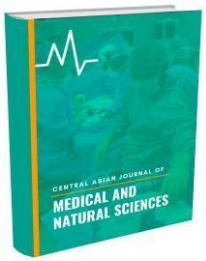

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Article

Changes in the Circadian Rhythm of Arterial Blood Pressure in Full-Term and Preterm Newborns Born to Mothers with Arterial Hypertension

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Abstract: Maternal arterial hypertension remains an important perinatal risk factor capable of influencing neonatal cardiovascular adaptation and the formation of physiological blood pressure regulation after birth. The present study aimed to evaluate changes in the circadian rhythm of arterial blood pressure among full-term and preterm newborns delivered from hypertensive pregnancies. A total of 45 newborns were examined, including 15 full-term and 30 preterm infants born to mothers diagnosed with arterial hypertension. Clinical observation included repeated assessment of systolic and diastolic arterial pressure, evaluation of cardiovascular adaptation, and analysis of circadian hemodynamic fluctuations during the neonatal period. The obtained findings demonstrated that preterm newborns showed significantly greater instability of arterial pressure, weaker day-night rhythm differentiation, and delayed cardiovascular adaptation compared with full-term infants. Episodes of transient hypotension, tachycardia, and peripheral circulation disturbances were observed more frequently among premature newborns. The study confirms the importance of continuous neonatal hemodynamic monitoring for early identification of cardiovascular maladaptation in infants exposed to maternal hypertensive disorders during pregnancy.

Keywords: Maternal Hypertension, Neonatal Blood Pressure, Circadian Rhythm, Preterm Newborns, Full-Term Newborns, Cardiovascular Adaptation, Neonatal Hemodynamics

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1. Introduction

The neonatal period is one of the most complex phases of early human life in terms of cardiovascular adaptation, as soon as the newborn organism is born, it must rapidly switch from the intrauterine circulation of the placenta to the independent regulation of systemic and pulmonary circulation. Stabilization of arterial blood pressure and progressive development of the circadian rhythm are among the numerous mechanisms contributing to this adaptation and of particular importance in ensuring an adequate cerebral perfusion, oxygen supply, and metabolic balance. These processes mature step-

by-step in the first days and weeks of life in normal newborns, but are potentially severely deranged by a variety of maternal and perinatal conditions [1].

Arterial hypertension in the mother is one of the most common morbid conditions of impaired fetal growth and neonatal adaptation disturbances. Chronic hypertensive disorders of pregnancy may lead to placental insufficiency, intrauterine hypoxia, endothelial dysfunction and chronic fetal stress, which can impact the immature cardiovascular system prior to delivery. Infants born to mothers with hypertension often exhibit systolic and diastolic blood pressure instability, altered vascular tone, impaired autonomic regulation and problems with establishing physiological day-night hemodynamic fluctuations during the neonatal period [2].

The mechanisms that underlie neurovascular autoregulation and circadian rhythm formation may be developmentally immature at lower gestations, resulting in these disturbances being more evident in premature infants. In recent neonatal studies, it has become clear that abnormalities of early blood pressure regulation not only affect the immediate adaptation of the newborn but also have important effects on long-term cardiovascular and neurological development during childhood. Inadequate postnatal maturation of ANS activity is considered to underlie reduced variability of AP and unstable circadian organization in preterm newborns, especially those who experienced adverse intrauterine conditions [3].

Meanwhile, if the neonate is hemodynamically unstable for a prolonged period after birth, he or she may be at risk for cerebral perfusion abnormalities, intraventricular hemorrhage, and delayed neurodevelopmental adaptation. Although the role of hemodynamic monitoring in the neonatal period is becoming increasingly recognized in the clinical setting, the features of the neonatal hemodynamic circadian rhythm in full term and preterm infants of mothers with arterial hypertension are still not well studied. To date, most studies have concentrated on individual blood pressure readings instead of considering the circadian blood pressure changes, and how this relates to gestational maturity. Hence it is important to evaluate the arterial pressure rhythm in these newborns in more detail, which may help to identify cardiovascular maladaptation earlier and optimize newborn monitoring in clinical practice [4].

2. Materials and Methods

The aim of the present clinical observational study was to assess the changes in arterial blood pressure (ABP) circadian rhythm in full-term and preterm newborns born from pregnant women with AHP. The investigation was conducted during a continuous observation period with special emphasis on early cardiovascular adaptation, stabilization of systemic hemodynamics and development of physiological blood pressure fluctuations during the neonatal period. Neonatal cardiovascular regulation is highly sensitive to intrauterine and postnatal influences and therefore all examinations were carried out under carefully standardized clinical conditions to minimize the external influences in the environment that might affect the cardiovascular parameters. A total of 45 newborn infants were included in the study. The studied group was divided into two clinical groups based on the gestational maturity at birth. The first group included 15 full-term newborns from mothers with an arterial hypertension diagnosis during pregnancy. The first group comprised 15 full-term newborns of mothers with an arterial hypertension diagnosis during pregnancy. The other group consisted of 30 preterm newborns born in similar maternal hypertensive situations. The diagnoses of maternal hypertension were verified by obstetric records and repeated arterial pressure measurements taken during the pregnancy, as well as clinical supervision by obstetric specialists. Infants with major congenital defects, severe congenital infections, chromosomal syndromes, and those with severe respiratory disease besides prematurity were excluded from the study to prevent other factors from affecting cardiovascular adaptation. All the newborns were examined

thoroughly right after the delivery by the neonatologists. The age of gestation, weight, Apgar score indicators, respiratory status, skin coloration, reflex activity and circulatory adaptation were recorded carefully. Systolic and diastolic arterial blood pressure were particularly studied since they are indicators of the functional maturity of the neonatal cardiovascular regulation and the activity of the autonomic nervous system. To assess blood pressure (BP) circadian variability, BP was measured using neonatal oscillometric monitoring devices fitted to neonatal patients and repeated at regular intervals throughout the day and night [5].

All of the above, plus arterial pressure assessment and heart rate monitoring, were performed during the entire neonatal adaptation period as well as clinical observation of sleep-wake cycles. A series of measurements were made in clinically stable periods in the preterm infants who needed supportive therapy, while avoiding the hemodynamic data being distorted by acute respiratory or metabolic changes. The acquired indicators were then compared between the two study groups to reveal possible differences in gestational maturity and the impact of maternal hypertension on the regulation of the neonatal circadian blood pressure [6].

Modern biomedical analysis techniques have been used to statistically process the collected clinical data. The quantitative data were presented as mean values ± SD and intergroup comparisons were made by Student's t-test and correlation analysis as appropriate. A difference was deemed statistically significant if $p < 0.05$ [7]. Ethical principles that were observed throughout the process of the study were in line with international research standards and all examinations were performed in the context of the normal clinical procedure for neonatal observation made by the institution approved by the medical protocols [8].

3. Results

The clinical data obtained was analyzed, and significant differences were found between full-term and preterm newborns born from mothers with arterial hypertension concerning the formation of circadian arterial blood pressure rhythm. The two groups had cardiovascular disturbances of adaptation at the neonatal stage, but these disturbances were significantly greater in premature infants. The differences observed seemed to be linked not only to the immaturity of gestation, but also to the effects of prolonged intrauterine exposure to the effects of maternal hypertensive disorders and placental circulatory insufficiency [9].

In the first study group of full-term newborns, there were moderate variations between day and night measurements of arterial blood pressure, but indicators for this parameter were relatively stable during the observation period. In most infants, the systolic blood pressure and diastolic blood pressure values gradually took up physiological neonatal values during the first days after birth. Nocturnal arterial pressure reduction and more stable heart rate regulation, which are considered as signs of circadian rhythm differentiation, could be detected in several newborns, although not fully developed. The clinical adaptation in this group was satisfactory in general and severe cardiovascular instability was found in isolated cases only.

Preterm newborns, on the other hand, showed very high variability of arterial pressure parameters during monitoring. In many of the infants in the second group, systolic and diastolic readings were unstable and there were irregular circadian variations in the hemodynamic activity along with less distinction between the day and night. Premature infants were more likely to experience transient hypotension, tachycardia, peripheral circulation disturbances and delayed cardiovascular adaptation than full-term newborns. In some instances, immature autonomic regulation seemed to disrupt the normal development of the physiological patterns of circadian rhythm [10]. The results yielded also showed that neonates born at lower gestational ages had a lower

capacity to sustain normal vascular tone and coordinated cardiovascular reactions during the process of neonatal adaptation. Frequently, the premature infants who were conceived by women with hypertension experienced longer recovery periods and heightened responsiveness to environmental factors such as feeding, handling, and sleep-wake cycles [11]. The hypothesis that maternal hypertension could have a negative impact on fetal autonomic cardiovascular regulation maturation prior to delivery is supported by these observations.

Table 1. Features of the rhythm of arterial blood pressure in studied newborns

Clinical indication	Full-term newborns (n=15)	Preterm newborns (n=30)
Stable systolic pressure	73.3%	36.7%
Day-night pressure differentiation	66.7%	23.3%
Episodes of transient hypotension	13.3%	46.7%
Cardiovascular adaptation disturbance	20.0%	56.7%
Tachycardia episodes	26.7%	53.3%
Peripheral circulation instability	13.3%	43.3%
Prolonged hemodynamic recovery	6.7%	50.0%

The presented data showed that the regulation of arterial blood pressure was significantly disturbed in newborns born preterm as compared to that of full-term babies, born to mothers with arterial hypertension. Autonomic cardiovascular control mechanisms are not fully developed in the early neonatal period, as evidenced by reduced circadian rhythm differentiation, vascular instability and increased hypotensive episodes in premature newborns [12].

4. Discussion

The findings from the present study indicate that maternal AHT could have a significant impact on the development of cardiovascular adaptation mechanisms in newborn infants, specifically premature infants. Normal physiological regulation of arterial pressure started around days 1–3 after birth, but the investigated newborns often showed circadian disorders of hemodynamic regulation, indicating immaturity of autonomic cardiovascular control. The differences detected between full term and preterm infants suggest that gestational maturity is an important factor in the establishment of stable blood pressure rhythm during the neonatal period. A key finding of this study was a smaller difference between daytime and nighttime arterial pressure readings in premature infants. The development of the circadian rhythm in healthy mature infants is indicative of the coordination between vascular tone regulation, neuroendocrine activity, sleep-wake cycles and autonomic nervous system adaptation. In the case of the preterm newborn infant of a mother who developed hypertension during the period of intrauterine development, however, there seems to be a longer delay before these regulatory mechanisms become functional after birth. These findings are consistent with the results of recent neonatal hemodynamic investigations which have also revealed delayed maturation of cardiovascular autonomic responses and poorer peripheral circulation regulation in premature infants [13].

In addition, the observed episodes of transient hypotension and cardiovascular instability in preterm infants may be related to chronic intrauterine stress from placental insufficiency and impaired uteroplacental perfusion. Fetal endothelial function, vascular resistance, and neurohumoral adaptation may be altered by exposure to maternal hypertension disorders at a long-term time. This means that the neonatal cardiovascular system can start the postnatal period with a reduced adaptive capacity. This mechanism

can have contributed to the higher sensitivity to external stress factors and longer hemodynamic stabilization of premature infants observed in this study [14].

Another key point is the possible neurological consequences of poor regulation of neonatal blood pressure. Stable systemic hemodynamics is of pivotal importance for adequate cerebral perfusion in early life, especially when cerebral autoregulatory mechanisms are immature, as is the case in premature infants. The recurrent changes in arterial pressure could thus predispose to cerebral hypoperfusion and to intraventricular hemorrhage and to delayed neurodevelopmental adaptation. In recent years, there is growing evidence in neonatal literature of the link between early cardiovascular instability and later neurological outcomes in the more vulnerable groups of newborns [15].

The data of the present study also highlight the need for ongoing assessment of hemodynamics in the newborn of a hypertensive pregnancy. However, in some cases, disturbances of circadian blood pressure regulation can only be detected by routine clinical observation, particularly during early adaptation when the regulation of cardiovascular function is very dynamic. In the neonate, the diagnosis of hemodynamic instability early in the course may help the neonatologist to optimize supportive therapy, minimize cardiovascular stress and improve long-term outcome in both full term and preterm infants [16].

The findings of the present study, although useful, have some drawbacks that should be noted. The number of subjects was still relatively small and longer follow-up periods are needed to assess potential long-term cardiovascular effects of disrupted neonatal circadian blood pressure regulation. However, the data presented here adds more clinical data on the effect of maternal arterial hypertension on neonatal cardiovascular adaptation and highlight the fragility of the premature infant in the early postnatal period.

5. Conclusion

The performed study has shown that the early neonatal period of the presence of the mother with arterial hypertension is accompanied by statistically significant violations of physiological arterial blood pressure rhythm, but the severity of these violations is significantly different depending on the maturity of the pregnancy. Full-term newborns tended to have relatively stable cardiovascular adaptation, with progressive development of day-night differences in BP, while premature infants were significantly more unstable in both systolic and diastolic BP adaptations and had delayed autonomic cardiovascular balance recovery, with less day-night differences in BP. The results obtained indicate that the maternal hypertensive disorders in pregnancy can have a negative impact on fetal cardiovascular development even before the baby is born. Chronic intrauterine exposure to decreased placental blood flow and endothelial dysfunction, as well as exposure to fetal hypoxic stress, seems to disrupt neurovascular regulatory mechanisms which maintain stable arterial pressure after birth. The influence is most noticeable in preterm newborns whose vascular adaptation process and autonomic nervous system is physiologically underdeveloped at the time of birth. A second major finding of the present study is that there is a strong association between unstable blood pressure control and the problems of neonatal adaptation in the first days of life. Transient hypotension, tachycardia, peripheral circulation disturbance and delayed stabilization of cardiovascular parameters occurred more frequently in premature infants. This hemodynamic instability may compromise the perfusion of the neonatal brain, and, if not promptly monitored and cared for, may lead to subsequent neurological and developmental problems. Continuous hemodynamic monitoring is also stressed for the clinical significance of the newborns of hypertensive pregnancies, particularly the preterm infants under intensive neonatal care. Use of careful evaluation of the circadian blood pressure rhythm might be beneficial in early detection of cardiovascular maladaptation and optimize individualized treatment strategies in the neonatal period. The presented results overall corroborate the increased risk factors for

impaired cardiovascular adaptation in newborns when their mother has arterial hypertension and the baby is premature. In order to gain a fuller understanding of the long-term cardiovascular and neurodevelopmental outcomes of disrupted neonatal circadian blood pressure regulation, additional large-scale studies with follow-up are required.

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