ORIGINAL ARTICLE ÖZGÜN ARAŞTIRMA

Can Tissue Oxygen Saturation Levels in the First 24 Hours Predict the Development of Patent Ductus Arteriosus in Premature Babies with Respiratory Distress Syndrome?

Respiratuar Distres Sendromlu Prematüre Bebeklerde İlk 24 Saatteki Doku Oksijen Satürasyon Düzeyleri Patent Ductus Arteriosus Gelişimini Öngörebilir mi?

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Abstract

Introduction: Patent ductus arteriosus (PDA) causes a substantial increase in morbidities in premature babies by causing changes in organ perfusion. Various echocardiographic parameters are used to diagnose PDA and determine whether it is hemodynamically significant (HsPDA). This study aimed to investigate the role of tissue oxygen saturation in the first 24 hours in predicting HsPDA in high-risk premature babies who received respiratory support because of respiratory distress syndrome.

Materials and Methods: In this prospective, observational study, cerebral, renal, and mesenteric regional tissue oxygen saturation levels were monitored by near infrared spectroscopy (NIRS) for the first 24 hours of the lives of preterm babies at ≤ 28 weeks of gestation. The NIRS data of babies with and without HsPDA as diagnosed by echocardiographic examination were compared.

Results: Eighty-one premature babies who had HsPDA were included in the study. In the control group 51 premature babies who had not HsPDA were evaluated. The median ± standard deviation (SD) gestational age of the babies included in the study was 26.9 ± 1 weeks, and the mean ± SD birth weight was 880 ± 218 g. Renal and mesenteric NIRS measurements during follow-up were lower in babies with versus without HsPDA, but the difference was not statistically significant.

Conclusion: Low renal and mesenteric stO2 values detected on the first day of life in high-risk infants may be associated with HsPDA. More studies are needed to reveal the effects of HsDPA on organs in these vulnerable babies with NIRS monitoring.

Keywords
Near-infrared spectroscopy, patent ductus arteriosus, premature

Anahtar kelimeler
Yakın kızıl ötesi spektroskopi, patent duktus arteriozus, prematüre

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Öz

Giriş: Patent duktus arteriozus (PDA) organ perfüzyonunda değişikliklere neden olarak prematüre bebeklerde önemli oranda morbidite artışına neden olur. PDA'yı teşhis etmek ve hemodinamik olarak anlamlı olup olmadığını (HdaPDA) belirlemek için çeşitli ekokardiyografik parametreler kullanılır. Bu çalışma, respiratuar distres

sendromu nedeniyle solunum desteği alan yüksek riskli prematüre bebeklerde, ilk 24 saat doku oksijen satürasyonunun HdaPDA'yı öngörmedeki rolününün araştırılması amaçladı.
Gereç ve Yöntem: Bu prospektif, gözlemsel çalışmada, ≤ 28 gebelik hafta doğan prematüre bebeklerin hayatlarının ilk 24 saatinde serebral, renal ve mezenterik bölgesel doku oksijen satürasyon seviyeleri yakın kızılötesi spektroskopi (NIRS) ile izlendi. Ekokardiyografik inceleme ile HdaPDA'sı olan ve olmayan bebeklerin NIRS verileri karşılaştırıldı.
Bulgular: Çalışmaya HdaPDA'sı olan 81 prematüre bebek dahil edildi. Kontrol grubunda HdaPDA'sı olmayan 51 prematüre bebek değerlendirildi. Çalışmaya alınan bebeklerin ortalama gebelik yaşı 26,9 ± 1 hafta, ortalama doğum ağırlığı 880 ± 218 gr idi. Takip sırasında renal ve mezenterik NIRS ölçümleri HsPDA'sı olan bebeklerde olmayanlara göre daha düşüktü, ancak fark istatistiksel olarak anlamlı değildi.
Sonuç: Yüksek riskli bebeklerde yaşamın ilk gününde saptanan düşük renal ve mezenterik doku oksijen satürasyon değerleri HdaPDA ile ilişkili olabilir. NIRS izlemi ile HdaDPA'nın organlar üzerindeki etkilerini ortaya çıkarmak için daha fazla çalışmaya ihtiyaç vardır.

Introduction

Patent ductus arteriosus (PDA) appears as an important cardiovascular problem in approximately two-thirds of premature babies born at ≤ 28 weeks of gestation (1). When PDA is hemodynamically significant (HsPDA), a decrease in cerebral, renal, and gastrointestinal perfusion and a decrease in the regional tissue oxygen saturation (rSO_2) levels in these organs occur (2,3). In addition, a left-to-right shunt develops and causes pulmonary hyperperfusion (4). All these changes result in an increase in pulmonary, cerebral, intestinal, and renal morbidity and mortality in this vulnerable population (4). An echocardiographic examination in the first 24–72 hours of life is recommended to assess these changes and to facilitate early diagnosis and close follow-up of HsPDA, especially in babies ≤ 28 weeks, who represent a high-risk group for these morbidities and often require a ventilator because of respiratory distress syndrome (RDS) (5). Most occurrences of intraventricular hemorrhage (IVH), which is an important morbidity in very low-birth-weight babies, occur within the first few days of life (6). Early diagnosis and treatment of PDAs contribute to a decrease in the frequency of pulmonary hemorrhage (7).

PDA and its hemodynamic effects can be recognized easily by echocardiography. This gold-standard method is also necessary to reveal other congenital, structural cardiac pathologies (3). However, in an extremely premature baby with extremely low birth weight, hemodynamic changes occur continuously, especially in the first days of life (8). Continuous and close monitoring of hemodynamic changes and management of them according to evidence are important to prevent related morbidities. It is not possible to monitor continuously with echocardiography.

Near-infrared spectroscopy (NIRS) is a noninvasive method for measuring tissue oxygenation by taking advantage of the difference in infrared light absorption between oxyhemoglobin and deoxyhemoglobin (9). It also provides data for calculating tissue oxygen consumption (9). NIRS provides continuous and real-time monitoring of the effects of HsPDA on cerebral, renal, and gastrointestinal perfusion and rSO_2. This study aimed to investigate the role of tissue levels of oxygen saturation in the first 24 hours in predicting HsPDA in high-risk, premature babies who received respiratory support because of RDS.

Materials and Methods

Study Design

This prospective, observational study was conducted in two different tertiary neonatal intensive care units (NICUs) over a 12-month period. Approval for the study was obtained from the Bursa Uludag University Faculty of Medicine Clinical Research Ethics Committee (decision no: 2012-26/11). Written informed consent was obtained from the parents of the babies before they were included in the study.

Study Population

Premature babies born at ≤28 weeks of gestation and receiving respiratory support with a diagnosis of RDS were included in the study. Babies with congenital malformations, with chromosomal abnormalities, and without parental consent were excluded from the study.

Study Protocol

The babies, who were born in the study centers, were resuscitated in accordance with the neonatal

resuscitation program and were stabilized in the NICUs. Respiratory support, pulse oximetry goals, oxygen, and surfactant therapy were carried out in line with the recommendations of the European consensus (10). The diagnosis of RDS was made according to clinical and radiologic findings.

Consent was obtained from the parents of the babies who met the study criteria. After consent, the cerebral, renal, and mesenteric rSO_2 levels of the babies were recorded for 24 hours with an NIRS device (Invos; Covidien). Neonatal NIRS probes were placed on the forehead for cerebral measurements and just above the hip, to the left of the spine, for renal measurements. Kidney localization was confirmed by ultrasound. A NIRS probe was placed in the left paraumbilical region for mesenteric measurements. At the same time, pulse oximetry (using a Covidien device) was monitored from the right wrist, and peripheral artery oxygen saturation levels were recorded. The 5-minute average of the recordings was calculated. Fractional tissue oxygen extraction (FTOE) was calculated from the data obtained.

An echocardiographic examination was performed in all patients between 48 and 72 hours (mean ± standard deviation, 58 ± 4 hours) after birth. According to the examination results, babies with HsPDA were included as group 1. The existence of the following criteria represented HsPDA: ductus diameter ≥ 1.5 mm, left atrium/aorta ratio ≥ 1.5 mm, and presence of retrograde flow in the descending aorta. The babies who did not meet any of these criteria represented the control group (group 2). Babies with HsPDA were treated primarily with ibuprofen. If contraindicated, paracetamol was given.

Prenatal and neonatal characteristics and demographic data of both groups were recorded. Babies were evaluated by ultrasound for IVH in the first 24 hours and on the third and seventh days. In addition to clinical and blood gas monitoring, daily creatinine values were monitored to assess renal function. Serum creatinine values > 1.5 mg/dL after the first day defined acute kidney injury.

Statistical Analysis

The data from babies in the groups with and without HsPDA were compared. SPSS (version 23; SPSS Inc., Chicago, IL) was used for statistical analysis. Results were expressed as percentages and means ± standard deviations (SDs) if distributed normally. The Shapiro-Wilk test was used to determine whether the data had a normal distribution. The t-test was used to compare the mean distribution of the two groups, and the chi-square test was used to compare the proportions of categorical variables. A p value of < 0.05 was considered significant.

Results

Eighty-one premature babies who had HsPDA were included in the study (group 1). In the control group 51 premature babies who had not HsPDA were evaluated (group 2). The median gestational age of the babies in group 1 was 26,8±1,1 weeks, and the mean birth weight was 860±152 g. In the control group, the median gestational age of the babies was 27,1±0,9 weeks, and the mean birth weight was 915±2032 g. The prenatal and neonatal characteristics of babies were similar in both groups (Table 1). IVH was significantly more common in the HsPDA group.

There was no difference between the groups in terms of cerebral NIRS measurements (Figure 1) and calculated FTEO values. Renal and mesenteric NIRS measurements during follow-up were lower in babies with HsPDA, but the difference was not statistically significant ($p > 0.05$; Figures 2,3). No metabolic acidosis or renal injury was observed in the babies in either group during the follow-up period.

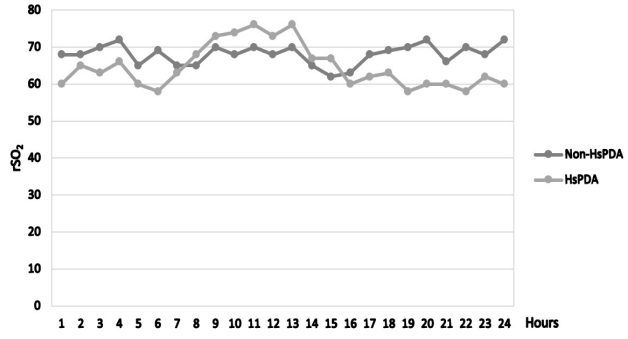

Figure 1. The cerebral tissue oxygen saturations of babies with and without hemodynamically significant patent ductus arteriosus. (HsPDA: hemodynamically significant patent ductus arteriosus, rSO2; regional saturation of oxygen)

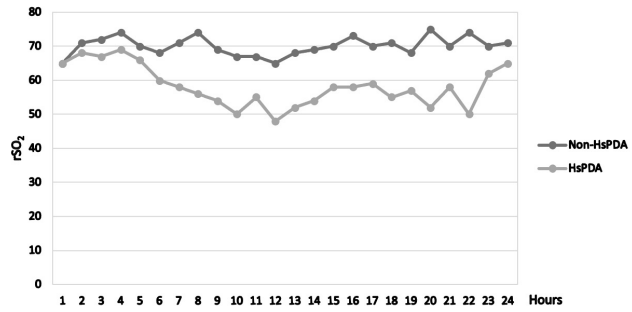

Figure 2. The renal tissue oxygen saturations of babies with and without hemodynamically significant patent ductus arteriosus. (HsPDA: hemodynamically significant patent ductus arteriosus, rSO2; regional saturation of oxygen)

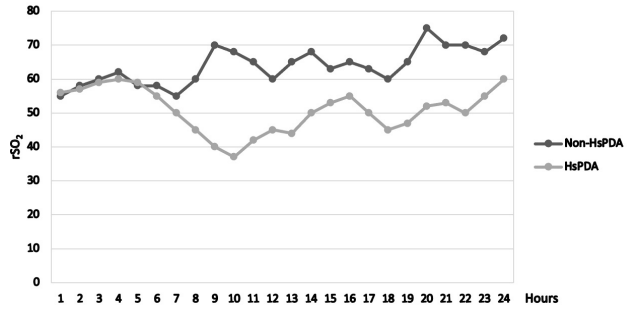

Figure 3. The mesenteric tissue oxygen saturations of babies with and without hemodynamically significant patent ductus arteriosus. (HsPDA: hemodynamically significant patent ductus arteriosus, rSO2; regional saturation of oxygen)

Table 1. Comparison of demographic and neonatal data of patients with and without HsPDA

	Group 1 (HsPDA) N:n= 81	Group 2 (Non-HsPDA) N:n= 51	p-value
Prenatal features			
Preeclampsia, n (%)	11 (14)	7 (14)	> 0,05
PROM, n (%)	18 (22)	9 (18)	> 0,05
Antenatal steroid treatment, n (%)	49 (60)	23 (45)	> 0,05
Neonatal features			
Birth weight (gr), med±sd	860±152	915±203	> 0,05
Gestational age (weeks), med±sd	26,8±1,1	27,1±0,9	> 0,05
Male, n (%)	45 (56)	29 (57)	> 0,05
Caesarean section, n (%)	68 (84)	43 (84)	> 0,05
Apgar score 1st minute, med±sd	4,1±2,1	4,1±2,1	> 0,05
Apgar score 5th minute, med±sd	6,2±1,3	6,4±1,8	> 0,05
Invasive ventilation, n (%)	45 (56)	27 (53)	> 0,05
Intraventricular Hemorrhage, n (%) • Grade 1 • Grade 2 • Grade 3 • Grade 4	43(53) 16 10 6 11	17 (33) 1 8 3 5	0,03
Necrotizing Enterocolitis, n (%)	27 (33)	14 (27,4)	> 0,05

HsPDA: Hemodynamically significant patent ductus arteriosus
PROM: Premature rupture of membranes

Discussion

HsPDA is an important cause of mortality and morbidity in premature babies. Therefore, early recognition and proper management are extremely important. Approximately two-thirds of premature babies with extremely low birth weights experience acute or chronic negative effects of PDA (11). Long-term exposure to the hemodynamic effects of PDA increases the likelihood of necrotizing enterocolitis, renal failure, retinopathy of prematurity, IVH, pulmonary bleeding, chronic lung disease, and mortality in these sensitive, premature babies (1,12,13). One possible mechanism driving these adverse effects is the change in organ perfusion caused by HsPDA (13-15). The diagnosis of HsPDA and the identification of its hemodynamic effects are possible with echocardiographic examination. However, this

method cannot provide continuous monitoring of premature babies.

In the past decade, the use of NIRS technology has increased rapidly in NICUs, especially in relation to premature morbidities (16). Arman et al. (15) found a significant correlation between NIRS measurements, and the blood flow velocities revealed by Doppler examinations of the middle cerebral artery, the superior mesenteric artery, and the renal artery. They reported that NIRS can be used to monitor organ perfusion in premature babies with HsPDA. In our study, we used NIRS monitoring in the first hours of life to predict the development of HsPDA in babies with RDS.

We found that cerebral rSO_2 values in babies with and without HsPDA were similar. Cerebral FTOE values have also been similar in babies with or without HsPDA. Costa et al. (16) reported a correlation between cerebral oxygenation and systemic flow during the first 48 hours (16). They also found that, in the first 24 hours of life, left cardiac output is a reliable indicator of systemic blood flow, and ductal steal does not affect cerebral blood flow. We believe that the similar cerebral rSO_2 values in both groups in our study reflect the physiological autoregulation mechanism. In addition, the evaluation of NIRS data as the averages of a certain time interval does not allow the detection of short-term fluctuations in the cerebrospinal blood flow that cause IVH, due to HsPDA.

However, Poon et al. (17) reported that closure of the ductus after treatment was associated with increased cerebral rSO_2 levels and decreased FTOE in infants who were treated for HsPDA after the second day lives of preterm babies. Similarly, Schwarz et al. (9) reported that cerebral oxygenation differed significantly between preterm infants with and without HsPDA who underwent echocardiography for clinical suspicion of HsPDA. They also reported that NIRS data could be used to guide PDA treatment decisions. Cohen et al. (18) also reported that the ductus diameter was associated with cerebral oxygenation over time and that decreased cerebral oxygenation over time may suggest HsPDA. In our study, low variability of cerebral tissue oxygenation in patients with, versus without, HsPDA in the follow-up assessment performed on the first day is consistent with the results of other studies. The lack of longer-term follow-up is a limitation of our study.

We observed that renal and mesenteric rSO_2 values during follow-up were lower in babies with HsPDA. Others have reported that renal and mesenteric rSO_2 measurements, especially after the sixth hour of follow-up, remain low; in our study, levels were lowest at a mean of 12 hours and remained low throughout follow-up (24 hours). However, even the largest difference between the two groups did not reach statistical significance. Chock et al. (14) reported that low renal rSO_2 values on NIRS monitoring were associated with HsPDA from the third day of life. They speculated that cerebral NIRS values were not affected by the negative effects of HsPDA because of autoregulation. Van Der Laan et al. (13) also reported no effect of HsPDA on renal and cerebral oxygenation from the third day of life. They noted that the lack of difference between the groups in their study might have resulted from how they defined HsPDA.

Petrova et al. (19) reported that PDA diameter did not affect renal and cerebral oxygenation and that mesenteric tissue oxygen values decreased with increasing PDA diameter. Arman et al. (15) found that mesenteric, cerebral, and renal flows did not correlate with PDA diameter. However, they also reported that both NIRS and blood flow rate measurements improved after treatment for PDA in correlation with each other.

We are aware that the fact that NIRS follow-up periods did not continue for a longer period in our study is an important limitation of our study. However, our aim in this study is to understand whether tissue oxygen saturation monitoring in different organs in the critical first hours of life will be associated with the development of HsPDA, not to diagnose HsPDA.

Conclusion

HsPDA continues to be an important clinical problem for extremely premature babies. New techniques that can be easily used at the bedside are required for the early recognition of HsPDA and continuous monitoring of its hemodynamic effects. Our study provides data on the use of NIRS monitoring in predicting HsPDA. NIRS monitoring from the first day of life can provide evidence-based data to facilitate the early recognition of HsPDA and its effect on organ perfusion levels. Decreases in renal and mesenteric rSO_2 values without clinical findings of PDA may be a warning of PDA.

Ethics

Ethics Committee Approval: Ethics committee approval was obtained from the Bursa Uludag University Faculty of Medicine Clinical Research Ethics Committee with decision number 2012-26/11.

Conflict of Interest: No conflict of interest was declared by the authors.

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