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RESEARCH

Integrative Pediatrics

Pulse Oximetric Saturation/Fraction of Inspired Oxygen Ratio Reflects Severity of Ductal Shunting

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Abstract

Although the physiology of left to right ductal shunting is well described, its clinical implications remain controversial. The $0_2Sat/Fi0_2$ ratio (SFR) is a non-invasive tool reflecting pulmonary oxygen diffusion. We present a retrospective review showing a significant reduction in SFR at 36 weeks postmenstrual age following early hemodynamically significant PDA.

Introduction

The clinical significance of patency of the ductus arteriosus (PDA) in preterm neonates remains one of the most enigmatic and controversial issues in modern neonatology. Although the physiology of left to right ductal shunting is well described, the clinical implications of this shunting on the lungs remain controversial. The $SatO_2/FiO_2$ ratio (SFR) is a noninvasive tool reflecting pulmonary O_2 diffusion impairment. It has been correlated with preterm respiratory disease [1], septic shock [2] and hypoxia [3]. SFR offers a continuous, reliable surrogate for the PaO_2/FiO_2 ratio regardless of whether the children are ventilated or breathing spontaneously without supplementary oxygen [4,5].

To date there are no data using SFR to study the early pulmonary effects of ductal shunting. In this retrospective study we hypothesized that significant ductal shunting impairs neonatal pulmonary oxygen diffusion which will be reflected by decreased SFR.

Methods

In this retrospective, observational study, records were retrieved for neonates <30 weeks gestational age (GA) born between 2017-2019 in the Shaare Zedek Medical Center. We routinely perform echocardiographic screening on preterm neonates during the first week of life. Babies were grouped by initial ductal status as either closed; open but hemodynamically insignificant (hisPDA); or hemodynamically significant (hsPDA).

Transcutaneous oxygen saturation (SpO_2) values were targeted between 90% and 94% throughout the study. SFR was calculated as $SpO_2/Fi0_2$ on day 7 of life and at 36 weeks postmenstrual age. The highest possible SFR value would be 476 in an infant with an SpO2 of 100% in 21% oxygen. For consistency, the first recorded oximeter and $Fi0_2$ readings of the morning on the day of the echocardiogram were selected for analysis.

No babies were treated for PDA (prophylactic or therapeutic) prior to their initial echocardiogram. hisPDAs were not treated. Our first line therapy for hsPDAs is acetaminophen, with ibuprofen as a second line. Infants with congenital heart disease and those who did not survive to 36 weeks were excluded from subsequent analysis. This retrospective study was approved by the local institutional review board.

Statistical analysis

Statistical analysis was carried out using MedCalc Statistical Software version 17.2 (MedCalc Software, Ostend, Belgium.) All data were first checked for normality using the Shapiro Wilks test. Continuous variables with a normal distribution were compared using ANOVA with post-hoc analysis by the Student-Newman-Keuls test. Continuous variables without a normal distribution were expressed as median [95% confidence interval] and were compared using the Mann-Whitney or Kruskal Wallis test. Categorical variables were compared using Fisher Exact test. Multivariable regression analysis was performed with SFR as the dependent variable and those variables found significant ($p<0.05$) by univariable analysis as independent variables to identify the

predictors of SFR outcome. For the purpose of analyses, we defined BPD as a supplemental requirement at 36 weeks' postmenstrual age and NEC according to Bell criteria stage 2 / 3.

Results

138 infants <30 weeks GA were born during the period specified. 32 expired before 36 weeks; two additional infants with complex congenital heart disease were excluded. The remaining 104 infants were grouped by ductal status (65-closed ducts; 17-hisPDAs and 22-hsPDAs). Babies with hsPDA had more BPD [14%-closed; 35%-hisPDA; 55% hsPDA respectively; p=0.005]. Babies with hsPDA had significantly lower SFR values at all time points. SFR in babies with hisPDA were decreased at 1 week postnatally, but similar to those of babies with closed ducts at 36 weeks (Figure 1).

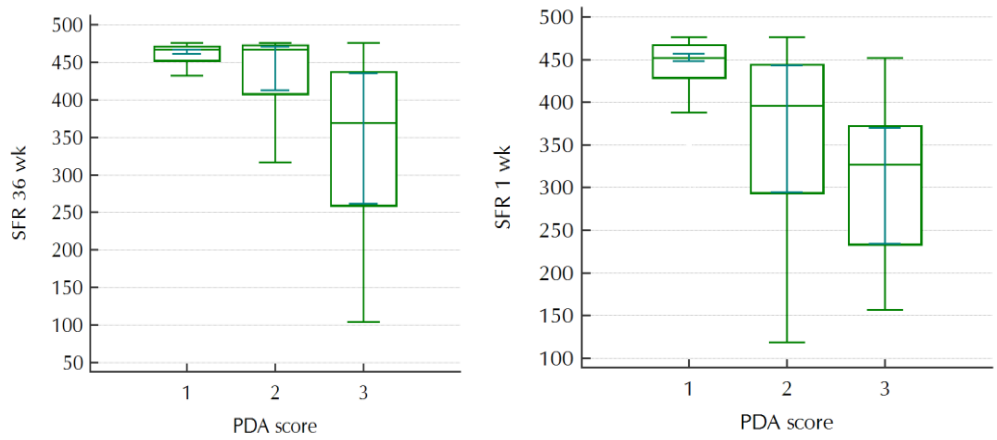

Figure 1. Median [95% confidence interval] SFR values at 1 week postnatal age, and at 36 weeks postmenstrual age as grouped by ductal status. SFR values in babies with hisPDA were decreased at 1 week postnatally [closed ducts 452[448,457] vs. hisPDA 396[294,442] vs. hsPDA 327[235,369]; p=0.00001], but were similar to those of babies with closed ducts at 36 weeks [467[461,467] vs. 467[413,471] vs. 369[262,436] respectively; p=0.000148].

We performed a multivariable regression analysis to identify the relative contributions of birth weight, GA, apgar scores and PDA severity to SFR. At 1 week of age, although PDA severity significantly affected SFR (p=0.0017), GA was the most significant contributor (p=0.0006). However, by 36 weeks, PDA severity was most significantly correlated with SFR (p=0.0098) while GA was no longer significant (p=0.2754).fracture.

Discussion

Signficant PDA shunting can increase pulmonary hydrostatic pressure and pulmonary edema, ultimately increasing the risk of BPD. The noninvasive SFR reflects pulmonary oxygen diffusion [1] and has been shown to be a reliable surrogate for the PaO_2/FiO_2 ratio in a variety of clinical settings [6].

Our data demonstrate a clear relationship between ductal severity within the first week of life and the subsequent SFR, consistent with a significant effect of ductal shunting on pulmonary oxygen diffusion. This is the first study documenting ongoing subclinical respiratory impairment, reflected by SFR, related to the severity of early ductal shunting. We believe that this supports an association between hemodynamically significant PDA and BPD [7].

Our results are consistent with those of Nobile et al. [1] who found significantly different 36 wk SFR between BPD and non-BPD infants. This observation raises the question as to whether the lower SFRs we noted at 36 weeks merely reflect developing BPD. In this context it is important to note that SFRs were significantly and similarly decreased in hsPDA infants from the first week of life – long before BPD. In addition, the results of the multivariable regression analysis confirm that PDA severity is the most significant contributor to SFR at 36 weeks.

Of note is the behavior of the different PDA subgroups. While the hsPDA shows consistently decreased lung perfusion over all three time slots, the hisPDA group showed only a transient effect, decreased at week 1 but not at 36 weeks.

The major limitation of this study is its retrospective nature. Second, although $Fi0_2$ and pulse oximetry measurements were close in time to each other, they were not recorded simultaneously. However, we believe that the observation that the severity ductal patency in the first week of life predicts

differences in SFR at 36 weeks does imply a pathogenic relationship.

References

1. Nobile S, Marchionni P, Gidiucci C, Correani A, Palazzi ML, et al. Oxygen saturation/FIO2 ratio at 36 weeks' PMA in 1005 preterm infants: Effect of gestational age and early respiratory disease patterns. *Pediatr Pulmonol*. 2019; 54: 637-643
2. Serpa Neto A, Cardoso SO, Ong DS, Espósito DC, Pereira VGM, et al. The use of the pulse oximetric saturation/fraction of inspired oxygen ratio for risk stratification of patients with severe sepsis and septic shock. *J Crit Care*. 2013;28: 681–686.
3. Tripathi RS, Blum JM, Rosenberg AL, Tremper KK. Pulse oximetry saturation to fraction inspired oxygen ratio as a measure of hypoxia under general anesthesia and the influence of positive end-expiratory pressure. *J Crit Care*. 2010; 25: 542.
4. Bernard GR, Artigas A, Brigham KL, Carlet J, Falke K, et al. The American-EuropeanConsensus Conference on ARDS: definitions, mechanisms, relevantoutcomes, and clinical trial coordination. *Am J Respir Crit Care Med*. 1994; 149: 818-824
5. Lobete C, Medina A, Rey C, Mayordomo-Colunga J, Concha A, et al. Correlation of oxygen saturation as measured by pulse oximetry/fraction of inspired oxygen ratio with Pao2/fraction of inspired oxygen ratio in a heterogeneous sample of critically ill children. *J Crit Care*. 2013; 28: 538.
6. Khemani RG, Patel NR, Bart RD 3rd, Newth CJL. Comparison of the pulse oximetric saturation/fraction of inspired oxygen ratio and the PaO2/fraction of inspired oxygen ratio in children. *Chest*. 2009; 135: 662-668.
7. Clyman RI, Hills NK, Liebowitz M, Johng S. Relationship between Duration of Infant Exposure to a Moderate-to-Large Patent Ductus Arteriosus Shunt and the Risk of Developing Bronchopulmonary Dysplasia or Death Before 36 Weeks. *Am J Perinatol*. 2019; 37: 216-223.

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