CORRELATION DEPENDENCE OF PARAMETERS OF N-TERMINAL BRAIN NATRIURETIC PEPTIDE (N-proBNP) AND ECHO-CARDIOGRAPHIC INDICATORS IN CHILDREN WITH CONGENITAL HEART DISEASES

Mamura Rakhmatillaeva, Dilnoza Abdurakhmanova, Oydin Ubaydullaeva
Tashkent Pediatric Medical Institute, Republic of Uzbekistan
E-mail: mamura.sabina@gmail.com

Abstract: Correlation dependence of the parameters of N - terminal cerebral natriuretic (NT-ProBNP) peptide and echocardiographic parameters for the diagnosis of pulmonary hypertension in children with CHD. For the study, 81 children aged 1 to 34 months were examined. The first group of CHD children without pulmonary hypertension, the second group - 56 CHD children with pulmonary hypertension. The results of our study show a statistically significant relationship between NT-ProBNP levels and structural features and pancreatic function during the development of PH with CHD.

Keywords: congenital heart defects; pulmonary hypertension; N-proBNP; echocardiography; ventricular septal defect; average pressure in the cavity of the right ventricle; sodium uretic peptide; correlation relationship; atrial septal defect; left-right shunt.

Relevance. Congenital heart defects (CHD) are the most common congenital malformations with an estimated prevalence of 8 out of 1,000 newborns. Congenital heart defects are associated with significant mortality and morbidity. Damage to the heart is irreversible due to a lack of regenerative potential, and usually patients may require surgery. Studying the biology of heart development is important not only for understanding the mechanisms and pathogenesis of congenital heart defects, but also in order to give us an idea about the development of new methods of prevention and treatment [1].

Pulmonary arterial hypertension (PAH) is a common clinical disease that can exist independently. This is basically a manifestation of many diseases when they progress to a certain stage, namely secondary PAH. In a clinic, a shunt from left to right congenital heart disease (CHD) will increase right-sided cardiac blood flow, thus damaging the pulmonary artery and causing PAH. Statistics show that about 4-10% of patients with CHD develop PAH. Global prevalence of PAH is about 1, and 80% of patients live in developing countries. The prevalence of PAH associated with CHD is about 25 people per million in the total population. PAH is very common in children, mainly due to CHD [2].

Republic of Uzbekistan is a region with a high birth rate, where this problem is very urgent. So, for 450-500 thousand annually born children, 0.6-0.8% are diagnosed with CHD. Among which more than half are vices with left-right discharge of blood, occurring with severe hypervolemia of the pulmonary circulation [4]. Pulmonary hypertension (PH), which

is observed in 10-35% of cases, is the most dangerous and formidable complication of the natural course of congenital malformations with left-right discharge. Pulmonary hypertension (PH) occurs at a certain stage in the development of congenital heart defects and large vessels with a systemic pulmonary shunt, that is, discharge of blood from left to right. Such defects include, in particular, a ventricular septal defect, an atrial septal defect, and an open arterial (botall) duct [5].

Natriuretic peptides are members of heart biomarkers that give a general idea of the structure and functioning of the heart in children.

Brain natriuretic peptide (BNP) is synthesized in the ventricles of the heart and is released in response to volume or pressure loading.

Pro-BNP, which is an inactive precursor, is split into BNP “active component” and N-terminal pro BNP (NT-pro BNP) “inactive final product”. [6].

Recently, it has been suggested that peptides should not be considered vasodilators, but physiological antagonists of vasoconstrictors. Thus, the active N - terminal cerebral natriuretic (N-proBNP) and inactive NT-proBNP peptide enter the bloodstream, while their secreted amounts are in close correlation. However, the half-life of these compounds is different and is 20 minutes for BNP, and about 120 minutes for NT "proBNP. [3]. In the myocardium of the atria and ventricles with hypoxia, clearance of NUP and NT-proBNP clearance of circulating NUP (ANP and BNP) is provided by two main metabolic pathways: intracellular cleavage in lysosomes and proteolysis under the influence of neutral endopeptidase [3].

Purpose of the study. To evaluate the correlation dependence of the parameters of the N - terminal cerebral natriuretic peptide (N-proBNP) and echo-cardiographic parameters to study pulmonary hypertension in children with CHD.

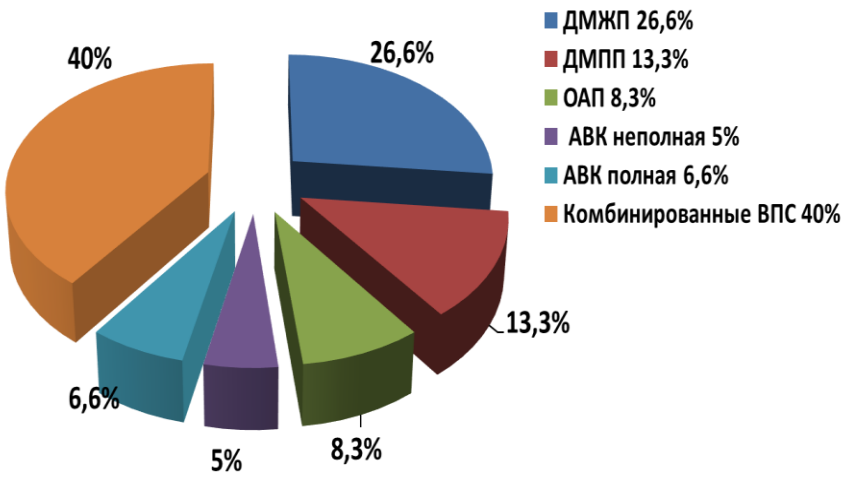
Materials and research methods

The studies were carried out at the Tashkent Pediatric Medical Institute clinic in the departments of pediatric cardiac rheumatology, cardiac surgery and the department of young children. To solve the problems, 81 children aged 1 to 34 months were examined. The work took into account the data of antenatal history and the results of ante- and postnatal diagnosis of CHD, clinical examination and laboratory-functional research methods (biochemical blood test, level of NT-proBNP, ECG, echocardiography, chest x-ray).

Results

The examined 81 children were divided into groups according to the given clinical and echocardiographic indications. Group 1 comprised 25 children with CHD without pulmonary hypertension; group 2 comprised 56 children with CHD and pulmonary hypertension.

Fig. No. 1. Types of CHD in the study



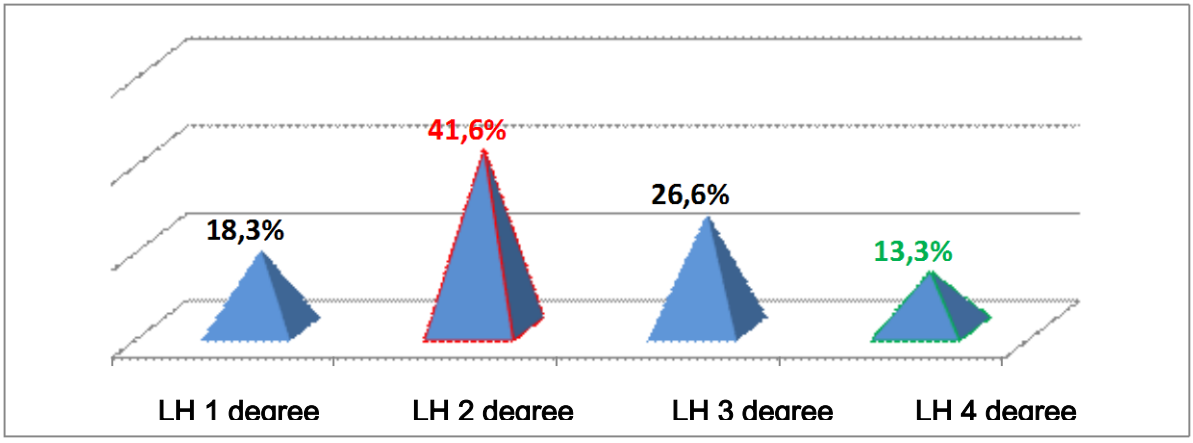
Ventricular septal defect
Atrial septal defect
Open aortic duct
incomplete atrioventricular canal
complete atrioventricular canal
Combined UPU

An analysis of the type of defect in the development of LH showed that congenital heart defects with an isolated blood shunt at the level of the interventricular septum in 26.6% of cases, defects with a blood shunt at the level of the atria in only 13.3% of cases, and combined heart defects up to 40% of cases .

To begin with, we examined the relationship of the degree of LH with the anatomical type of CHD.

To this aim, we analyzed 81 echocardiograms of young children with congenital heart defects complicated by pulmonary arterial hypertension of various degrees. Pulmonary hypertension was determined according to Burakovsky, and the first degree of pulmonary hypertension was diagnosed in 18.3, the second degree in 41.6, the third degree in 26.6% and the fourth degree of pulmonary hypertension in 13.3% of children (Fig. 2).

Fig. 2.Distribution of patients by LH degree.



The degree of LH was determined by the ratio of systolic pressure in LA to systemic blood pressure, taking into account the classification of Burakovsky V.I. et al.: up to 30% -1 degree, 30% -70% - 2 degree, 70% -100% - 3 degree, more than 100% - 4 degree.

We distributed the combination of pulmonary hypertension with the type of congenital defect in the following table (Table 1), where such combinations of various nosological forms are presented.

Table №1.

The relationship of various heart defects with the degree of pulmonary hypertension

Порок сердца		**LH 1 degree**	**LH 2 degree**	**LH 3 degree**	**LH 4 degree**	Total
VSD	n	15	9	7	3	34
	%	44.1%	26,4%	20,5%	8,8%	
ASD	n	3	2	0	0	5
	%	60%	40%	-	-	
VSD+ASD	n	-	2	1	-	3
	%		66,6%	33,4%		
VSD+OAD	n	2	2	-	-	4
	%	50%	50%			
OAD	n	3	1	-	-	4
	%	75%	25%			
VSD+TMV	n	5	4	1	-	10
	%	50%	40%	10%		

As can be seen from the table, patients with VSD are twice as likely to be complicated with different degrees of LH. In our practice, I degree LH was more observed between patients with VSD in 15 (44.1%). We noted only in children with a malignant hypertrophy of the III-IV degree of LH. For the most part, among patients with ASD, 3/5 (60%) had grade I LH. 2/3 (66.6%) of patients had grade II LH. In equal patients with VSD + ASD, I-II degree LH was observed. In ¾ (75%) patients with OAD, grade I LH was noted. In half (50%) of patients with VSD + TMV, LH I degree was observed.

Thus, congenital heart disease of VSD is most often complicated with LH. We must timely identify the defect and prescribe treatment to prevent complications and their height. In patients with combined congenital malformations of VSD + ASD complicated with LH I degree often proceeds unnoticed, and patients are treated even with advanced complicated LH II degree.

This means that children with one defect (group I) are twice as likely to be complicated by LH of the first degree. In our study, we noted that in children with benign prostatic hypertrophy, LH of the III-IV degree is observed, which leads to pulmonary hypertensive crisis, which develops at 6-7 months of age.

In children with combined defects (group II), LH I-II degree was noted.

As a result of the analysis, it was revealed that pulmonary hypertension of the III-IV degree was registered in patients with congenital malformations formed by one nosological form. Congenital heart defects with a blood shunt at the level of the interventricular septum are more likely to develop high pulmonary hypertension than CHD with an atrial septal defect. The most unfavorable is the combination of defects of the interventricular septum and atrial septum.

As can be seen from the table, VSD is complicated by pulmonary hypertension of the 1st degree in 15 (44.1) patients, VSD + TMV- in 5 (50%) patients, VSD in 3 (60%) and OAD

in 3 (75%) patients, VSD + OAD-in 2 (50%) patients. VSD in 9 (26.4%) patients and a combination of VSD with TMV - in 4 (40%) patients - most often leads to LH of the 2nd degree. Pulmonary hypertension of the 3rd degree is complicated by benign prostatic hypertrophy in 7 (20.5%) patients and concomitant malformations of pancreatic hypertrophy and pulmonary hypertension in 1 (33.4%) and pulmonary hypertension in 1 (10%) patients. 4th degree pulmonary hypertension is most common in cases of benign prostatic hypertrophy in 3 (8.8%) patients.

The analysis showed that congenital heart defects with a blood shunt at the level of the interventricular septum are more likely to develop pulmonary hypertension than CHD with an atrial septal defect. Also, CHD with VSD are often complicated by pulmonary hypertension of the 3-4th degree.

During the observation process, in the 1st and 2nd group of the study, NT-proBNP-cerebral natriuretic (BNP) peptides were determined, the indicators of which were compared with the parameters of echocardiography. The performance of which was directly proportional to the performance of NT-proBNP.

A direct correlation was also found between echocardiographic systolic pressure in the pulmonary artery and right-hand cardiac catheterization indicators initially: RVSP RCCI (corr. 0.88, $p < 0.05$) and TPVR RCCI (corr. 0.71, $p < 0.05$). The correlation data indicate that the higher the RVSP and TPVR indicators according to RCCI, the higher the APLA measured using echocardiography.

Comparison of APLA data obtained using echocardiography and RCCI showed a strong correlation between these methods. Therefore, in patients with IPH, it is necessary to use echocardiography as a screening method for assessing APLA. However, due to some limitations of the method (for example, poor visualization of the regurgitation jet or its eccentric orientation), which lead to errors in the measurement of APLA, it is necessary to use additional parameters to objectify this method.

Table №2

Right ventricular echocardiographic and plasma NT-proBNP levels

Indicators	**Indicator value in groups**	
	1st (n=25)	2nd (n=56)
RV, mm	24 ± 0,9	27± 1,5
APRV, mmHg Art.	11,6 ±1,2	17,5±0,95
Pulmonary trunk, mm	24 ±2	28 ±1,5
Vtk regurgitation, m / s	3,0 ±0,7	3,8±1,2
SGPmax in LA, mmHg ct	5,1±1,8	25±3,4
NT-proBNP, fmol / ml	606,0±150,9	1525,5±1029,0

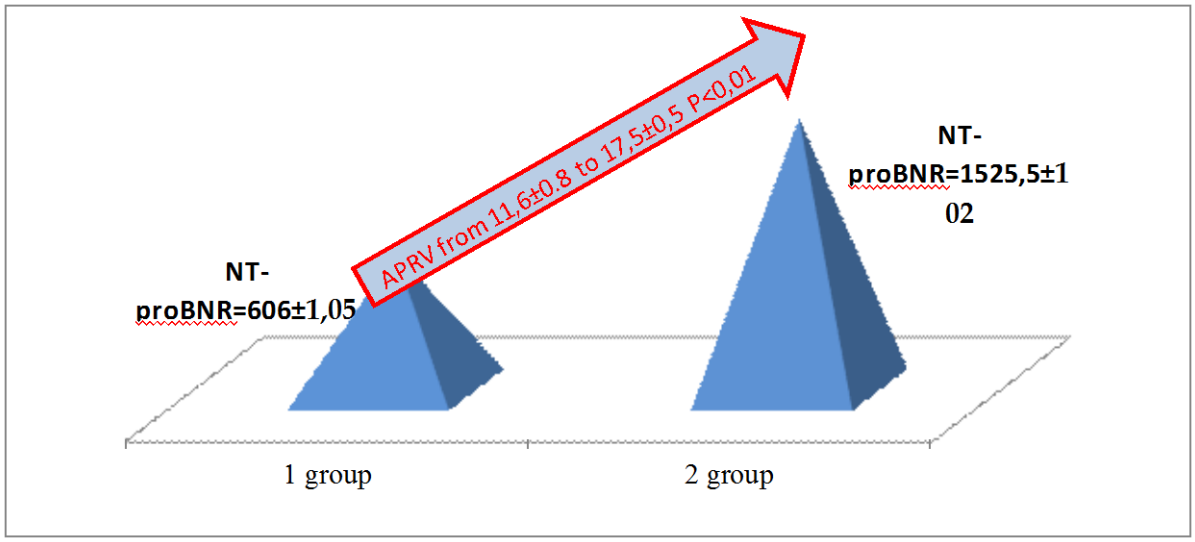
RV - the size of the cavity of the right ventricle, mm;
APRV - the average pressure in the cavity of the right ventricle, mm RT. Art.
SGPmax - maximum systolic pulmonary pressure gradient.
Vtk regurgitation - blood flow velocity of tricuspid regurgitation
NT-proBNP-cerebral natriuretic (BNP) peptides.

Table №3.
Correlation between the levels of NT-proBNP in blood plasma and the corresponding echocardiographic parameters of the RV.

Indicators	APRV, mmHg Art.		SGPmax in LA, mmHg	
	r	P	r	P
NT-proBNP. in 1st group	0,744	0,014*	0,005	0,068
NT-proBNP. in 2nd group	0,563	0,034*	0,645	0,024*

Of the echocardiographic parameters, parameters of the pancreatic diastolic function such as APRV, mmHg, significantly correlated with the level of NT-proBNP in the group with CHD complicated by LH. Art. by the value of which they judge the degree of LH.

Fig. № 3



Thus, based on the results of echocardiography, a positive correlation was observed between systolic pulmonary pressure and serum BNP and the amount of shunt from left to right. The results of our study demonstrate a statistically significant relationship between NT-proBNP levels and the developmental features of RV structure and function disorders during the development of LH in CHD.

Conclusions

Based on the results of echocardiography, a positive correlation was observed between systolic pulmonary pressure and serum BNP and the amount of shunt from left to right. The

results of our study demonstrate a statistically significant relationship between NT-proBNP levels and the developmental features of RV structure and function disorders during the development of LH in CHD.

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