

Evaluation of Tissue Perfusion Status in Moderately Preterm Infants

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Research

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Abstract

Background: The newborn babies require multiple physical of adjustment hemodynamic changes after birth, Perfusion index (PI) can help to evaluate peripheral tissue perfusion .

Objective: To investigate the tissue perfusion status and circadian rhythm in moderately premature infants.

Methods: As a prospective study, it monitored indicators including perfusion index(PI), blood pressure(BP) (systolic BP and diastolic BP) , pulse rate(PR), respiratory rate(RR), oxygen saturation(SpO₂) and body temperature of moderately preterm infants of hemodynamical stability in the morning and night within 8 days after birth from July 2019 to October 2019.

Results: The mean PI values of moderately preterm infants within 8 days after birth were(1.1±0.5) on Day 1, (1.1±0.5) on Day 2, (1.3±0.5) on Day 3, (1.3±0.5) on Day 4, (1.4±0.6) on Day 5, (1.4±0.5) on Day 6, (1.5±0.6) on Day 7, and (1.5±0.5) on Day 8. There was no difference of statistical significance between PI values in the morning and night (P >0.05). PR from Day 6 to 8 after birth were higher than those from Day 1 to 3 (P <0.05). PR increased significantly on Day 7 and 8 compared with those on Day 4 and 5 (P <0.05). BP from Day 3 to 8 was significantly higher than that on Day 1 (P <0.05), and BP from Day 4 to 8 were higher than that on Day 2. There was a weak positive correlation between PI values and gestational age (GA) (r =0.097), PR(r =0.067) and Time (day) (r =0.284) , and a negative correlation with SpO₂ (r =-0.113)(P<0.01). The calculation of PI value under non-standardized regression is represented by the following equation: $PI = 2.253 + 0.057 \times GA (\text{week}) + 0.062 \times \text{Time} (\text{day}) - 0.03 \times \text{SpO}_2 (\%)$.

Conclusions: PI and PR of moderately preterm infants were growing within 8 days after birth, while BP was relatively lower after birth and gradually increased to a stable level on Day 3 to 4. PI and BP circadian rhythms associated with tissue perfusion weren't established on Day 8 after birth.

Background

The newborn babies require multiple physical adjustment, which is especially the case for preterm newborns, as hemodynamic changes of cardiac output caused by a rapid fall in pulmonary vascular resistance is playing a crucial role at this point. Hemodynamic stability has been connected with necrotizing enterocolitis(NEC), intraventricular hemorrhage, late onset sepsis, and shock. Unstable hemodynamics may lead to significant changes in perfusion and cause organ damages or even death, thus increasing the disability rate and mortality of premature infants [1]. In recent years, pulse oximetry monitor and noninvasive blood pressure monitor have been widely used in the neonatal ward, which, to some extent, have promoted preliminary stability assessment of newborn babies' blood circulation. However, as blood pressure is affected by humor and sympathetic nervous system, and for adults the increase of parasympathetic excitability at night will make the blood pressure dip [2], it is probably not a good indicator of peripheral perfusion. Perfusion index (PI), a ratio of the pulsatile (arterial blood) against

non-pulsatile (static blood) signals of blood flow in the peripheral tissue calculated by a simple and noninvasive method, could help to evaluate peripheral perfusion [3].

Therefore, in this paper, correlations between PI value and blood pressure(BP) (systolic BP and diastolic BP), pulse rate(PR), respiratory rate(RR), oxygen saturation(SpO₂), circadian rhythm are evaluated by continuously monitoring data of preterm infants under stable conditions within 8 days after birth.

Therefore, in this paper, the relationship between PI value and blood pressure(BP) (systolic BP and diastolic BP), pulse rate(PR), respiratory rate(RR), oxygen saturation(SpO₂), circadian rhythm are evaluated through continuously monitoring data of preterm infants under stable conditions within 8 days after birth.

Methods

The observational study was conducted consecutively in the Neonatology Department of Children's Hospital of Shanxi from July 2019 to October 2019. The criteria for subjects include: (1) preterm infants of 32 to 36 weeks' gestational age (GA). (2) Admitted within 6 hours after birth. (3) Apgar score of 8 at 1min and 10 at 5min. (4) Hemodynamically stable preterm newborns, characterized by smooth breathe, normal color and cry, normal position and activity, normal muscle strength and muscle tone. (5) No need for oxygen and respiratory support. Exclusion criteria include: newborns with infection, congenital heart diseases(CHD), NEC, continuous apnea episodes, hyperpyrexia($\geq 37.5^{\circ}\text{C}$), and pneumothorax during hospitalization.

Study design

All enrolled preterm infants were assessed by physical examination and laboratory tests to clarify their physical conditions (smooth breathing, normal color and cry, normal position and activity, normal muscle strength and muscle tone) after admission, and every morning their conditions were checked. The pulse oximeter was placed on the foot of preterm newborns under quiet state for half an hour after feeding between 8:00–10:00 in the morning and 22:00–0:00 in the night. The following data was then recorded: PI, PR, SpO₂, BP, RR and body temperature (T). PI and PR were detected by Masimo Radical-7 (USA) monitor, and SpO₂ was read for 3 consecutive times in 6 seconds to obtain the average value.

Statistical Analyses

The Kolmogorov Smirnov test was used to quantify the data of normal distribution, which was expressed as mean \pm standard deviation ($m \pm SD$). Two groups of parametric variables were compared by T-test and variance analysis was adopted for multi-group comparison. $P < 0.05$ was considered statistically significant. Pearson correlation coefficient was used to analyze the correlation of variables while multiple linear regression analysis was applied to establish multiple linear regression equations. All statistical calculations were processed by SPSS22.0 in Windows (IBM SPSS Statistic).

Results

A total of 95 preterm infants of 32 to 36 weeks' gestational age were admitted to the Neonatology Department of Children's Hospital of Shanxi. 1 patient suffered from NEC on Day 8 after birth, 1 patient was suspected of sepsis due to persistent fever during hospitalization, and 6 patients were excluded due to incomplete information. 87 preterm infants were involved in the study. with a mean GA of (34.4±1.1) week(W), BW(birth weight) of (2142.6±384.8) g, 48M and 43F, and mean Apgar score of (9.8±0.4) at 1 min and (9.9±0.3) at 5 min after admission.

The mean PI, PR, BP, SpO₂, T values of preterm infants during 8 days after birth are shown in Table 1. The PI values of the preterm infants was in a growing trend after birth, which increased significantly from Day 5 to 8 compared Day 1 and 2 ($P<0.05$), and the PI values on Day 7 and 8 were much higher than those from Day 1 to 4 ($P<0.05$). However, there was no significant differences among the PI values on the other days ($P>0.05$). PR increased gradually after birth, with the values from Day 6 to 8 after birth much higher than those from Day 1 to 3 ($P<0.05$) PR increased significantly on Day 7 and 8 compared with those on Day 4 and 5 ($P<0.05$), and PR increased significantly on Day 8 compared with Day 6 ($P<0.05$). There was no significant differences between the PR values from Day 1 to 5 ($P>0.05$). BP from Day 3 to 8 were significantly higher than that on Day 1 ($P<0.05$), Day 4 to 8 were higher than that on Day 2, while the value stayed stable in the other days ($P>0.05$) (Figure 1). T values on Day 2 and 3 after birth were higher than that on Day 1. On Day 6, the value was lower than that on Day 2 ($P<0.05$), and for the remaining days, the values were similar ($P>0.05$). There was no significant difference for RR and SpO₂ during the period.

BP (Systolic BP and diastolic BP) in the morning and night were similar ($t=1.691$, $P=0.194$; $t=0.370$, $P=0.543$) from Day 1 to Day 8. PI in the morning and night from Day 1 to Day 8 were similar ($P>0.05$) (Table 2). There was difference of statistical significance for PI values among different gestational ages ($F=6.233$, $P<0.001$), and PI value increased along with gestational age (Table 3).

The results of Pearson correlation analysis showed a weak positive correlation between PI value with GA ($r=0.097$), PR ($r=0.067$) and Time ($r=0.284$), a negative correlation with SpO₂ ($r=-0.113$) ($P<0.01$) (Table 4). Multiple linear regression analysis was adopted with PI the dependent variable, while GA, PR, Time and SpO₂ as independent variables. The calculation of PI value under non-standardized regression model was based on the following equation: $PI = 2.253 + 0.057 \times GA \text{ (week)} + 0.062 \times \text{Time (day)} - 0.03 \times \text{SpO}_2 \text{ (%)}$ (Table 5).

Discussion

As an optical plethysmography parameter related to systemic perfusion, PI can serve as a sensitive reflection of the perfusion level of peripheral tissues, with correlation to the ventricular output [3,4]. Sivaprasath et al. proposed that PI value was positively correlated to pulse pressure, systolic BP and diastolic BP to different degrees among children aged 1~12 years to different degrees. The decline of PI

value may predict impending shock, but was not reliable for the detection of hypotension [5]. It is found that PI and PR of moderately preterm infants in the first 8 days after birth were growing slowly at the points of time in our study, similar to findings from previous researches home and abroad [6–8]. A positive correlation between PI and PR was also found, but there was no significant correlation between PI and BP. A physiological theory holds that BP is decided by cardiac output (heart stroke volume and PR) and peripheral vascular resistance (arterial compliance, ratio of systemic blood flow to systemic vascular volume) while neonatal BP is affected by multiple factors, including GA, age in days, BW, postnatal age, antenatal hormone, patent ductus arteriosus, temperature. So far, there is no unified definition of hypotension, weakening its credibility as an indicator for evaluation. Therefore, blood flow maybe a better indicator of perfusion than BP. Neonatal myocardial contractile elements were significantly fewer compared with older children and adults. The immature myocardial cells tended to exhibit higher basal contractile state and were more sensitive to cardiac afterload [9], hence the mobilization of cardiac reserve may firstly be characterized by an increase in PR rather than BP despite instability of systemic blood perfusion. All infants, especially premature infants, experience a series of hemodynamic changes during transitional period after birth, including intrauterine to extrauterine changes, decreased pulmonary arterial pressure, shunting of blood flow from systemic circulation to pulmonary circulation, closure of ductus arteriosus, and increased volume of systemic circulation. A PR value between 120 and 160 bpm and coupled with weak myocardial contraction means that cardiac reserve could be achieved by increasing PR to maintain tissue perfusion. Even in the absence of adequate tissue perfusion during the compensatory period of shock, peripheral blood vessels are responsive to ischemic stimuli via sympathetic nervous system and humoral regulation. This is also one of the reasons that many newborns have tachycardia together with or without increased BP and no hypotension during the compensatory period of shock. However, the inflammatory reaction during shock can seriously affect the microcirculation of adjacent tissues and skin, as indicated by significant decrease of PI value of peripheral blood flow in the first 45 seconds after ischemic stimulus [10]. Our study showed that BP of moderately preterm infants was lower after birth, and tended to stabilize on Day 3 to 4 after birth. PI and PR were recorded until Day 10 after birth in the primary study, which was found to be growing while there was not much change in BP. However, part of the data was eliminated because the patients were discharged. Therefore, arterial BP is not an accurate indicator to evaluate neonatal peripheral tissue perfusion while PI, which reflects the ratio of arterial blood flow against non-arterial blood flow, is considered more reliable in this regard. Theoretically, the cardiac reserve capacity would increase with ages. As the PR of infants and young children is lower than that of newborn infants, the PR value of preterm infants should gradually decrease and stabilize at a certain stage. However, at least on Day 8 after birth, we have not seen a drop in RP. Whether there is a similar trend of PR for term infants will be the focus of future studies.

Previous studies focusing on PI values at different ages claimed the median PI of preterm infants with GA < 32W was 0.9 on the first day after birth, 1.8 at 24 hours after birth [11,12], and 3.0 for children 1~3 years old [5]. Our research showed that PI values for preterm infants with GA 34~36W were significantly higher than those with GA 32~33W, which would grow with age, suggesting that PI was related to the

maturity of preterm infants. Meanwhile the correlation analysis in our study showed that PI is related to GA (W), Time (day) and SpO₂ (%), which were incorporated into the equation for the calculation of PI. In this equation, SpO₂ is easy to be measured as both GA and time are objective indicators. The results of the equation were similar to those of previous studies, making it a useful tool to predict the normal value of PI in moderately preterm infants within 8 days after birth. It maybe also apply to term infants and earlier preterm infants. Previous studies reported that low PI value below 0.7 indicated left heart obstructive disease [13]. In our study, it is found the PI value of a preterm infant suffering from severe NEC on Day 8 eventually turned to surgery, before which the PI value dropped from 1.5 to a much lower level of 0.76, suggesting that PI could be a signal of low systemic perfusion level. Significant decline of PI value during neonatal shock should be taken as a reference based on the normal value of individuals for liquid recovery treatment. The PI equation obtained in this study is helpful to evaluate the node of fluid resuscitation. We tried to resuscitate a 2-day-old preterm infant of GA 34W with PI value of 0.28 from severe shock. When the PI value gradually increased to 1.9, saline dilatation was terminated. Unfortunately, the infant developed pulmonary hemorrhage. Therefore, it is necessary to explore the node of PI value for different infants during fluid resuscitation to improve the prognosis of infants with shock.

PI is the pulse index of blood flow, which is influenced by multiple factors such as muscle contraction, temperature, blood shunting, invasive procedures, neonatal posture, circadian rhythm, etc. The data was measured when the infants were in a quiet state with minimum invasive procedures to ensure the accuracy of data. Due to the circadian rhythm of sympathetic-parasympathetic nervous system and various activities, BP dipping of adults and older children within 24 hours is usually higher than 10% [14,15], a phenomenon gradually formed as a result of the development and maturity of children and the effect of various factors. The paper found no difference in BP and PI values between the morning and night within 8 days after birth, probably due to the instability of sympathetic-parasympathetic nervous system in the early postnatal period of the preterm infants, which prevented the establishment of the circadian rhythms associated with BP and PI at the end of Day 8 after birth. Yet in the primary stage of the study, namely on Day 10 after birth, no difference was found in BP values in the morning and night while there were differences for PI. However, the data was eliminated given the absence of some data might lead to a deviation. Therefore, it remains unknown whether the circadian rhythm related to PI of moderately preterm infants could be established 10 days after birth.

Conclusion

The paper established an equation incorporating a series of PI values for moderately preterm infants within 8 days after birth, which was helpful for the primary assessment of peripheral perfusion in individuals. However, the circadian rhythms related to BP and PI haven't been established yet, which requires further studies to explore the specific conditions of individuals for clinical decision-making.

Abbreviations

PI: Perfusion index; BP: blood pressure(systolic/diastolic blood pressure); PR: pulse rate; RR: respiratory rate; SpO₂: oxygen saturation; NEC: necrotizing enterocolitis; GA: gestational age

Declarations

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Authors' contributions

GY and YZ have contributed equally to this work. KL, YZ and GY had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. KL and YZ designed the study and draft the manuscript, GY assisted with study design, collected data and conducted data analysis. SN, MZ and FG coordinated the data collection. All authors read and approved the final manuscript.

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Ethics approval and consent to participate

The Institutional Ethics Committee in our hospital approved the study protocol (Protocol number:201967). We collected all baseline data including clinical examinations in our study after getting written informed consent from their parents or legal guardians.

Competing interests

The authors hereby declare no competing conflict of interest regarding any aspect of this article.

Availability of data and materials

All data generated or analysed during this study are included in this published article, but are available from the authors on request.

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