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Original article

Perfusion index in preterm newborns during the first week of life and association with neonatal morbimortality: a prospective observational study

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Abstract

Introduction: Perfusion index (PI) is a noninvasive method of peripheral perfusion measurement. Previous publications suggest that PI might be an useful and accurate predictor of morbidity and mortality risk in preterm newborns. This study aims: 1) to assess the PI values of preterm newborns (< 37 weeks) in the first seven days of life according to gestational age; 2) to assess differences in PI values between healthy preterm newborns and those who developed adverse outcomes during the neonatal period.

Material and methods: This is a prospective observational study performed in a Neonatal Intensive Care Unit that enrolled 60 preterm newborns with less than 37 weeks admitted between 1st February 2016 and 1st February 2017. Post-ductal PI was evaluated in the newborns' feet in the first hour and at 24 hours, 48 hours, 72 hours and 168 hours of life. The presence of an adverse outcome and/or death in the neonatal period was assessed in clinical records, along with several other clinical variables.

Results: We found a non-significant trend towards decreasing PI values in the first 2 days of life, with an increase at 48 hours and stable values at 72 hours after birth. PI values had an inverse relationship with gestational age (p for linear trend: 24 hours, p = 0.029; 48 hours, p = 0.001; 72 hours, p = 0.037; 168 hours, p = 0.001). The most prevalent adverse outcomes were shock (n = 8, 13.2%), anemia (n = 10, 16.7%) and intraventricular hemorrhage grade > 2 (n = 10, 16.7%). Median PI values were found to be significantly lower in newborns with an adverse outcome (0.90 vs. 0.70 at 24 hours; 0.87 vs. 0.72

at 48 hours; 0.91 vs. 0.79 at 72 hours; and 0.90 vs. 0.80 at 168 hours) and/or death in neonatal period (0.87 vs. 0.55 at 1 hour; 0.80 vs. 0.70 at 24 hours; 0.81 vs. 0.55 at 48 hours; 0.88 vs. 0.74 at 72 hours; and 0.89 vs. 0.49 at 168 hours).

Conclusions: PI values differed according to gestational age and to the presence of comorbidities, confirming that it might represent a valuable tool in the early identification of adverse outcomes in the neonatal period.

Keywords

Perfusion index, pulse oximeter, post-ductal, preterm, mortality, morbidity.

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Introduction

Preterm newborns, mainly those admitted to Neonatal Intensive Care Units (NICUs), are known to be at risk of developing several adverse outcomes, which ultimately can lead to an increase in morbimortality, especially during the first week of life. The development of hemodynamic instability that, when prolonged, may lead to an acute organ failure, is in part due to the immaturity of the cardiovascular and autonomous systems. The assessment and the maintenance of adequate tissue oxygen supply are generally considered primary objectives [1-4].

In clinical practice, tissue perfusion and oxygenation is usually assessed by noninvasive techniques essentially based on macrocirculatory parameters, such as systemic blood pressure (BP), heart rate (HR), oxygen saturation (SpO_2) and functional echocardiography [5, 6]. However, it is suggested that these methods are poor representatives of microcirculatory functioning [6].

During circulatory failure, the classical mechanism of peripheral vasoconstriction diverts blood flow from less important tissues to essential organs. This calls attention for the fact that, particularly in preterm newborns, techniques monitoring microcirculation in less vital tissues could allow to early identify vital tissue hypoperfusion, before the installation of decompensated shock leading to organ failure [7, 8]. It is important to note that indirect measures actually used for assessment of microcirculation, such as urine output, capillary refill time and serum lactate levels, are considered insensitive markers of tissue perfusion, especially in the first days of life, when extra-uterine life adaptation occurs. In face of this, new hemodynamic monitoring methods have been studied and the perfusion index (PI), translating the real time variations of the pulse oximetry signal in the peripheral circulation, has emerged as an easily applicable, noninvasive and continuous parameter that reflects changes in the cardiac output and vasomotor tone [9, 10]. The PI is a numeric value that results from the ratio between pulsatile signal, determined by arterial blood flow, and no pulsatile signal, determined by skin, subcutaneous tissue, venous blood flow and other local tissues. The value is based in signals derived from the amount of infrared light absorbed by each component at any specific moment and is related with pulse strength [9-11]. When hypoperfusion occurs, local vasoconstriction implies that the pulsatile signal has decreased and, because no pulsatile signal maintains equal with a constant amount of light absorbed, the PI value decreases, reflecting the lower peripheral perfusion. Globally, changes in PI value can be associated with changes in cardiac output and vasomotor tone [9].

Usually, pre-ductal PI values are higher than post-ductal ones due to the shunt of blood through the patent ductus arteriosus, which is strictly dependent on pulmonary vascular resistances, and these events are more marked in preterm newborns. Because of this, monitoring post-ductal PI is a more reliable measure of microcirculation and systemic response to hypoperfusion and allows a more precise comparison between newborns [12, 13].

In recent studies with newborns, PI has been reported to be associated with gestational age, pulse pressure, peripheral temperature, capillary refill time, mean arterial pressure and oxygen saturation [11, 14]. Its application has been explored in several specific settings, such as in states of inflammatory systemic responses [15], in detection of subclinical chrorioamnionitis [16], in the screening or early detection of hemodynamic instability associated

with congenital heart diseases [17, 18], patent ductus arteriosus [19], low superior vena cava flow [20], and in response to volume restitution and blood transfusion [21]. Moreover, previous studies have reported positive correlations between post-ductal PI and indirect measures obtained by near-infrared spectroscopy (NIRS), another noninvasive technique of microcirculation monitoring [22].

Despite all this, only a few studies have focused on the relevance of PI in preterm infants and more studies are needed to determine the prognostic value of PI, in order to strengthen and standardize the application of this tool as a clinical marker of illness in this age group [9, 23-25].

The present study aimed to evaluate post-ductal PI values in a population of preterm newborns during the first week of life, according to their gestational ages, and to evaluate the association between PI and the occurrence of adverse outcomes, such as disease and/or death during the neonatal period.

Material and methods

Study design and sample

We conducted a prospective observational study that aimed to enroll preterm infants admitted to the NICU of Centro Materno-Infantil do Norte (Porto, Portugal), a tertiary center, between 1st February 2016 and 1st February 2017. All preterm newborns with less than 37 weeks were eligible for the study protocol. Newborns with major congenital malformations and/or cases in whom technical limitations occurred in PI data collection were excluded. We finally enrolled 60 preterm newborns in the study.

Data collection and variable definition

Data on demographic and general maternal characteristics were abstracted from clinical records. Newborns' sex, gestational age, anthropometric data and Apgar score were recorded at birth.

Newborns were classified in three groups, as stated by the World Health Organization gestational age classification: less than 28 weeks (extremely preterm), from 28 weeks to less than 32 weeks (very preterm), and from 32 weeks to less than 37 weeks (moderate to late preterm) [26].

PI measurements were assessed with Masimo Radical-7 SET® (Masimo Corp) and, according to the equipment settings, they were recorded between the values of 0 and 20. Post-ductal PI values were obtained with the sensor placed in one of the feet at the first hour of life and on day 1 (24 hours), day 2 (48 hours), day 3 (72 hours) and, whenever the newborn was still in the NICU, on day 7 (168 hours) of life. The PI values were recorded after a stable pulse wave obtained for a minimum period of 10 seconds, to minimize artifacts in the record.

The presence of at least one of the following clinical situations was considered as an adverse outcome: asphyxia, shock (cardiogenic, hypovolemic and/or distributive), respiratory distress syndrome, anemia, sepsis, pneumonia, necrotizing enterocolitis, patent ductus arteriosus (PDA) with hemodynamic significance and intraventricular hemorrhage (grade higher than 2). The occurrence of death during the neonatal period was also considered. In the absence of the former conditions, the newborns were classified as healthy preterm.

Statistical analysis

The statistical analysis was performed using the software Statistical Package for the Social Science (SPSS Inc., Chicago, IL, USA), version 24. Continuous variables were expressed as mean ± standard deviation (SD) or as median (25th percentile [P25]-75th percentile [P75]) if skewed. Differences between groups in independent continuous variables were assessed by Student's T-test or by Mann-Whitney or Kruskal-Wallis. Trends for PI values according to gestational ages were assessed with linear regression. Differences between groups in paired continuous variables were assessed by Wilcoxon test. Chi-square tests were used for categorical variables. Linear trend in PI values was tested using linear regression models with classes of gestational age included as independent continuous variables. A two-tailed p-value of < 0.05 was considered as statistically significant.

Legal considerations

The study was approved by the Ethics Committee of Centro Hospital do Porto (CHP), the Research Coordinating Office of the Department of Education, Training and Research of CHP and the Clinical Direction. Informed consent was obtained from legal representatives of all infants.

Results

A total of 60 newborns (60% male) were recruited for this study. The median gestational age was 31.4

(24.1-35.3) weeks. Thirteen (21.7%) infants were extremely preterm, 22 (36.7%) infants were very preterm and 25 (41.7%) infants were moderate to late preterm. The general characteristics of the study population, according to gestational age groups, are presented in **Tab. 1**.

Sex distribution and maternal age were similar between gestational age groups. The anthropometric characteristics, birthweight, length and head circumference were significantly higher among the preterm with higher gestational age.

Apgar score were lower among the preterm with lower gestational age. The extreme preterm group presented lower Apgar score values at the 1st (5 [3-5] vs. 8 [6-9] vs. 8 [7-9], $p < 0.001$), at the 5th (6 [5-7] vs. 9 [8-10] vs. 9 [9-10], $p < 0.001$) and at the 10th minutes (7 [5-7] vs. 10 [9-10] vs. 10 [9-10], $p < 0.001$) than the very preterm and the moderate to late preterm groups, respectively.

The extreme preterm group presented more frequently adverse outcomes (100% vs. 45% vs. 40%, $p = 0.006$, in extreme, very and moderate to late preterm groups, respectively) and death during the neonatal period (62% vs. 4.5% vs. 0%, $p < 0.001$, in extreme, very and moderate to late preterm groups, respectively).

The PI measurements in the first 7 days of life, according to gestational age groups, are presented in **Tab. 2**. In all gestational age groups, PI values at 48 hours after birth were lower than at 72 and 168 hours. No differences were found in the PI values between gestational age groups at the first hour, but at all other measurements the PI values increased with gestational age (p for linear trend: 24 hours $p = 0.029$, 48 hours $p = 0.001$, 72 hours $p = 0.037$, 168 hours $p = 0.001$).

When considering the occurrence of adverse outcomes, newborns that developed disease presented significantly lower PI values at all times, with the exception of the first hour (**Tab. 3**). Newborns who died during the neonatal period presented significantly lower PI values at all times recorded (**Tab. 3**).

Discussion

In the present study, we found that PI values differed according to gestational age, being lower in extremely preterm newborns and higher in moderate to late preterm. Moreover, we showed that PI values suffered higher variations during the first hours of life, with a tendency to later stabilize at around 72

Table 1. Characteristics of the study population.

Variables	Total (n = 60)	Extremely preterm (n = 13)	Very preterm (n = 22)	Moderate to late preterm (n = 25)	p[a]
Maternal age, years	31.5 ± 3.9	32.8 ± 4.3	30.9 ± 4.4	31.5 ± 3.1	NS
Gestational age, weeks	31.4 (24.1-35.3)	26.3 (24.1-27.5)	29.8 (28.1-31.8)	32.4 (32.2-35.3)	NS
Male sex	36 (60.0%)	7 (53.8%)	15 (68.2%)	14 (56.0%)	NS
Birthweight, g	1,444 ± 548	763 ± 198	1,367 ± 347	1,865 ± 416	< 0.001
Length, cm	8.3 ± 4.7	32.2 ± 3.5	38.7 ± 2.6	41.2 ± 3.6	< 0.001
Head circumference, cm	28.2 ± 3.6	23.8 ± 1.8	27.8 ± 2.1	30.9 ± 2.7	< 0.001
Apgar score at 1 minute	8 (5-9)	5 (3-5)	8 (6-9)	8 (7-9)	< 0.001
Apgar score at 5 minutes	9 (7-10)	6 (5-7)	9 (8-10)	9 (9-10)	< 0.001
Apgar score at 10 minutes	9 (8-10)	7 (5-7)	10 (9-10)	10 (9-10)	< 0.001
Adverse outcome	32 (53.3%)	13 (100%)	10 (45.2%)	10 (40.0%)	0.006
Shock	8 (13.3%)	6 (46.2%)	1 (4.5%)	1 (4.0%)	
Intraventricular hemorrhage grade > 2	10 (16.7%)	8 (61.5%)	1 (4.5%)	1 (4.0%)	
Anemia	10 (16.7%)	5 (38.5%)	2 (9.0%)	3 (12.0%)	
Asphyxia	1 (1.7%)	1 (7.7%)	-	-	
Necrotizing enterocolitis	4 (6.7%)	1 (7.7%)	1 (4.5%)	2 (8.0%)	
PDA with hemodynamic significance	4 (6.7%)	2 (15.4%)	1 (4.5%)	1 (4.0%)	
Neonatal death	9 (15%)	8 (61.5%)	1 (4.5%)	-	< 0.001

The results are presented as mean ± standard deviation, as median (P25-P75) or as absolute frequencies (percentage).
[a]Kruskal-Wallis for comparison between the three groups of newborns.
NS: no significance; PDA: patent ductus arteriosus.

Table 2. Distribution of perfusion index (PI) values in newborns, at first 7 days of life, according to gestational age.

Hours of life	Total (n = 60)	Extremely preterm (n = 13)	Very preterm (n = 22)	Moderate to late preterm (n = 25)	p[a]
1 hour	0.81 (0.64-1.08)	0.74 (0.37-1.35)	0.83 (0.66-1.03)	0.80 (0.66-1.09)	NS
24 hours	0.80 (0.63-0.98)	0.56 (0.40-0.86)	0.85 (0.64-1.00)	0.80 (0.68-0.99)	0.029
48 hours	0.80 (0.59-0.90)	0.53 (0.33-0.72)	0.75 (0.56-0.99)	0.85 (0.78-0.90)	0.001
72 hours	0.89 (0.62-0.97)	0.60 (0.52-0.85)	0.90 (0.69-1.09)	0.91 (0.78-0.98)	0.037
168 hours	0.85 (0.70-1.00)	0.60 (0.48-0.73)	0.83 (0.71-1.00)	0.90 (0.82-1.20)	0.001

The results are presented as median (P25-P75)
[a]P-values for linear trend across groups of gestational age were calculated by linear regression.
NS: no significance.

Table 3. Characterization of perfusion index (PI) values, on the first 7 days of life, according to the occurrence of adverse outcomes and neonatal death.

Hours of life	Adverse outcome			Neonatal death		
	Yes (n = 32)	No (n = 28)	p[a]	Yes (n = 9)	No (n = 51)	p[a]
1 hour	0.73 (0.60-0.87)	0.90 (0.69-1.35)	NS	0.55 (0.35-0.86)	0.87 (0.67-1.10)	0.043
24 hours	0.70 (0.62-0.94)	0.90 (0.71-1.00)	0.009	0.70 (0.41-0.95)	0.80 (0.66-0.98)	0.005
48 hours	0.72 (0.57-0.89)	0.87 (0.75-0.99)	0.008	0.58 (0.52-0.67)	0.81 (0.67-0.90)	0.001
72 hours	0.79 (0.60-0.90)	0.91 (0.78-1.20)	0.005	0.74 (0.54-0.93)	0.88 (0.69-0.96)	0.043
168 hours	0.80 (0.69-0.93)	0.90 (0.80-1.00)	0.033	0.49 (0.34-0.75)	0.89 (0.71-1.00)	0.042

The results are presented as median (P25-P75).
[a]Mann-Whitney U to access differences between newborns with and without adverse outcome and between newborns with and without neonatal death.
NS: no significance.

hours of life. Interestingly, we were able to describe that PI values are lower in preterm newborns with pathological adverse outcomes and in those that died during the neonatal period.

The post-ductal PI trends observed along the first 3 days of life may reflect the physiological variability of the peripheral microvascular blood flow that characterizes the transitional period in which a hypoperfusion-reperfusion cycle occurs [27, 28]. The preterm heart is structurally and functionally immature and is not capable of adapting to relatively small changes in preload and afterload, in order to effectively deliver oxygen and nutrients to the tissues. Briefly, the sudden increase in systemic vascular resistance due to cord clamping cannot be immediately compensated by the immature myocardium, with insufficient contractile reserve, which may determine a peripheral hypoperfusion state. A reflex increase in cardiac output tends to occur over the first 48 to 72 hours of life of neonates and depends on gestational age [27].

So far few studies have explored the use of PI in newborns but, globally, the PI values and trends observed in our study are similar to others previously published. We found that PI values stabilized at 72 hours, independently of gestational age, at a median value of 0.89 (0.62-0.97). Hakan et al. reported that PI values reached a steady state on the 5th day of life and Hawkes et al. also described a high variability of PI values in the transitional period [12, 24]. Both groups of authors concluded that this initial period is marked by high PI variability, which is concordant with our findings [12, 24]. Hakan et al., Vidal et al. and Kinoshita et al. reported median PI values similar to those described in our study but Cresi et al. reported somehow higher values [12, 19, 23, 29]. These differences might be explained by the inclusion of a sample of newborns with a different distribution of gestational ages, possibily with different clinical and hemodynamical states. Naturally, if extreme and very preterm babies are over- or sub-represented in the samples considered, especially if the samples are small, the conclusions obtained might substantially differ.

In our study, we described lower PI values among preterm newborns with pathological adverse outcomes. In previous studies, De Felice et al., Granelli and Ostman-Smith, and Laere et al. also

described significant lower PI values in infants with high severity diseases [14, 17, 30]. According to De Felice et al., a PI equal to or lower than 1.24 is an accurate predictor of illness severity [14]. Granelli and Ostman-Smith showed that a PI value below 0.7 was linked with left obstructive heart disease [17]. Takahashi et al. revealed a positive correlation between PI and superior vena cava flow, with values below 0.44 being predictors of low superior vena cava flow in very low birth weight newborns [20]. Also, Tuten et al. reported that, at 24 hours of life, PI values lower than 0.5 could be used as an early predictor of retinopathy of prematurity and bronchopulmonary dysplasia [31].

In the context of vascular compromise, peripheral vasoconstriction is an early event that reflects the deviation of blood from less important structures to vital organs. This concept suggests that monitoring microcirculation can result in early detection of hypoperfusion conditions avoiding the development of acute organ dysfunction and failure. For assessment of peripheral perfusion in newborns, a number of methods are currently available, such as laser Doppler, spectral orthogonal polarization, sidestream dark field, visible light technology, amplitude integrated electroencephalogram, NIRS and PI. While none of these methods is currently validated to monitor microcirculation in preterm newborns in clinical practice, pulse oximetry technology is widely diffused in NICUs and PI is a value that can be readily and easily acquired. In our study, we reinforced the observation that PI values might be considered a parameter of microcirculation monitoring and that they might be used as an additional tool for prediction of morbidity and mortality risk in preterm newborns.

The major strength of the present study is that it included a relatively large sample of newborns, encompassing a wide range of gestational ages. Nonetheless, the need for a detailed analysis and the comparison between gestational age groups implicate that some comparisons are made between smaller subgroups, which might limitate our ability to find significant differences. This situation also didn't allow the comparison of PI values between preterm newborns with adverse outcome and/or neonatal death according to gestational ages groups.

Another important limitation is due to the fact that PI records were not always performed by the same medical staff member. Although it has been recently implemented a standardized protocol for PI measurement in our NICU, inter-variability between observers might have occurred, affecting the results. Moreover, although we tried to ensure perfect conditions at the time of PI values recording, some potential artifacts, not controlled in our study protocol, such as light exposure, skin color, peripheral temperature, peripheral perfusion and other movement artifacts, might have influenced the records obtained. Moreover, previous studies reported that PI might also be influenced by circadian rhythms, feeding periods, intravenous treatments, body temperature, peripheral perfusion state and newborn position (prone vs. supine) [29, 32, 33], factors that we also could not account for in the present analysis. In fact, the absence of a standardized methodology for PI values recording might represent the major limitation for clinical extrapolation of evidence about this index.

Conclusion

In conclusion, we described PI values variation according to gestational age and during the first 7 days of life and we were able to associate PI values with the presence of neonatal adverse outcomes.

In the future, we believe that multicentric and randomized controlled clinical trials are needed in order to standardize protocols of PI use in clinical practice and to reinforce previous findings in this field. We also consider of utmost importance the definition of reference values for PI in this specific group of newborns, in order to allow the establishment of PI as a prognostic value of morbimortality, integrated in clinical decision algorithms.

Declaration of interest

The Authors declare that they do not have any potential conflicts of interest. No specific funding was obtained for the present study.

References

1. Creasy R, Resnik R, Iams J, Lockwood C, Moore T. Maternal-Fetal Medicine: Principles and Practice. 6th ed. Philadelphia, PA: Saunders Elsevier, 2009.
2. Wu TW, Azhibekov T, Seri I. Transitional Hemodynamics in Preterm Neonates: Clinical Relevance. Pediatr Neonatol. 2016;57(1):7-18.
3. Shina S, Donn S. Fetal-to-neonatal maladaptation. Semin Fetal Neonatal Med. 2006;11(3):166-73.
4. Osborn D. Diagnosis and treatment of preterm transitional circulatory compromise. Early Human Dev. 2005;81(5):413-22.
5. De Backer D, Creteur J, Preiser JC, Dubois MJ, Vincent JL. Microvascular blood flow is altered in patients with sepsis. Am J Respir Crit Care Med. 2002;166(1):98-104.

6. Bujis E. Critically ill children and the microcirculation: Go with the flow? Erasmus University Rotterdam. 2013. Available at: http://hdl.handle.net/1765/51532, last access: June 2017.
7. Lima A, Bakker J. Noninvasive monitoring of peripheral perfusion. Intensive Care Med. 2005;31(10):1316-26.
8. Lima A, Bakker J. Clinical monitoring of peripheral perfusion: there is more to learn. Crit Care. 2014;18(1):113-5.
9. Piasek C, Van Bel F, Sola A. Perfusion index in newborn infants: a noninvasive tool for neonatal monitoring. Acta Paediatr. 2014;103(5):468-73.
10. Lima A, Beelen P, Bakker J. Use of a peripheral perfusion index derived from the pulse oximetry signal as a noninvasive indicator of perfusion. Crit Care Med. 2002;30(6):1210-3.
11. Kroese J, van Vonderen JJ, Narayen IC, Walther FC, Hooper S, te Pas AB. The perfusion index of healthy term infants during transition at birth. Eur J Pediatr. 2016;175(4):475-9.
12. Hakan N, Dilli D, Zenciroglu A, Aydin M, Okumus N. Reference values of perfusion indices in hemodynamically stable newborns during the early neonatal period. Eur J Pediatr. 2014;173(5):597-602.
13. Unal S, Ergenekon E, Aktas S, Beken S, Altuntas N, Kazanci E, Kulali F, Hirfanoglu I, Onal E, Turkyilmaz C, Koc E, Atalay Y. Perfusion index assessment during transition period of newborns: an observational study. BMC Pediatr. 2016;16:164.
14. De Felice C, Latini G, Vacca P, Kopotic, RJ. The pulse oximeter perfusion index as a predictor for high illness severity in neonates. Eur J Pediatr. 2002;161(10):561-2.
15. Dammann O, Kuban KC, Leviton A. Perinatal infection, fetal inflamatory response, withe matter damage, and cognitive limitations in the children born preterm. Ment Retard Dev Disabil Res Rev. 2002;8(1):46-50.
16. De Felice C, Vecchio D, Criscuolo M, Lozupone A, Parrini S, Latini G. Early postnatal changes in perfusion index in term newborns with subclinical chorioamnionitis. Arch Dis Child Fetal Neonatal Ed. 2005;90(5):411-4.
17. Granelli A, Ostman-Smith I. Noninvasive peripheral perfusion index as a possible tool for screening for critical left heart obstruction. Acta Paediatr. 2007;96(10):1455-9.
18. Kuehl K, Loffredo C, Ferencz C. Failure to diagnose congenital heart disease in infancy. Pediatrics. 1999;103:743-7.
19. Vidal M, Ferragu F, Durand S, Baleine J, Batista-Novais AR, Cambonie G. Perfusion index and its dynamic changes in very preterm neonates with patent ductus arteriosus. Acta Paediatr. 2013;102(4):373-8.
20. Takahashi S, Kakiuchi S, Nanba Y, Tsukamoto K, Nakumara T, Ito Y. The perfusion index derived from a pulse oximeter for predicting low superior vena cava flow in very low birth weight infants. J Perinatol. 2010;30(4):265-9.
21. Kanmaz H, Sarikabadayi Y, Canpolat E, Albug N, Ogut SS, Dilman U. Effects of red cell transfusion on cardiac output and perfusion index in preterminfants. Early Hum Dev. 2013;89:683-6.
22. Zaramella P, Freato F, Quaresima V, Ferrari M, Vianello A, Giongo D, Conte L, Chiandetti L. Foot pulse oximeter perfusion index correlates with calf muscle perfusion measured by near-infrared spectroscopy in healthy neonates. J Perinatol. 2005;25(6):417-22.
23. Kinoshita M, Hawkes CP, Ryan CA, Dempsey EM. Perfusion index in the very preterm infant. Acta Paediatr. 2013;102(9):398-401.
24. Hawkes G, O'Toole J, Kenosi M, Ryan CA, Dempsey EM. Perfusion index in the preterm infant immediately after birth. Early Hum Dev. 2015;91(8):463-5.
25. Jardim J, Rocha R, Silva G, Guimarães H. Peripheral perfusion index-reference range in healthy Portuguese term newborns. J Pediatr Neonat Individual Med. 2014;3(1):e030109.
26. World Health Organization. Preterm birth. www.who.int/mediacentre/factsheets/fs363/en/, last update: November 2015, last access: March 2017.
27. Hillman NH, Kallapur SG, Jobe AH. Physiology of transition from intrauterine to extrauterine life. Clin Perinatol. 2012;39(4):769-83.
28. Wu T, Azhibekov T, Seri I. Transitional hemodynamics in preterm neonates: clinical relevance. Pediatr Neonatol. 2016;57:7-18.
29. Cresi F, Pelle E, Calabrese R, Costa L, Farinasso D, Silvestro L. Perfusion index variations in clinically and hemodynamically stable preterm newborns in the first week of life. Ital J Paediatr. 2010;36:6-11.
30. Laere D, O'Toole J, Voeten M, McKiernan J, Boylan GB, Dempsey E. Decreased variability and low values of perfusion index on day one are associated with adverse outcome in extremely preterm infants. J Pediatr. 2016;178:119-24.e1.
31. Tuten A, Dincer E, Topcuoglu S, Sancak S, Akar S, Hakyemez Toptan H, Özalkaya E, Gokmen T, Ovalı F, Karatekin G. Serum lactate levels and perfusion index: are these prognostic factors on mortality and morbidity in very low-birth weight infants? J Matern Fetal Neonatal Med. 2017;30(9):1092-5.
32. Shani R, Schulze KF, Ohira-Kist K, Kashyap S, Myers MM, Fifer WP. Interactions among peripheral perfusion, cardiac activity, oxygen saturation, thermal profile and body position in growing low birth weight infants. Acta Paediatr. 2010;99:135-9.
33. Hummler HD, Engelmann A, Pohlandt F, Hogel J, Franz AR. Decreased accuracy of pulse oximetry measurements during low perfusion caused by sepsis: Is the perfusion index of any value? Intensive Care Med. 2006;32(9):1428-31.