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COMMENT

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Oxygenation in the NICU: there is more to it than meets the eye

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IMPACT:

- Dormishian and colleagues in their study address an issue that care teams in the NICU encounter on a daily basis, regarding motion artifacts during oxygenation monitoring.
- In our commentary, we discuss the available tools that allow continuous noninvasive monitoring of oxygenation in the NICU, and modalities that increase the time premature infants spend in the desired SpO_2 range and impact their clinical outcomes.

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Oxygenation instability due to frequent hypoxemic episodes is common among premature infants, mainly during the first weeks of life. It was recognized to contribute to severe retinopathy of prematurity (ROP) in the early 90s[1] and has since been associated with various other morbidities such as bronchopulmonary dysplasia (BPD), motor impairment, and even death.[2,3]

In the neonatal intensive care unit (NICU), oxygen saturation (SpO_2) is the measure used to assess the oxygenation status of infants. To measure SpO_2, pulse oximeters pass two wavelengths to a photoreceptor and extract the pulsatile elements of the transmitted light to estimate arterial oxygen saturation. Keeping premature infants within a predefined SpO_2 target range is of major significance. This has been evaluated in large blinded RCTs and found to affect death and neonatal morbidities.[4] However, this is a challenging task as premature infants were found to spend more than 50% of the time outside the target SpO_2 range.[5,6] Different interventions have been suggested to increase the time spent within the target SpO_2 range. Among these interventions are two modalities that were found to increase the time spent in the desired SpO_2 range and impact clinical outcomes.

First is the automated oxygen delivery system. This system uses real-time continuous SpO_2 data to make adjustments in fraction of inspired oxygen (FiO_2). Several respiratory support devices with automated oxygen control systems are currently available in the NICU and are able to deliver invasive and non-invasive support. Recently, Nair et al. reviewed the current evidence of automated oxygen delivery in the NICU.[7] All studies included in the review reported significantly higher proportion of time in SpO_2 target range, lower proportion of time in the hypoxemia and hyperoxia range, and a reduced need for manual adjustments while the infants were supported by a respiratory support device with an automated oxygen delivery system. These results are promising. However, all studies were of short duration, varying from 2 to 48 h, and evidence regarding the impact of this improved oxygenation stability on clinical outcomes is lacking.[7]

Second, a tool that can help the bedside team objectively quantify the time the infant spent in different SpO_2 ranges is the SpO_2 histogram. The SpO_2 histograms are integrated into the bedside monitors and present the time the infant has spent in each SpO_2 value, in different time intervals- from the last 30 min to the last 24 h. Using the SpO_2 histograms to document oxygenation instability among premature infants in the NICU increases the percentage of time infants are in the target SpO_2 range[8] and is associated with a reduction in BPD, severe ROP, and death.[8,9] Furthermore it has been found to be helpful in objectively assessing the impact of different interventions, such as position change[10] and doxapram treatment, on the oxygenation instability of premature infants.

However, both of these tools rely on reliable SpO_2 readings. False SpO_2 readings due to improper probe placement or motion artifacts alter the SpO_2 histogram (as the monitor usually uses a sample rate of 1 Hz to generate the histogram) and might give the care team a false picture of the oxygenation status of the infant. When using the automated oxygen delivery system, erroneous SpO_2 readings might lead to an unnecessary increase in FiO_2 and result in hyperoxia.

The reliability of pulse oximeter in premature infants during motion is being addressed in the current issue of *Pediatric Research* by Dormishian et al. in their study "Pulse oximetry reliability for detection of hypoxemia under motion in extremely premature infants."[11] By simultaneously monitoring SpO_2 with two separate probes placed on different extremities of premature infants ≤28 weeks gestational age, they studied the reliability of SpO_2 during intermittent hypoxia episodes associated with motion. Hypoxemia episodes were defined as true or false based on the differences between the SpO_2 readings of the two probes during motion artifacts. They showed that most desaturation episodes were true, even in the presence of motion artifacts. This is an important message to the bedside care team. Misjudging a hypoxemic event as false, potentially exposes the infant to a longer period of hypoxemia and its risks. Future development of SpO_2 monitors is needed to overcome motion artifacts, in order to

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achieve continuous reliable monitoring of premature infants' oxygenation status.

Another modality that is available in the NICU and can be used for continuous oxygenation monitoring is transcutaneous measuring of the partial pressure of O_2 ($tcPO_2$). In this modality, the sensor heats the skin, thereby arterializing the capillary bed underneath and increasing oxygen diffusion through the outer layer of the skin. The agreement between the measured PO_2 at the skin surface and the true arterial PO_2 depends on factors that influence the oxygen dissociation curve (blood pH, hemoglobin level, etc.) and oxygen consumption by the heated skin and the electrode. Historically $tcPO_2$ monitors suffered from a bad reputation in the NICU due to poor accuracy, technical difficulties, and safety events resulting in skin burns. Recently, with a newly developed sensor, good agreement and correlation are achieved at lower temperatures and are therefore safer.[12] The advantages of this sensor are that it is not affected by motion, unlike SpO_2 probe that relies on good signal quality from the pulse oximetry, and that it may better indicate hyperoxia when the SpO_2 is at the range of its plateau. This might be of significance in extremely premature infants, or in term infants with pulmonary hypertension. This was nicely demonstrated in premature infants in the study of Srivatsa et al.[13] when ambient air hyperoxia (infants were in room air) occurred more frequently in the group without ROP and "iatrogenic" hyperoxia (when the infants were exposed to excessive oxygen administration) occurred more frequently in the group with severe ROP. The main disadvantage of $tcPO_2$ compared to SpO_2 is that it responds more slowly to changes in oxygenation and that it requires a calibration period that does not allow its use during neonatal resuscitation. Both methods might be affected by tissue perfusion. In the NICU, a good agreement was found between $tcPO_2$ and PaO_2 among premature infants, except for samples taken during proven sepsis.[14] Among infants born ≥34 weeks' gestation, bias (mean difference) between $tcPO_2$ measures and capillary PO_2 was not significant. However, a significant bias was demonstrated when $tcPO_2$ was compared to arterial PO_2. Of note, there was wide precision (standard deviation of the differences) in all.[15] As both devices (pulse oximeters and $tcPO_2$ monitors) have their advantages and limitations it appears that combining these two modalities in the NICU may be helpful. Clinical studies are needed to assess the possible complementary contribution of the two devices.

Dormishian and colleagues in their study[11] address a practical clinical question that care teams in the NICU encounter on a daily basis. They highlight a specific question regarding motion artifacts during oxygenation monitoring and open a wider window to the unresolved issue of oxygenation instability in extremely premature infants. The oxygenation instability that premature infants experience during their first weeks of life may impact their short and long-term outcomes. Increasing awareness and understanding of available tools that allow continuous noninvasive monitoring of oxygenation in the NICU, better monitoring of true oxygenation status, defining the threshold of harmful oxygenation instability, and developing tools that can improve oxygenation stability are needed in the NICU.

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COMPETING INTERESTS

This article is original, is not being considered for publication elsewhere, and has not been published previously. The authors declare no competing interests.

ADDITIONAL INFORMATION

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