

Review

How Do We Monitor Oxygenation during the Management of PPHN? Alveolar, Arterial, Mixed Venous Oxygen Tension or Peripheral Saturation?

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Abstract: Oxygen is a pulmonary vasodilator and plays an important role in mediating circulatory transition from fetal to postnatal period. Oxygen tension (PO_2) in the alveolus (PAO_2) and pulmonary artery (PaO_2) are the main factors that influence hypoxic pulmonary vasoconstriction (HPV). Inability to achieve adequate pulmonary vasodilation at birth leads to persistent pulmonary hypertension of the newborn (PPHN). Supplemental oxygen therapy is the mainstay of PPHN management. However, optimal monitoring and targeting of oxygenation to achieve low pulmonary vascular resistance (PVR) and optimizing oxygen delivery to vital organs remains unknown. Noninvasive pulse oximetry measures peripheral saturations (SpO_2) and a target range of 91–95% are recommended during acute PPHN management. However, for a given SpO_2 , there is wide variability in arterial PaO_2 , especially with variations in hemoglobin type (HbF or HbA due to transfusions), pH and body temperature. This review evaluates the role of alveolar, preductal, postductal, mixed venous PO_2 , and SpO_2 in the management of PPHN. Translational and clinical studies suggest maintaining a PaO_2 of 50–80 mmHg decreases PVR and augments pulmonary vasodilator management. Nevertheless, there are no randomized clinical trials evaluating outcomes in PPHN targeting SpO_2 or PO_2 . Also, most critically ill patients have umbilical arterial catheters and postductal PaO_2 may not be an accurate assessment of oxygen delivery to vital organs or factors influencing HPV. The mixed venous oxygen tension from umbilical venous catheter blood gas may assess pulmonary arterial PO_2 and potentially predict HPV. It is crucial to conduct randomized controlled studies with different PO_2/SpO_2 target ranges for the management of PPHN and compare outcomes.

Keywords: oxygenation; PPHN; oxygen tension

1. Introduction

Persistent pulmonary hypertension of the newborn (PPHN) occurs when there is impaired pulmonary vascular transition during birth due to disruption of pulmonary vasodilator mechanisms. Impaired transition from fetal to neonatal circulation leads to elevated pulmonary vascular resistance (PVR), right-to-left or bidirectional shunts at patent foramen ovale (PFO) and/or patent ductus arteriosus (PDA) leading to hypoxemia [1]. Both term and preterm neonates are at risk for PPHN [2–5]. The course of preterm neonates in the neonatal intensive care unit (NICU) is further complicated by the development of bronchopulmonary dysplasia (BPD) and can potentially be associated with pulmonary hypertension (PHT) [6–8]. The incidence of PPHN in neonates are often underestimated but is thought to be around 1.8 to 2/1000 live births [1,5,9]. In infants with PPHN, several studies report poor

long-term neurodevelopment outcomes and higher early mortality rates despite pulmonary vasodilator therapies [1,10,11]. At birth, with the initiation of spontaneous breathing or with positive pressure ventilation (PPV) and with adequate lung inflation, the pulmonary blood flow (PBF) increases by 8 to 10-fold along with a decrease in PVR. As the fetus grows in a relatively hypoxemic environment, increase in oxygen tension seems to play a significant role in decreasing PVR at birth [12]. Optimal oxygenation is necessary to meet tissue demand, especially in vital organs such as brain and heart and to prevent hypoxic pulmonary vasoconstriction (HPV). This review discusses the role of oxygen tension (PO_2) and pulse oximetry (SpO_2) during the management of PPHN. With lack of clinical evidence on optimal oxygenation in PPHN, this manuscript reviews data from both term and preterm translational models associated with high PVR in the perinatal period.

2. Discussion

Understanding the relationship of fetal oxygenation, PVR, pulmonary blood flow (PBF) in both the fetus and newborn is critical to managing a neonate with PPHN.

2.1. Relation of PO_2 and Fetal PVR

The fetus develops with placenta serving as an organ of gas exchange. The highest PO_2 within the fetal circulation is approximately 32–35 mmHg in the umbilical vein. There is a further decrease in PO_2 to 25–28 mmHg in the ascending aorta supplying the developing brain and myocardium [13–15]. The placenta protects the fetus from maternal hyperoxia and hypoxia [14,15]. As observed in translational studies, during maternal hyperoxia/hypoxia, the distribution of blood in the placenta, channeling of blood to and from the fetal liver by ductus venosus, and alteration of PVR (increase/decrease) avoids excessive fluctuations in fetal PO_2 [16]. The relationship of fetal PVR to PO_2 is dependent on the gestational age (GA) of the fetus [17]. By term gestation, PVR decreases dramatically in response to increased fetal PO_2 [18].

2.2. Gestational Age, Fetal PVR, and PO_2

The changes in PVR to PO_2 in relation to GA were studied in fetal ovine model [19]. Ovine fetuses at different GA of 0.6 (103–104/term ~150 days), 0.74 (112–119 days), 0.80 (121–130 days), and 0.90 (132–138 days) were exposed to hypoxia or hyperoxia by adjusting the oxygen exposure to the ewe. Pulmonary vasoconstriction and vasodilation were observed at term gestation when exposed to low and high PO_2 . Hypoxia and hyperoxia did not have a significant effect on PVR at 0.6 and 0.74 gestation. In humans, maternal hyperoxia did not alter fetal PBF at 20–26 weeks GA but increased PBF and reduced atrial and ductal shunting at 31 to 36 weeks [20]. Extrapolating from these findings, the pulmonary vascular response to PO_2 seems to increase with advancing gestational age.

2.3. Effect of PO_2 on PVR at Birth

During normal transition, spontaneous breath initiated by the newborn infant ventilates the lung and increases alveolar oxygen tension, which increases PBF reducing PVR, successfully switching from fetal to neonatal circulation [21]. Multiple factors such as mode of delivery (vaginal delivery results in more rapid reduction in PVR compared to an elective cesarean section), maturity, antenatal glucocorticoids, temperature (hypothermia increases PVR), mode of cord clamping and asphyxia (related to higher PVR), could affect transition at birth [22]. These factors affect the balance between the vasoconstrictors (endothelin-1, thromboxane), and vasodilators (prostacyclin and endothelium derived nitric oxide), which exert their effects on the pulmonary artery smooth muscle cells (PASMC). In addition to these factors, oxygen (O_2) seems to play a greater role in the regulation of PVR by having a direct effect on PASMC. Oxygen stimulates the increased production of pulmonary endothelial nitric oxide (NO), which is a potent pulmonary vasodilator birth [22].

2.4. Oxygen and Hypoxic Pulmonary Vasoconstriction (HPV)

A fundamental difference between pulmonary blood vessels and systemic vessels is their ability to constrict in response to hypoxia [23]. Regional HPV diverts blood away from underventilated alveoli and promotes ventilation-perfusion (V/Q) matching. HPV is mediated by PO_2 surrounding the precapillary pulmonary arteriole (Figure 1) and is influenced both by mixed venous (pulmonary arterial) PVO_2 and alveolar PAO_2 [24]. The stimulus for HPV is dictated by the equation $P(\text{stimulus})O_2 = PVO_2^{0.375} \times PAO_2^{0.626}$. Based on this equation, it is clear that alveolar PAO_2 is the predominant factor determining the severity of HPV. Acidosis exacerbates HPV in neonatal animal models [15].

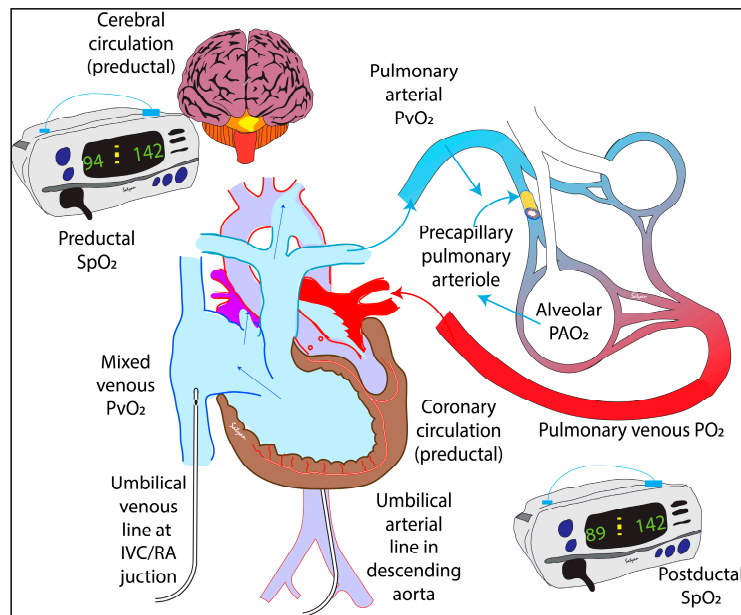


Figure 1. The primary determinant of hypoxic pulmonary vasoconstriction is the precapillary pulmonary arteriole. The oxygen tension at this site is determined by alveolar PAO_2 and pulmonary arterial PO_2 . In the absence of lung disease, pulmonary venous PO_2 and alveolar PAO_2 are usually similar. In the absence of significant shunts, preductal PaO_2 is reflective of pulmonary venous PO_2 . Umbilical venous PO_2 is similar to mixed venous PO_2 and pulmonary arterial PO_2 in the absence of a left-to-right atrial/ductal shunt. Oxygen delivery to the brain and heart is based on preductal PaO_2 and SpO_2 . Postductal PaO_2 (from an umbilical arterial line) can be low and does not predict PVR or oxygen delivery to vital organs. Copyright Satyan Lakshminrusimha.

2.5. Supplemental Oxygen and PO_2 during the Transition

Oxygen supplementation is the most common resuscitative measure for newborns in the delivery room. American Academy of Pediatrics Neonatal Resuscitation Program (AAP NRP) recommends that supplemental O_2 be initiated at concentrations of 21% O_2 in term and 21–30% O_2 in preterm neonates and to titrate based on prespecified preductal saturations [25]. Given the ease and universal use of pulse oximetry, preductal oxygen saturations (SpO_2) could be the most efficient way of targeting oxygenation in the delivery room and the neonatal intensive care unit (NICU). However, for a given saturation range, the achieved PO_2 could vary widely and the extremes of SpO_2 have low accuracy [26]. In a newborn requiring resuscitation, hypoperfusion could also decrease the accuracy of SpO_2 .

2.6. Oxygen Tension in Spontaneous Air Breathing Infants

The concept of normoxemia in a transitioning newborn is not well defined. A healthy newborn, who transitioned from placenta to lungs as an organ of gas exchange, sees a rise in arterial oxygen tension (PaO_2) by 30–40 mmHg from fetal values. The increases in alveolar PAO_2 and arterial PaO_2

along with ventilation play an important role in decreasing PVR and increasing PBF. In a study of near term gestation lambs (comparable to human term neonates), the use of 21% O₂ lead to PaO₂ values of 50–60 mmHg [12]. The observed decrease in PVR from fetal life occurred at a PaO₂ of 52.5 ± 1.7 mmHg, also known as the change point [12]. The change point is the PaO₂ value at which there is a change in the slope of PVR–PaO₂ scatter plot. In human neonates, who were previously on respiratory support and were weaned to room air and breathing spontaneously, 176 samples of arterial blood gas were analyzed [27]. The analysis showed that 80% of the PaO₂ values were between 40–80 mmHg and the average PaO₂ was 64 mmHg. In a study involving 10 neonates, the average PaO₂ was 77 ± 4.5 mmHg in quiet asleep compared to a PaO₂ of 70 ± 6.5 mmHg in active sleep [28]. In this study, the quiet sleep was defined as no eye movement or activity, while active sleep had frequent small movements, and the site of blood draw (pre vs. post ductal) is not known [28]. A recent study, defined normoxemia in neonates with a PaO₂ range of 50–80 mmHg [29]. Based on these observations, the PaO₂ in normal neonates mostly ranges between 50–80 mmHg. Achieving a similar preductal PaO₂ value during the management of PPHN neonates appears prudent.

2.7. Oxygen Tension and PPHN

In a neonate with PPHN secondary to failed transition or underlying lung pathology, the elevated pulmonary pressures often lead to shunting of blood from pulmonary to the systemic circulation, leading to profound and labile hypoxemia despite PPV and supplemental oxygen. Adequate oxygenation to achieve preductal PaO₂ in the 50–80 mmHg range (similar to normal neonates) remains the cornerstone of PPHN management in both term and preterm neonates.

2.8. Alveolar PAO₂ and its Effect on PPHN

The alveolar PO₂ (PAO₂), which can be calculated using the inspired O₂ concentration and arterial oxygenation and carbon dioxide tension, is a major determinant of HPV [30]. In the presence of parenchymal lung injury and or immature lungs, alveolar hypoxia could exacerbate pulmonary vasoconstriction. Studies done four decades ago, comparing newborn and adult ovine models, have shown that alveolar hypoxia leads to more significant HPV leading to redistribution of pulmonary circulation away from hypoxic lung in newborn lambs compared to adult sheep (Figure 2).

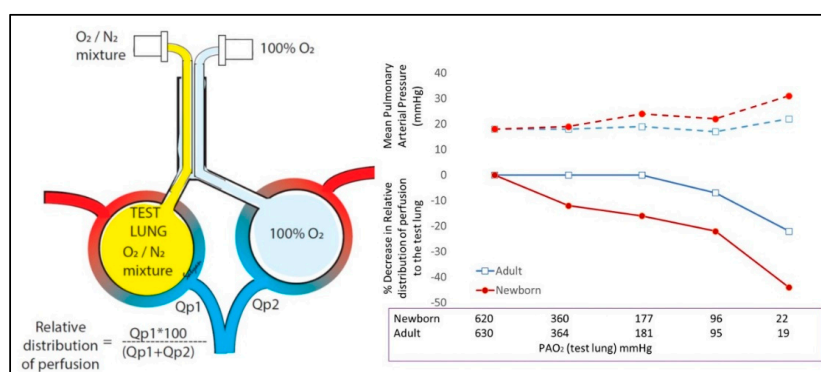


Figure 2. Created using data from Custer et al. [31]. Importance of alveolar hypoxia in directing lung blood flow. Neonatal lambs and adult sheep were instrumented. Each lung was intubated with a different endotracheal tube. One lung was ventilated with 100% oxygen and the other test lung with varying concentrations of oxygen mixed with nitrogen. Relative distribution of perfusion was calculated with Qp1 (blood flow to test lung) and Qp2 (blood flow to the 100% oxygen lung) using the formula shown in the figure. Lower PAO₂ had a profound effect on pulmonary vasoconstriction in newborn ovine model (red line) compared to adults (blue line).

In adult sheep, alveolar PAO₂ had to drop to 19 mmHg to observe significant redistribution of blood flow away from the hypoxic lung. In sharp contrast, reduction of alveolar PAO₂ below

360 mmHg (equivalent to ventilation with 50% oxygen), lead to HPV and redistribution of blood away from the hypoxic lung (Figure 2).

However, HPV occurred only with severe alveolar hypoxia in adult lambs exacerbating ventilation-perfusion mismatch [31]. These results suggest that HPV in response to alveolar hypoxia is more prominent and severe, and occurs at higher PAO₂ levels during the neonatal period compared to adult life.

Table 1 shows the effect of inspired oxygen concentration on preductal arterial (PaO₂), PVR and alveolar PAO₂ (calculated using PaCO₂), in control term gestation lambs and lambs with PPHN induced by antenatal ductal ligation (a model of primary PPHN without any lung disease). [12] In control lambs without lung disease or PPHN, low PVR is achieved by ventilation with 21% oxygen with alveolar PAO₂ in the 90–100 mmHg range.

Table 1. Effect of PAO₂ on control and PPHN ovine models on PVR [12]

Parameters	O ₂ (%)	PaCO ₂ (mmHg) *	PaO ₂ (mm Hg) *	PVR (mmHg/mL/kg/min) *	PAO ₂ (mmHg) Calculated *
Control	21	42 ± 2	57 ± 6	0.28 ± 0.01	94.5 ± 6.2
PPHN	21	44 ± 3	23 ± 2	1.6 ± 0.2	92.0 ± 5.3
PPHN	50	39 ± 3	36 ± 8	1.0 ± 0.1	301.3 ± 11.3
PPHN	100	47 ± 5	40 ± 5	1.0 ± 0.1	641.3 ± 10.5

* Mean and standard error of mean.

However, in lambs with PPHN, use of 21% oxygen leads to normal PAO₂ but low PaO₂ compared to non-PPHN controls, and is associated with high PVR. Increasing calculated PAO₂ by increasing inspired oxygen led to a decrease in PVR (Table 1) [12]. In this model of primary PPHN, inspired oxygen concentration of 50% was needed to elicit maximal decrease in PVR. Although alveolar hypoxia worsens PPHN, hyperoxia (PAO₂ > 300 mmHg) did not have any additional vasodilator effect. Pulmonary vasodilator response to hyperoxia may not be sustained and could blunt the vasodilator response to inhaled nitric oxide (iNO) [32]. A concern with alveolar PAO₂ is that it is calculated using mathematical equations and in heterogenous lung disease, different areas of the lung may have different PAO₂ values.

In an acute meconium aspiration model of ovine PPHN, SpO₂ range of 90–94% was associated with an increase in PaO₂ alone without an increase in PAO₂ and resulted in a marginal improvement in PVR and PBF. At SpO₂ of 93–97% an increase in both PaO₂ and PAO₂ were necessary to achieve optimal decrease in PVR (Figure 3). With the high prevalence of PHT among extremely preterm infants, it is critical to understand the role of PAO₂ in regulating PVR [33]. Kinsella et al. evaluated the pulmonary vasodilator effect of iNO, oxygen and lung distension on developing pulmonary circulation [34]. In preterm lambs at 115 days GA (0.78 of term), pulmonary vasodilation was more prominent with rhythmic lung distension compared to supplemental oxygen or iNO [34]. In near term lambs, 100% oxygen and iNO led to profound pulmonary vasodilation [34]. We speculate that in the setting of extreme prematurity and respiratory distress syndrome in the absence of classic PPHN physiology, iNO and alveolar hyperoxia may not be effective in decreasing PVR compared to term neonates.

2.9. Arterial Oxygen Tension and Its Effect on PPHN

Predictal arterial oxygenation (PaO₂) is typically used to assess the severity (based on oxygenation index), management, and evaluate response to therapy in PPHN [35]. In neonates with PPHN treated with adequate ventilation and supplemental oxygen, a predictal PaO₂ of < 40 mmHg reflects hypoxemia. Secondary to right-to-left shunting across the ductus, there may be a pre and post ductal difference in SpO₂ and PaO₂. No clinical studies to date have studied the effect of maintaining various levels of PaO₂ in the management of PPHN. As mentioned previously, a predictal PaO₂ of > 52.5 ± 1.7 mmHg decreased PVR in ovine models without PPHN, while a PaO₂ of > 59.6 ± 15.3 mmHg was required to decrease PVR in a PPHN model [12]. In a preterm RDS model, a PaO₂ of > 58 mmHg was required to

decrease in PVR [17]. Similarly, the change point for preductal PaO₂ was 45 ± 0.1 mmHg in a model of asphyxia with meconium aspiration syndrome.

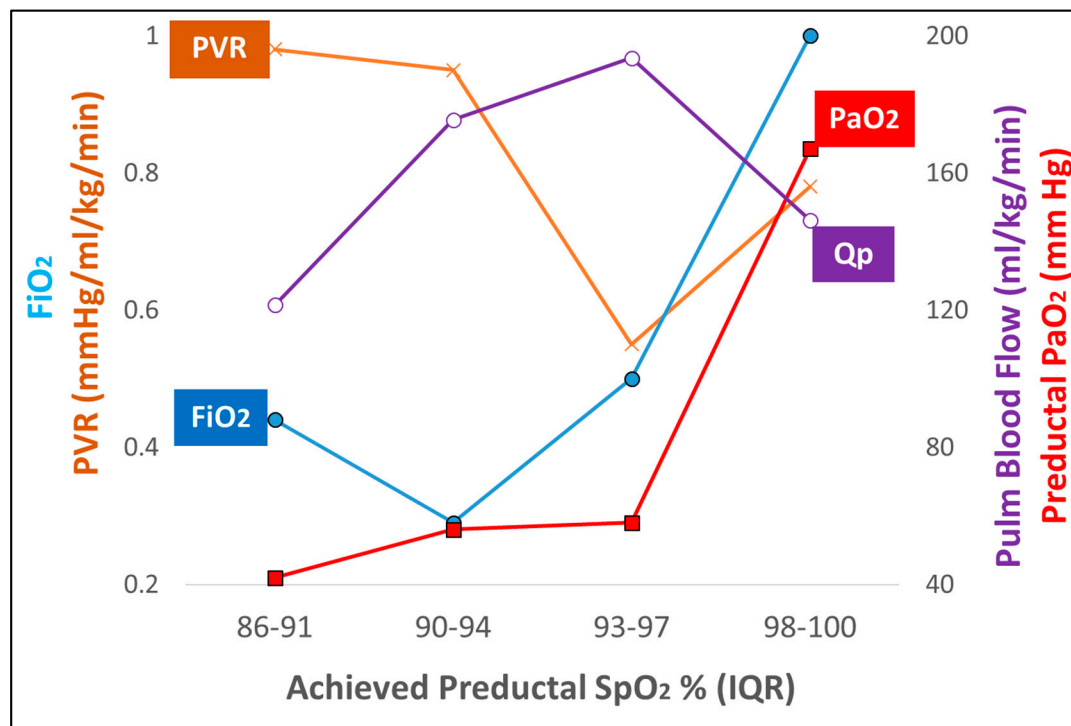


Figure 3. A graph depicting the relationship of inspired oxygen, PVR, left pulmonary blood flow, arterial oxygenation and preductal SpO₂ is illustrated in an ovine model of meconium aspiration model with PPHN. [36] The pulmonary vascular resistance (PVR—brown cross), pulmonary blood flow (Qp—purple open circles), FiO₂ (blue circles) and PaO₂ (red squares) at different preductal saturation (SpO₂) ranges are shown. Preductal SpO₂ in high 80 s resulted in high PVR and low Qp. Preductal SpO₂ in the low–90 s was associated with increased PaO₂, increased Qp, low FiO₂ and high PVR (due to high pulmonary arterial pressure—not shown). Preductal SpO₂ in the mid–90 s was associated with FiO₂ in the 0.5 range with lowest PVR, highest Qp in this model. Increasing FiO₂ to 1.0 increased PaO₂ and SpO₂ but did not result in further increase in Qp or decrease in PVR. For detailed statistical analysis, please refer to Rawat et al. [36]. Copyright Satyan Lakshminrusimha.

Recently, we have shown that in a model of asphyxia and meconium aspiration with PPHN during the first 6 h post-resuscitation, targeting a preductal SpO₂ of 95–99% and achieving 93–97% SpO₂ with a corresponding PaO₂ of 58 ± 19 mmHg was associated with the lowest PVR (0.55 ± 0.15 mmHg/mL/kg/min), with an inspired oxygen requirement of $50 \pm 21\%$ [36]. In this study, the SpO₂ range of 90–94% had a similar PaO₂ (56 ± 11 mmHg), but the corresponding PVR was much higher with a significantly lower inspired oxygen requirement ($29 \pm 17\%$) [36]. These results shown in Figure 3 outline the importance of alveolar PAO₂ in addition to arterial PaO₂ in mediating lower PVR. While the PaO₂ in the 90–94% SpO₂ group and 93–97% SpO₂ group were identical, we speculate that the difference in FiO₂ contributed to the marked decrease in PVR in the 93–97% group (Figure 3).

With the available data, preductal PaO₂ has a high utility in neonates with PPHN as it dictates the amount of oxygen delivered to the cerebral and coronary circulation. In summary, targeting preductal arterial oxygenation in the clinically accepted range of normoxemia (50–80 mmHg), could help in managing PPHN by optimizing oxygen delivery, but is not the only factor determining PVR. Providing adequate FiO₂ to maintain optimal alveolar PAO₂ is also important in mediating pulmonary vasodilation. Avoiding extremely high PaO₂ (>100 mmHg) and PAO₂ (>300 mmHg) may potentially facilitate response to other pulmonary vasodilators, reducing high cumulative oxygen exposure and

toxicity [12,30,32]. The optimal PaO₂ range during acute phase of PPHN warrants further clinical trials focusing on both short-term and long-term outcomes.

3. Post-Ductal PaO₂ (PDPaO₂) and PPHN

Given the easy arterial access path in neonates, a high umbilical arterial catheter (UAC), with its tip in the thoracic portion of the descending aorta, is the most commonly placed arterial access in the NICU [37]. When blood gas is obtained from the UAC, it usually reflects post-ductal (PDPaO₂) unless the ductus arteriosus is closed (Figure 1) [35]. Labile hypoxemia, in the presence of shunting from pulmonary to systemic circulation, could present with pre and post ductal PaO₂ gradient of 10–20 mmHg, which often goes in hand with pre and post ductal SpO₂ difference and is characteristic of PPHN. In the absence of shunting, a PDPaO₂ could reflect preductal PaO₂. In a clinical trial comparing the blood gas to saturation values, out of 800 arterial blood gas samples collected, 88% of the samples were postductal, which reflects the extensive use of PDPaO₂ to evaluate and guide therapy when supplemental oxygen is needed [27]. Using preductal SpO₂ to adjust FiO₂ is preferred to the use of PDPaO₂ during management of PPHN. However, absence of a preductal to postductal oxygenation gradient does not rule out bidirectional ductal shunting and low PBF [35].

3.1. Mixed Venous Oxygen Tension (PvO₂) and Management of PPHN

The mixed venous PO₂ typically refers to oxygen tension in the pulmonary artery [38]. Since umbilical venous catheters (UVC) are commonly placed in the NICU, the blood gas obtained from a UVC is used as a proxy for mixed venous gas [39]. The PVO₂ could assess the tissue oxygenation in neonates.

In a clinical study involving 22 neonates with respiratory failure requiring mechanical ventilation, PVO₂ had an inverse relationship with arterial-venous oxygen content difference ($r = -0.528$) and fractional oxygen extraction ($r = -0.592$). The position of UVC (high in the right atrium or near PFO vs. low in the inferior vena cava) could affect the PVO₂ measurements and may not accurately reflect the pulmonary arterial PO₂ especially if they are also being used to infuse fluids.

In our lab, in a meconium aspiration model and a preterm RDS model, a PVO₂ demonstrated a change point of 25 and 32 mmHg respectively [40,41] (Figure 4). The utility of PVO₂ from the UVC during the management of PPHN requires further exploration.

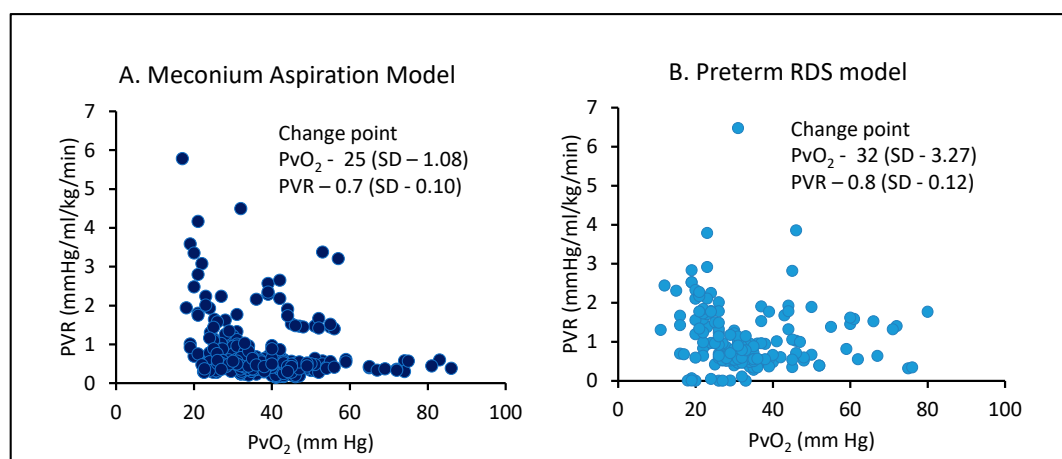


Figure 4. The scatterplot between PVR and PVO₂ is shown in (A) meconium aspiration model and (B) preterm RDS model. The PVO₂ was obtained from the main pulmonary artery blood gas. The MCMC model using SAS 9.4 (NC) estimated change point. Copyright MR/PC/SL.

3.2. Effect of Transfusion, pH and Temperature on Relationship between SpO₂ and PaO₂ in PPHN

The influence of transfusion, temperature and acidity (pH) on SpO₂ and PaO₂ could be explained by oxygen dissociation curve. Oxygen dissociation curve (ODC) explains the relationship between

oxygen saturation of the hemoglobin (plotted in y -axis) and oxygen tension (plotted in x -axis), which is essential for oxygen absorption in the lungs and delivery to the tissues [42]. A right shift in the curve is associated with release of O_2 to the tissues and a left shift is associated with O_2 absorption from the lungs. Fetal hemoglobin (HbF) is the predominant type during fetal and neonatal period. Secondary to high affinity of HbF to O_2 the ODC is shifted to the left in neonates and this could lead to higher oxygen saturation for lower PaO_2 . Thus, for a PaO_2 of approximately 40 mmHg, the SpO_2 could be between 85–93%, and for a SpO_2 of 97% the PaO_2 could be > 100 mm Hg [27]. Factors such as blood transfusions affect the ODC. The packed red blood cell transfusion that predominantly has HbA (adult hemoglobin), could alter the oxygen affinity moving the ODC to the right affecting the relation between SpO_2 and PaO_2 [42]. PPHN, respiratory failure and carbon dioxide retention with low pH could move the ODC right with lower affinity of Hb to O_2 , which affects the SpO_2 for a given PaO_2 . Lastly, temperature affects the blood gas analysis unless the values are corrected for body temperature [43].

The solubility of a gas increases with lower temperature and it is important to analyze blood gas and correct it for body temperature. In infants undergoing whole body hypothermia for moderate to severe hypoxic ischemic encephalopathy (HIE), periodic assessment of PaO_2 corrected for body temperature is important to avoid hypoxia and exacerbation of PPHN. Uncorrected PaO_2 and SpO_2 may not be reliable and targeting these values could potentially lead to hypoxemia during whole body hypothermia as shown in Figure 5 [43]. Thus, it is important that blood transfusions, pH and temperature be taken into account while managing an infant with PPHN. Periodically checking arterial blood gases and trying to maintain preductal PaO_2 in the 50–80 mmHg range may be beneficial in the management of PPHN by avoiding HPV.

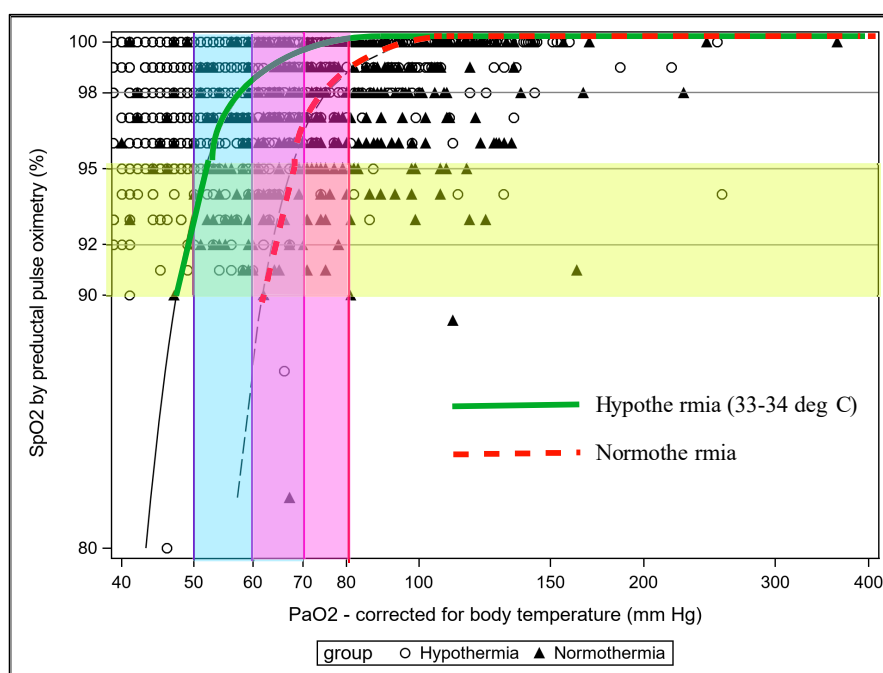


Figure 5. The relation between SpO_2 (y -axis) and PaO_2 (x -axis) in hypothermia and normothermia is shown. In normothermia and hypothermia, the relationship between SpO_2 and PaO_2 is altered. Targeting a preductal corrected PaO_2 of 50–80 mmHg may require preductal SpO_2 in the mid- to high 90 s during management of severe PPHN on whole body hypothermia. Copyright Satyan Lakshminrusimha.

4. Conclusions

In the management of PPHN, arterial oxygen tension plays an essential role in establishing the diagnosis, assessing the severity, guiding treatment, facilitating specific pulmonary vasodilator therapy, evaluating the response to therapy, and escalating care if needed. Since an UAC placement is standard

of care, the disadvantage of having PDPaO₂ could be a limitation, especially in severe PPHN with labile hypoxemia with ductal shunts. Preductal oxygenation dictates oxygen delivery to brain and heart. Hypoxic pulmonary vasoconstriction is associated with low alveolar oxygen tension and mixed venous oxygen tension. While SpO₂ provides a continuous, non-invasive assessment of preductal oxygenation, periodic blood gas evaluation is warranted especially in the presence of hypothermia or acidosis. Further clinical trials are warranted to assess the utility of preductal, postductal, and umbilical venous PO₂ in addition to preductal SpO₂ in the management of PPHN.

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