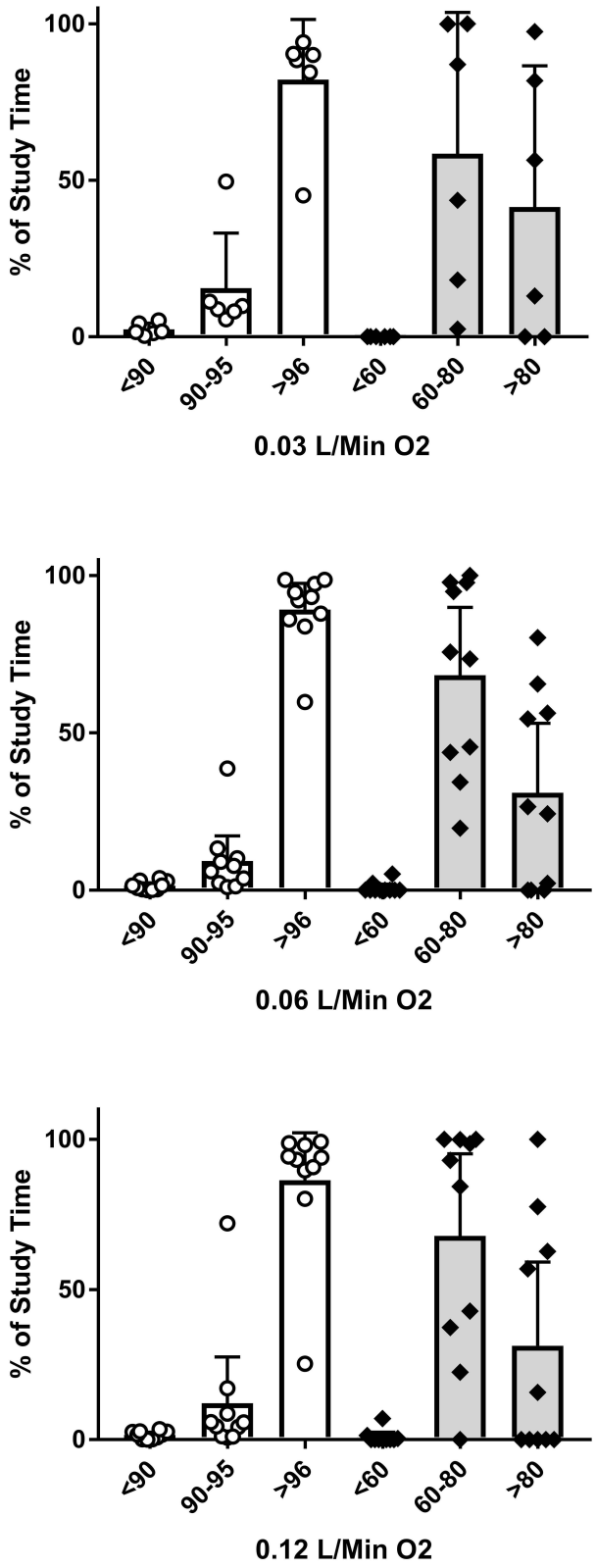

Figure 1 Comparison of POX and NIRS data: The comparison of data between POX (white bars) and NIRS (grey bars) at different oxygen flow rates was performed. Shown are the means with 95% confidence interval. Regardless of O2 flow rate, infants were rarely hypoxemic, but instead were in the hyperoxemia category (POX >96%) most of the time. We did not find any dose relation with increasing flow rate.

values of <60%. The POX of >96% (hyperoxemia) was compared to NIRS values of >80% and the target range of 90%–96% was compared to NIRS values of 60%–80%. Infants on any amount of oxygen were rarely hypoxemic with an average time of 1.75% (POX < 90%). Similarly, regardless of O2 flow rate, infants were in the hyperoxemia category (POX > 96%) most of the time at 87% (Figure 1). Infants on any oxygen were in the target saturation range (POX 90–96%) only 11% of the time. We did not find any dose relation with increasing flow rate from 0.03 lpm to 0.06 lpm to 0.12 lpm (82.1% with flow 0.03 lpm vs 92.5% with flow 0.06 lpm vs 87% with flow 0.12 lpm). While infants did not spend much time in saturations <60% (0.27% of time), the average time an infant remained within the target NIRS range (60–80%) was better than POX data with an average time of 62.8%. The time with hyperoxia was also better at 37% time with NIRS >80%. Similar to POX data, we did not find a dose response with increasing flow rate and the time in the hyperoxemic range >80% (41.5% with flow 0.03 lpm vs 34.4% with flow 0.06 lpm vs 34.8% with flow 0.12 lpm).

Discussion

While the burden of BPD remains unacceptably high, research on prevention and strategies for best outcomes continues to show promise.[17] Both hypoxia and hyperoxemia are detrimental in the preterm population and can lead to poor neurodevelopmental outcome. As such, we sought to identify the minimum safe high and low oxygen flow rate for infants with moderate BPD going home on oxygen. In addition, there is little data on the NIRS technology in infants not on O2 and as such these data are quite novel. We performed POX and NIRS studies on preterm infants going home in room air to determine the normal data for POX and NIRS without oxygen. We were happy to confirm previous data that there is an approximate difference of 20% between the POX and NIRS values with POX being higher than NIRS. Reason for higher POX values is the pulse oximeters detect the pulsatility of the blood flow and give readings, which are very close to arterial oxygen saturation. In contrast, the NIRS collects data from the tissue microcirculation, which contains arterial, venous, and capillary components. RcSO2 is an average value with approximately 75–85% of the signal originating from venules. Thus, NIRS reflects mainly cerebral venous oxygen saturation. We were intrigued that most infants not on supplemental oxygen have POX values well above 96% for the majority of the time. This obviously becomes relevant in the context of potential hyperoxia for the oxygen treated BPD study group.

For the study group, our aim was to determine the percentage of time the infant remains within the target saturation range and to find the adequate oxygen flow rate for these infants going home on low flow nasal cannula. For all infants on any oxygen, we did not find any dose relation with increasing flow rate from 0.03 lpm to 0.06 lpm to 0.12 lpm. Similarly, the average time an infant remained within the set NIRS range was also lower than expected. Again, we did not find any dose relation with increasing flow rate and the time in the hyperoxemic range >80%.

Based on these POX and NIRS findings, it is reasonable to suggest that home oxygen of 0.06 to 0.12 lpm is probably adequate to protect against hypoxemia and hyperoxemia. We could not find any correlation between POX and NIRS values. Even though we see that infants spend most of the time with higher POX saturations >96% the NIRS was not the same. It is possible that the brain does not see the higher values due to the cerebral autoregulation. Cerebral autoregulation is the ability of the brain to maintain perfusion and oxygenation in response to different stresses. Impaired autoregulation has been associated with poor neurodevelopmental outcomes. Although preterm infants have impaired cerebral autoregulation at birth, we hypothesise that the infants close to going home may have developed enough autoregulation capability that it does not see the impact of hypoxia or hyperoxia immediately. However, to test this hypothesis, we would need a separate study.

Limitations

Most of the time the preterm infants remained in the hyperoxemic range for POX in all flow rates. Guidelines suggest that POX greater than 96% is potentially hyperoxemic. True hyperoxemia is only known by measuring blood gas with a PO2 >150 mmHg or measuring oxygen free radicals. This as this would be too invasive. The other limitation is that we did not show a clear dose response to oxygen flow rate. Our sample size is small, and it is possible that we missed the dose response. The data are statistically strong, and this seems unlikely. The standard of care in our institution and at most centers in North America is 0.03–0.12 lpm. As such, this dose would not have been ethically feasible. An animal model is likely needed to assess dose response and oxygen-free radicals.

Conclusion

This is the first report showing the normal NIRS values of relatively healthy preterm infants. There is no correlation between the cerebral NIRS values and POX values over a short time. This is likely due to the cerebral autoregulation; however, this report was not designed to study the effects of cerebral autoregulation in these infants. NIRS still plays an important adjunct role as a monitoring device, which gives us insight into the brain oxygen saturation. We suggest that the NIRS numbers should be considered in the management of preterm infants along with other monitoring tools but not as stand-alone. We suggest the flow rate of 0.06–0.10 lpm is safe for home O2 with moderate BPD, however the final decision would lie on the discharging physician and neonatal team.

Abbreviations

BPD, Bronchopulmonary dysplasia; NICU, Neonatal intensive care unit; NIRS, Near Infrared Spectroscopy; SpO2, Saturation of peripheral Oxygen; MABP, Mean arterial Blood Pressure; LED, Light Emitting Diode; O2Hb, Oxy hemoglobin; HHb, Deoxy-Hemoglobin; RcSO2, Regional cerebral saturation of Oxygen; SO2, Saturation Oxygen; FTOE, Fractional Tissue Oxygen extraction; MRP, Most Responsible Physician; RCT, Randomized control trial; GA, Gestational Age.

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Disclosure

The authors report no conflicts of interest in this work. This paper was uploaded to the University of Saskatchewan repository as a thesis on 20 February 2024.[18]

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