

Assesment of Pleth Variability Index in Moderate-late Preterm Infants

Orta-Geç Preterm İnfantlarda Pletismografik Variabilite İndeksi Değerlendirilmesi

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Cite as: Işık Ş, Kanmaz Kutman HG, AKIN MŞ, Ertekin Ö, Oğuz ŞS. Assesment of Pleth Variability Index in Moderate-late Preterm Infants. Forbes J Med 2023;4(1):84-8

ABSTRACT

Objective: The pleth variability index (PVI) allows the non-invasive detection of hemodynamic changes but is not yet commonly used in neonates. This study determined reference values for PVI in spontaneously breathing moderate to late preterm newborns during the first 12 hours of life and evaluate the relationship between these values and respiratory morbidity.

Methods: The study included infants born at 32-37 weeks of gestation who had good spontaneous respiratory effort, were hemodynamically stable and were hospitalized in a tertiary neonatal intensive care unit. PVI, perfusion index (PI), oxygen saturation, and heart rate were prospectively monitored every 2 s for the first 12 h postnatally. Basic characteristic findings were obtained from patient records.

Results: Data from a total of 58 patients were analyzed. The mean PVI was $21\pm 4.3\%$ and mean PI was $0.85\pm 0.25\%$. Comparison of patients who required respiratory support ($n=43$) and those who received no respiratory support ($n=15$) showed that the heart rate (137.5 ± 10.6 vs. 129.7 ± 9.6 , $p=0.01$) is significantly higher and PI ($0.8\pm 0.2\%$ vs. $0.9\pm 0.3\%$, $p=0.03$) is significantly lower in the respiratory support group. Moreover, PVI levels were found to be slightly higher in infants who get respiratory support ($21.7\pm 4.5\%$ vs. $19.2\pm 3.2\%$, $p=0.05$).

Conclusion: PVI can be successfully measured in moderate-to late preterm newborns. More extensive studies are needed to obtain information on the clinical use of PVI, interpretation of abnormal results, its association with neonatal morbidities, and treatment management.

Keywords: Preterm, pleth variability index, pulse oximeter

ÖZ

Amaç: Pletismografik variabilite indeksi (PVI) hemodinamik değişiklikleri non-invaziv olarak tespit edebilen, yenidoğanlarda henüz sık olarak kullanılmayan bir araçtır. Bu çalışmanın amacı yaşamın ilk 12 saati boyunca spontan soluyan ılımlı ve/veya geç preterm yenidoğanlarda PVI için referans değerleri belirlenmesi ve bu değerlerin solunumsal morbiditeler ile ilişkisinin saptanmasıdır.

Yöntem: Üçüncü basamak yenidoğan yoğun bakım ünitesinde yatırılarak izlenen 32-37 gebelik haftaları arasında doğmuş, spontan solunum çabası iyi olan, hemodinamik olarak stabil olan bebekler dahil edildi. Prospektif kesitsel olarak hayatın ilk 12 saati boyunca perfüzyon indeksi (PI), PVI, oksijen satürasyonu ve kalp hızı; 2 saniyede bir ölçüm yapılacak şekilde monitorize edildi. Temel karakteristik bulgular hasta kayıtlarından elde edildi.

Bulgular: Toplam 58 hastanın verisi analiz edildi. Ortalama PVI değeri $21\pm 4,3$, PI değeri ise $0,85\pm 0,25$ olarak bulundu. İnvaziv olmayan solunum desteği gerektiren ($n=43$) ve hiç solunum desteği almayan ($n=15$) hastalar kıyaslandığında kalp hızı, satürasyon, PI benzer bulunurken; PVI ($21,7\pm 4,5$ ve $19,2\pm 3,2$) değeri solunum desteği alanlarda daha yüksek olmasına rağmen istatistiksel anlama ulaşmadı ($p=0,05$).

Received/Geliş: 14.09.2022

Accepted/Kabul: 28.11.2022

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Sonuç: PVI ılımlı ve geç preterm yenidoğanlarda başarılı şekilde ölçülebilmektedir. PVI'nin klinik kullanımı, anormal sonuçların yorumlanması, yenidoğan bebeklerde morbiditeler ile ilişkisi ve tedavi yönetimi ile ilgili bilgi verecek daha geniş kapsamlı çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Preterm, pletismografik variabilite indeksi, nabız oksimetre

INTRODUCTION

Pulse oximetry has been used in neonatal monitoring for many years. It is the most widely used non-invasive method to monitor critically ill patients.^{1,2} The signal consists of two components, the pulsatile arterial component and the non-pulsatile component from other light-absorbing tissues such as connective tissue, bone, and venous blood. Oxygen saturation is an analysis of the pulsatile component.

The perfusion index (PI) is a numerical measure of peripheral perfusion derived from a pulse oximeter. The PI is the ratio of the pulsatile component [alternating current (AC) to the non-pulsatile component direct current (DC)] of light reaching the detector, expressed as a percentage ($PI = [AC / DC] \times 100$).³

Numerous studies have investigated PI in neonates. The median PI value for healthy neonates was determined to be 1.7% in these studies. PI reflects changes in peripheral blood flow, and a PI value lower than 1.24% was shown to be a marker for assessing the severity of neonatal disease.³

The pleth variability index (PVI) is a non-invasive and continuous measure of the dynamic change in PI occurring during one or more respiratory cycles ($PVI = [PI_{\text{maximum}} - PI_{\text{minimum}}] / PI_{\text{maximum}} \times 100$). Today, PVI is used to identify hemodynamic changes in adult patients, to determine right atrium volume, and in the management of fluid and inotropic therapy. Data on PVI values in neonates are still scarce.

In this study, we determined reference values for PVI in spontaneously breathing moderate to late preterm (32-37 weeks) neonates and determine the relationship between these values and neonatal morbidities.

METHODS

This prospective, cross-sectional study included infants who were born between 32 and 37 weeks of gestation, had good spontaneous respiratory effort, were hemodynamically stable and were admitted to the neonatal intensive care unit. Infants with perinatal asphyxia, sepsis, or known cardiac or pulmonary anomalies, and those that required inotropic therapy were excluded. The study was approved by the Ethics Committee of Zekai Tahir Burak Maternity and Teaching Hospital (9/2016).

In our tertiary neonatal intensive care unit, which serves as a referral center, preterm infants are managed using standard protocols. Infants admitted to intensive care

within the first 24 h of life receive 70-80 mL/kg electrolyte-free fluid therapy. After hemodynamic stabilization, enteral feeding (preferably with breast milk) is started if not contraindicated.⁴ Infants with a Silverman-Anderson score of ≥ 6 are provided respiratory support starting with non-invasive methods.⁵ Respiratory distress syndrome (RDS) and patent ductus arteriosus (PDA) were diagnosed according to the guidelines of the Turkish Neonatology Association.^{6,7}

The same guidelines were used for treatment and management.

As soon after admission as possible, infants were monitored with the Masimo Radical-87[®] monitor, which has a program to measure PVI. To ensure standardization, the sensor was attached to the right lower extremity in all infants. During the first 12 h of life, PI, PVI, oxygen saturation, and heart rate were measured every 2 s. Data stored on the monitor were transferred to a personal computer using the TrendCom data transfer program and analyzed by a blinded researcher.

Statistical Analysis

The data were analyzed using Statistical Package for the Social Sciences (SPSS) version 17.0 (SPSS, Chicago, IL). Student's t-test or chi-square test was used for normally distributed data and Mann-Whitney U test was used for non-normally distributed data. Correlations were analyzed using Pearson or Spearman correlation coefficients. The results were expressed as mean \pm standard deviation, median and range, or frequency and percentage. $P < 0.05$ was considered statistically significant.

RESULTS

Data from a total of 58 infants were analyzed. The neonates were born at a median gestational age of 34 weeks (range, 32-37) and median birth weight of 2115 g (range, 870-3900), 48 (82.7%) were born by cesarean delivery, and 30 (51.7%) were male. Eleven (18.9%) infants were born from multiple pregnancies, and 22 (38%) had received antenatal steroids. PDA was detected in 5 infants (8.6%), and 3 of them (5.1%) received medical treatment for hemodynamically significant PDA. Seven patients (12%) were diagnosed with RDS. Among all infants, the mean PVI was $21 \pm 4.3\%$ and the mean PI was $0.85 \pm 0.25\%$. The 10th, 50th, and 90th percentile values for PVI were 16.6%, 19.6%, and 27%, respectively (Table 1).

We did not find any correlation with gestational age and birth weight with PI, PVI, saturation, or heart rate ($p>0.01$). Heart rate was weakly negatively correlated with PI ($r=-0.35$, $p=0.007$) and PVI ($r=-0.26$, $p=0.04$) values.

Comparison of neonates who required non-invasive respiratory support ($n=43$) and those who did not receive any respiratory support ($n=15$) showed that heart rate and PI was significantly changed in the respiratory support group (Table 1). Moreover, PVI values were slightly higher in the respiratory support group compared with infants who did not obtain respiratory support (Table 2).

DISCUSSION

The results of this study demonstrate that PVI can be measured successfully in preterm infants regardless of

their gestational age and birth weight. PVI was slightly higher in infants who needed non-invasive respiratory support compared with those who did not. This finding may be related to decreased venous return to the heart with positive end-expiratory pressure, as well as with the underlying condition associated with the need for respiratory support.

Today, devices are used to monitor the heart rate, oxygen saturation, and respiratory rate of all infants admitted to neonatal intensive care. Recently, PI has also become a routinely monitored parameter in many intensive care units. Many studies have been published examining normal values and the relationship between PI and morbidities in term and preterm newborns.⁸⁻¹² The median PI values in our study were similar to those reported in a previous study investigating normal values in preterm infants.¹²

In contrast to PI, PVI is an understudied parameter in neonates, especially preterm neonates. Studies have shown that PVI is inversely associated with cardiac preload in adults and children and may be useful in predicting fluid response in mechanically ventilated patients and during surgery.¹³⁻¹⁷ In a study by Bagci et al.¹⁸ investigating the effect of PVI monitoring during surgery on predicting fluid non-responsiveness, PVI was continuously monitored in 29 term infants on mechanical ventilation, and the upper limit of the reference range for PVI was found to be 18%. The median PVI was 23% [interquartile range (IQR), 20-25] during arterial hypotension and decreased to 16% (IQR, 13-18) after volume replacement. The authors concluded that PVI may be a useful indicator of volume-responsive hypotension during surgery in neonates. In another study including healthy term infants, the median PVI in the first day of life was 20% and PVI values were

Table 1. Demographic characteristics of patients

GA; weeks, median (min-max)	34 (32-37)
Birth weight, g, median (min-max)	2115 (870-3900)
ACS, n (%)	22 (38)
Male gender, n (%)	30 (51.7)
C/S, n (%)	48 (82.7)
PROM, n (%)	13 (22.4)
Multiple gestation, n (%)	17 (18.9)
Surfactant treatment, n (%)	7 (12)
hsPDA, n (%)	5 (8.6)
PI	0.85±0.25
PVI	21±4.3

GA: Gestational age, ACS: Antenatal corticosteroids, C/S: Cesarean section, PROM: Prolonged rupture of membranes, hsPDA: Hemodynamically significant patent ductus arteriosus, PI: Perfusion index, PVI: Pleth variability index, min-max: Minimum-maximum

Table 2. Comparison of the groups who get respiratory support or not

	Respiratory support (n=43)	No respiratory support (n=15)	p
GA; weeks mean±SD	33.9±1.6	33.9±1.4	0.92
ACS, n (%)	17 (39%)	5 (33%)	0.55
Male gender, n (%)	23 (53%)	7 (46%)	0.78
C/S, n (%)	36 (83%)	12 (80%)	0.65
PROM, n (%)	7 (16%)	6 (40%)	0.056
MSAF, n (%)	0	1 (6%)	0.25
Surfactant treatment, n (%)	7 (16%)	0	0.17
hsPDA, n (%)	5 (11%)	0	0.31
SpO ₂	97.4±1.2	97.2±1.6	0.6
Heart rate	137.5±10.6	129.7±9.6	0.01
PI	0.8±0.2	0.9±0.3	0.03
PVI	21.7±4.5	19.2±3.2	0.05

GA: Gestational age, ACS: Antenatal corticosteroids, C/S: Cesarean section, PROM: Prolonged rupture of membranes, hsPDA: Hemodynamically significant patent ductus arteriosus, PI: Perfusion index, PVI: Pleth variability index, SD: Standard deviation

positively correlated with heart rate and PI and negatively correlated with oxygen saturation.¹⁹ Although the mean PVI value in our study was similar to that reported in term infants, it was not associated with any vital signs other than heart rate. In a study by Yiğit et al.²⁰ evaluating the effect of the delivery method on PI and PVI values in 125 healthy term babies, PI and PVI values were found to be higher in the cesarean delivery group. The authors suggested that the high heart rate, PI, and PVI values observed in the cesarean group may be associated with the more pronounced hemodynamic changes that occur in these infants during the postpartum transition period. Our findings of higher heart rate and PVI in infants who required non-invasive respiratory support may be related to the small number of patients in the group receiving respiratory support.

In a study conducted with 45 neonates born before 29 weeks of gestation, PI and PVI were monitored, and serial echocardiography was performed to evaluate for PDA during the first postnatal week. The median PVI was 22% (18-27) and showed no change during the study period but differed according to the ductal flow pattern. PVI was lower in neonates with growing or pulsatile PDA compared with those with pulmonary hypertension and closed or closing PDA.²¹

PVI reflects the degree of change in PI caused by respiration over a certain period and is therefore greatly affected by the current state of the cardiopulmonary system. PVI enables reliable prediction of cardiac preload responsiveness, provided that the cardiopulmonary interaction between respiratory cycles is stable and pressure changes in the chest cavity are sufficiently pronounced. Therefore, the higher PVI in infants with RDS and need for respiratory support may have been a result of their high respiratory rate and larger fluctuation in PI.

Study Limitations

Our study includes infants in the preterm group within a certain week range. Although the number of patients is the highest reported in this group, it is still a small sample size. In our study, the relationship between PVI and other common preterm morbidities was not examined.

CONCLUSION

To our knowledge, this study has the largest sample size, which evaluates PVI values in hemodynamically stable preterm infants. Further and larger studies must explain the relationship between PVI and morbidities in preterm neonates and determine how it can be effectively applied in the management of these morbidities.

Ethics

Ethics Committee Approval: The study was approved by the Ethics Committee of Zekai Tahir Burak Maternity and Teaching Hospital (9/2016).

Informed Consent: Consent form was filled out by all participants.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: Ş.I., H.G.K.K., Design: Ş.I., H.G.K.K., Ö.E., Data Collection or Processing: Ş.I., M.Ş.A., Analysis or Interpretation: Ş.I., H.G.K.K., Ş.S.O., Literature Search: Ş.I., M.Ş.A., Ö.E., Writing: Ş.I., H.G.K.K., Ş.S.O.

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

Financial Disclosure: The authors declared that this study received no financial support.

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