

Determination of plasma B-type natriuretic peptide concentrations in the neonatal period

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ABSTRACT

Objective: Determine plasma NT-ProBNP concentration in the neonatal period. **Objects and methods of the study:** Prospective, cross-sectional study on 96 children from 1 day to 28 days at the Vietnam National Children's Hospital. Quantifying the plasma NT-ProBP concentration and comparing between age groups, gender, and preterm – full-term infants. **Results:** NT-ProBNP concentration was highest at 1 day of age and then gradually decreased with age with a statistically significant difference ($p < 0.05$). There is a negative linear correlation between NT-ProBP concentration and age ($r = -0.82$; $p < 0.05$). There was no difference in NT-ProBNP concentration according to gender ($p > 0.05$). NT-ProBNP concentrations in preterm infants were higher than in full-term infants ($p < 0.05$). **Conclusion:** NT-ProBNP concentration increases after birth and gradually decreases with age. There were differences in NT-ProBNP concentrations between full-term and preterm infants but no differences by gender.

Keywords: concentration, NT-ProBNP, neonatal.

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INTRODUCTION

B-type natriuretic peptide (NT-ProBNP and BNP) is released due to an increase in pressure and volume of the heart chambers, especially the left ventricle. B-type natriuretic peptide has the effect of causing natriuresis, diuresis, and vasodilation [1], [2]. Quantification of plasma NT-ProBNP concentration is a test that has been widely used in the diagnosis and monitoring of heart failure treatment as well as cardiovascular diseases in children and has shown high sensitivity and specificity. Currently, NT-ProBNP is an important biomarker in indications for intervention and treatment of congenital heart disease in children.

Studies have shown that NT-ProBNP is valuable in diagnosing a number of diseases in the neonatal period such as persistent pulmonary hypertension, patent ductus arteriosus, etc. However, NT-ProBNP concentrations change with age days old during this period. Specifically, this index increases at the time of birth, increases highest within the first 48 hours, and gradually decreases within 1 week after birth [3], [4], [5]. Therefore, when evaluating the role of NT-ProBNP in cardiovascular diseases during this period, it is necessary to pay attention to reference values of this index in newborns. Currently in Vietnam as well as in the world, there is no official reference index of NT-ProBNP plasma of infants and children. To clarify this issue, we conducted the study

"Determining plasma NT-ProBNP concentrations in the neonatal period".

OBJECTS AND METHODS

Objects of the study

Healthy newborns come for a health check at the Vietnam National Children's Hospital.

Criteria for selection

Age: 1 day to 28 days - Children are determined to be healthy through clinical examination and paraclinical tests.

Criteria for exclusion

Birth asphyxiated newborn

Children with respiratory failure, cardiovascular disease, and severe infections.

Design methods of the study

Design of the study: Prospective, cross-sectional study

Sample selection method and sample size: Select convenience samples. There were 96 infants from 1 day old to 28 days old who met the selection criteria and were included in the study.

Time and location of the study:

Time: from April 2017 to October 2019.

Location: Clinic of Vietnam National Children's Hospital.

The study's variables

Age: divided into age groups: patients' ages are divided into groups according to days of age after birth: 1 day, 2 days, 3 days, 4 days, 5 to 7 days, 8 to 14 days, and 15 to 28 days.

Gender: male, female

Preterm infants: defined when born before 37 weeks of gestational age. Babies < 28 weeks are extremely premature; From 28 - < 34 weeks is premature.

NT-ProBNP concentration (pg/ml).

Steps to conduct the study

Newborns are determined to be healthy when they come for a health check-up by taking medical history, clinical examination, and paraclinical investigation tests. Conducted quantification of plasma NT-ProBNP concentration using electrochemiluminescence immunoassay on Roche's Cobas e601 machine of the Department of Biochemistry, Vietnam National Children's Hospital. The quantitative method is carried out in accordance with the procedures (sample preservation and sampling method, quantitative method) of the Ministry of Health. The unit of plasma NT-ProBNP concentration is pg/ml.

Data processing and analysis

Data in the study were processed using SPSS software version 22. Data are presented as: median, min value and max value with the 25th and 75th Interquartile range for non-standard distribution. Using Mann - Whiney test to compare the median of 2 independent samples for non-standard distribution.

Ethical considerations in the study

The child's family explained the study content and agreed to participate. The study does not affect the patient's health. Patient information is guaranteed to be confidential.

RESULTS

General characteristics

In this study, we selected 96 patients who met the criteria for selection of the study. The study

results are presented as follows:

Table 1. General characteristics of the study objects

Characteristics	Quantity	Percentage	
Age	1 day	11	11.5%
	2 days	13	13.5%
	3 days	9	9.4%
	4 days	12	12.5%
	5-7 days	14	14.6%
	8-14 days	18	18.6%
	15-28 days	18	18.6%
Gender	Boy	42	43.8%
	Girl	54	56.2%
Gestational age	Preterm	63	65.6%
	Full-term	33	34.4%
Average age (days)	15 ± 13.12		
Average weight at birth (grams)	3012 ± 2314		

There are no significant differences in gender between the two groups of boys and girls. The 15-28 days and 8-14 days groups account for the highest proportion (both 18.6%), followed by the 5-7 days old group (14.6%). The average age of the study objects was 15 days and the average birth weight was 3012 grams.

NT-ProBNP concentration in the neonatal period

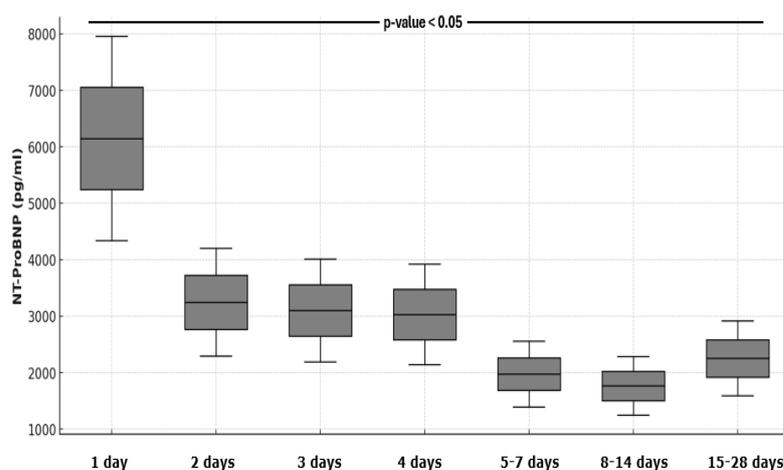


Figure 1. NT-ProBNP concentration by day of age

NT-ProBNP concentration is highest at 1 day of age and then gradually decreases with age. The difference in NT-ProBNP concentrations between age groups is statistically significant ($p < 0.05$).

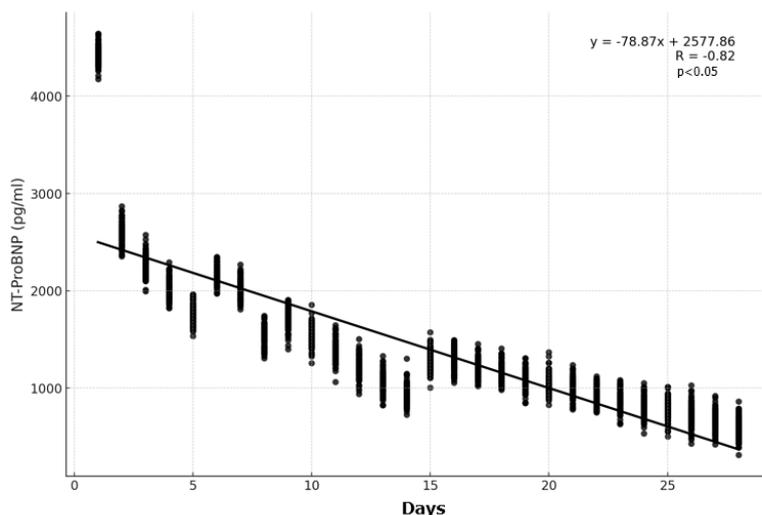


Figure 2. Correlation of NT-ProBNP concentrations with age

NT-ProBNP concentration gradually decreases with age and there is a negative linear correlation between these two indices ($r = -0.82$; $p < 0.05$).

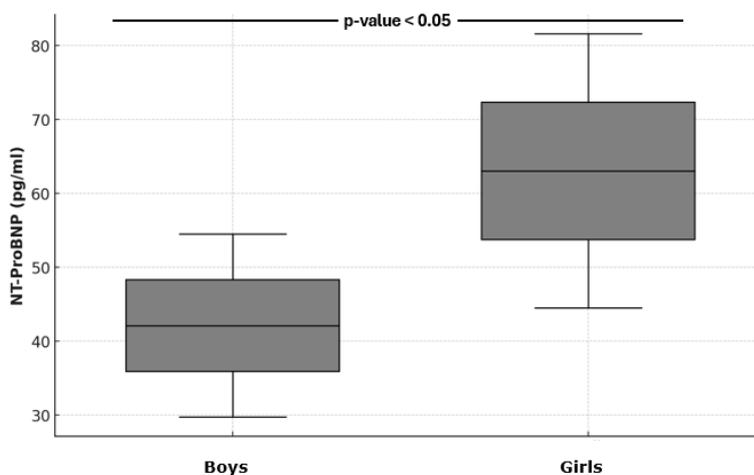


Figure 3. NT-ProBNP concentrations by gender

There is no statistically significant difference in NT-ProBNP concentration according to gender between males and females ($p > 0.05$).

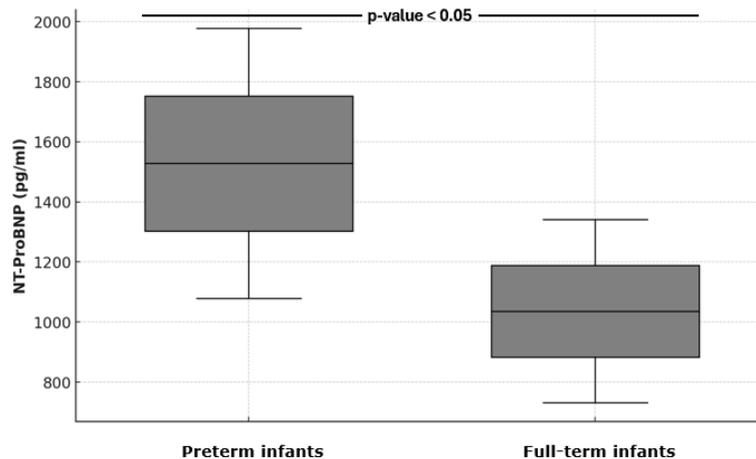


Figure 4. NT-ProBNP concentrations in full-term and preterm infants

NT-ProBNP concentrations in preterm infants are higher than in full-term infants with a statistically significant difference with $p < 0.05$.

DISCUSSIONS

Our study results show that NT-ProBNP concentration is highest at 1 day of age and then gradually decreases with age with a statistically significant difference ($p < 0.05$) (Figure 1). This result is similar to the study of Thomas S. Mir et al. on 153 healthy full-term newborns. According to Thomas S. Mir, plasma NT-ProBNP concentrations increased significantly in the first 2 days after birth and gradually decreased after the 2nd day ($p < 0.0001$). Plasma NT-ProBNP concentration on the 2nd day was 3 times higher than at the time after birth. After this marked increase, NT-ProBNP concentrations gradually decreased and became stable on the 3rd day after birth. The author commented that the obvious increase in the first days shows that NT-ProBNP has a physiological role in the change in perinatal circulation from the fetus to the neonatal period. Postpartum circulatory changes that increase ventricular pressure and volume are also a factor that stimulates NT-proBNP secretion [2]. According to Mir TS et al., NTproBNP concentration increases within 48 hours and

gradually decreases during the first week after birth. During the first days, elevation of NT-proBNP helps reduce postpartum ventricular pressure and helps reduce preload. The high water and collagen ratio of the neonatal heart causes decreased ventricular compliance leading to increased release of NT-proBNP levels. This index is high in the first days after birth and may be related to increased systemic vascular resistance, pulmonary blood flow and increased pulmonary artery pressure after birth. After the end of this period of change, plasma NT-ProBNP concentrations tend to stabilize [4]. Meanwhile, Johns M.C et al. believe that increased NT-ProBNP concentrations in newborns may be due to physiological dehydration occurring in the first week after birth. The increase or decrease in NT-proBNP concentration is correlated with physiological weight loss in newborns [6].

Other studies also reported different values for NT-ProBNP concentrations in the neonatal period. The authors suggest that the reference range varies depending on the time of testing and sampling method [7], [8].

Natriuretic Peptides are thought to not cross the placenta and therefore any change in NT-ProBNP concentration in the neonate requires an accurate assessment of the infant's condition [9]. Authors Rauh M et al. state that B-type Natriuretic peptide is useful for diagnosing or excluding heart failure in newborns. Therefore, assessing cardiovascular disease in newborns by quantifying NT-ProBNP concentrations should pay attention to reference values in the first week after birth [3]. After the neonatal period, studies show that NT-proBNP concentrations continue to gradually decrease with age and then stabilize from 4 months to 15 years of age and there is no significant difference between the sexes [6], [7].

When analyzing the correlation between NT-ProBNP concentration and age, the results showed that there was a negative linear correlation between these two indices ($r = -0.82$; $p < 0.05$) (Figure 3). Rauh M et al. also commented that there was a negative correlation between NT-ProBNP concentration and age ($r = -0.45$; $P < 0.001$) [3].

In our study, plasma NT-ProBNP concentrations did not differ by gender (between boys and girls) with ($p > 0.05$). Other studies around the world also show that there are no significant differences in NT-ProBNP concentrations according to gender in healthy children during the newborn period [3], [4]. In the study of Nir A et al., after 10 years of age, serum NT-proBNP concentrations began to differ between the two sexes, specifically NT-ProBNP concentrations in boys were lower than in girls. According to this author, this difference may be related to the concentration of estrogen (activating the gene for synthesizing

diuretic peptide) and androgen (reducing the concentration of diuretic peptide) [7].

In our study, the results showed that NT-ProBNP concentrations in preterm infants were higher than in full-term infants. Similarly, in the study of Fritz AS et al., the results showed that children with gestational age < 28 weeks had significantly higher NT-proBNP values than children with gestational age ≥ 28 weeks, especially in the first week after birth. This result shows a significant influence of gestational age on NT-proBNP concentrations. Therefore, the author suggests that in preterm infants without complications, NT-proBNP concentrations in the first week of life depend on gestational age at birth [10].

CONCLUSIONS

Research to determine plasma NT-ProBNP concentrations in 96 healthy newborns at the Vietnam National Children's Hospital, we conclude: NT-ProBNP concentration increases after birth and gradually decreases with age. There were differences in NT-ProBNP concentrations between full-term and preterm infants but no differences by gender.

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