Diagnostic Value of "Brain Natriuretic Peptide" in Children with Hemodynamically Significant Heart Disease

Hemodinamik Olarak Önemli Kalp Hastalığı Olan Çocuklarda "B Tipi Natriüretik Peptid"in Tanısal Önemi

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ABSTRACT Objective: To investigate the diagnostic value of Brain Natriuretic Peptide (BNP) in children with hemodynamically significant heart disease. **Material and Methods:** The patients were eveluated by physical examination and with 2-D and Doppler echocardiography. Patients were classified according to presence or absence of hemodynamically significant heart disease, as Group 1 and Group 2, respectively. Patients in Group 1 were further subclassified into patients with normal left ventricular end-diastolic dimention (LVEDD) and patients with above normal LVEDD, as Group 1-A and 1-B, respectively. Group 1-C consisted of patients with clinical findings of congestive heart failure (CHF) and Group 1-D those without CHF on physical examination. **Results:** The median serum BNP level was found to be 600 pg/mL in Group 1-A and 340 pg/mL in Group 1-B (Interquartile ranges 1382 and 1513, respectively) ($p>0.05$). Nonetheless, in Group 1, mean serum BNP level was found to be significantly higher in Group 1-B as well as in Group 1-A compared to Group 2, and this difference was found to be statistically significant ($p< 0.05$). Mean serum BNP level was found to be 740 pg/mL in Group 1-C and 270 pg/mL in Group 1-D (Interquartile ranges 1400.75 and 1710.75, respectively) ($p> 0.05$). However, mean serum BNP level was significantly higher in Group 1-C as well as in Group 1-D than it was in Group 2, and this elevation was found to be statistically significant ($p< 0.05$). The difference between pulsed wave tissue Doppler results of Group 1-B and Group 1-A were insignificant ($p> 0.05$). Similarly,the difference between pulsed wave tissue Doppler findings of Group 1-C and Group 1-D were insignificant ($p> 0.05$). **Conclusion:** BNP is a successful biochemical marker of left ventricular dysfunction that can be used in the diagnosis and follow-up of children with heart disease.

Key Words: Brain natriuretic peptide-35; heart defects, congenital; ventricular dysfunction

ÖZET Amaç: B tipi natriüretik peptitin (BNP) hemodinamik yönden önemli kalp hastalığı olan çocuklarda diagnostik önemini araştırmaktır. **Gereç ve Yöntemler:** Olgular fizik muayene ve ekokardiyografik incelemeler sonucunda hemodinamik yönden önemli kalp hastalığı olanlar (Grup 1) ve olmayanlar (Grup 2) şeklinde ikiye ayrıldı. Hemodinamik yönden önemli kardiyak hastalığı olan Grup 1' deki olgulardan sol ventrikül diyastol sonu çapları normal olanlar Grup 1-A, normalin üstünde olanlar 1-B, ayrıca fizik muayene esnasında konjestif kalp yetersizliği bulguları olanlar Grup 1-C, olmayanlar Grup 1-D olarak sınıflandırıldı. **Bulgular:** Ortanca serum BNP düzeyi Grup 1-A'da 600 pg/mL, Grup 1-B'de 340 pg/mL (çeyrekler arası genişlik sırasıyla 1382 ve 1513) bulundu ($p> 0.05$). Ancak ortalama serum BNP düzeyi hem Grup 1-A'da hem de Grup 1-B'de Grup 2'ye kıyasla belirgin yüksek saptandı ve bu fark istatistiki yönden anlamlı idi ($p< 0.05$). Ortanca serum BNP düzeyi Grup 1-C'de 740 pg/mL, Grup 1-D'de 270 pg/mL (çeyrekler arası genişlik sırasıyla 1400.75 ve 1710.75) bulundu ($p>0.05$). Gerek Grup 1-C'de gerekse Grup 1-D'de ortalama serum BNP düzeyi Grup 2'ye göre belirgin yüksekti ve bu yükseklik istatistiksel olarak anlamlı idi ($p< 0.05$). Darbeli dalga doku Doppler sonuçları yönünden Grup 1-A ile 1-B arasında istatistiksel olarak anlamlı fark yoktu ($p>0,05$). Keza, Grup 1-C ile Grup 1-D arasında da darbeli dalga doku Doppler sonuçları yönünden istatistiksel olarak anlamlı fark bulunmadı ($p> 0.05$). **Sonuç:** BNP sol ventrikül disfonksiyonunu göstermede başarılı bir biyokimyasal parametredir ve bu yüzden pediyatrik kardiyolojide tanıda ve izlemde kullanılabilir.

Anahtar Kelimeler: Beyin natriüretik peptid; kalp kusurları, doğumsal; ventriküler disfonksiyon

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Although being less common in infants and children than in adults, heart disease is a significant cause of morbidity and death in infants and children. Congenital structural cardiac abnormalites and acquired heart diseases may result in pulmonary hypertension and heart failure.[1]

Cardiac B-type natriuretic peptide and the N-terminal segment of its pro-hormone (NT-proBNP) are a strong biomarkers in the diagnosis and prognosis of heart diseases.[2] Brain natriuretic peptide is synthesized as a pro-hormone containing 108 amino acids and then it is cleaved into BNP consisted of 32 amino acids and N-terminal BNP (NT-BNP).[3] The natriuretic peptide system has a similar role in health and disease in the paediatric age Group as in adults.[1]

BNP shows natriuretic, diuretic, and vasodilator effects.[4] It exerts its diuretic and natriuretic effect by influencing renal hemodynamics or directly via tubular effect. It increases glomerular filtration rate by afferent arteriolar dilatation and efferent arteriolar vasoconstriction. Blocking the angiotensin-II–mediated water and sodium reabsorption in the proximal tubule and the effect of vasopressin in the collecting duct, it increases natriuresis and diuresis. It causes arterial and venous dilatation by leading to relaxation in vascular smooth muscle. Consequently, preload and afterload decrease.[5] In addition, it prevents the fibrotic and proliferative processes in the myocardium.[6,7] Reducing peripheral vascular resistance with its vasodilator effect, BNP increases cardiac output and decreases filling pressures and pulmonary capillary wedge pressure. Because of its antimitogenic effects, it is believed that release of BNP shows a modulating effect in the pathologies affecting vascular wall such as atherosclerosis, hypertension, and restenosis. Moreover, BNP inhibits central and peripheral sympathetic nervous systems, increases vagal tonus, prevents renin-aldosteron release, and blocks effects of endothelin-I and angiotensin-II.[8-10]

Today, developments in ultrasound technology allow us to quantitatively determine the systolic and diastolic functions of myocardium directly from myocardium (the tissue in which sample volume is added). Through this technologic development called tissue Doppler imaging, it is possible to determine systolic and diastolic flows of myocardium independently from preload.[11,12]

In this study, we examined hemodynamic state using transthoracic echocardiography and the correlation of hemodynamic state with brain natriuretic peptide in children with congenital heart disease.

MATERIAL AND METHODS

Fifty-four children with heart disease who were admitted to our clinic during the 8-month period between December 2005 and July 2006 were included in the study. All subjects were initially assessed by physical examination, chest X-ray and 12-lead electrocardiography. Transthoracic echocardiographic examinations of the subjects were performed using Vivid 3 echocardiography with 3.5 or 5 MHz transducer. During the transthoracic echocardiographic examination, type of intracardiac lesion and its hemodynamic significance and left ventricular systolic and diastolic functions were assessed. Tissue Doppler measurements were performed with the sample volume placed 5 mm from lateral mitral annulus and using angle correction in the apical 4 chamber position. S velocity, early (E' velocity) and late (A' velocity) diastolic lateral mitral annular velocities, isovolemic relaxation time (IVRT), ejection time (ET) and isovolumic contraction time (ICT) were assessed.

In our study, all subjects were divided into two Groups as either hemodynamically significant (Group 1; n= 34) or non-significant cardiac lesions (Group 2; n= 20) as detected by physical examination and echocardiography.

Patients in Group 1 were further subclassified into patients with normal left ventricular end-diastolic dimention (LVEDD) and patients with above normal LVEDD, Group 1-A and 1-B, respectively. Group 1-C consisted of patients with clinical findings of congestive heart failure (CHF) and Group 1-D those without CHF on physical examination.

Serum BNP levels of the subjects were measured at Biosite triage MeterPlus device using BNP Test stripes.

This study was performed according to the Helsinki declaration principle and was approved by the local ethics committee. Informed consent was obtained from each patient.

STATISTICAL ANALYSIS

In statistical analysis performed using SPSS, the differences between age, body weight, serum BNP levels, M MODE values, and pulsed wave tissue Doppler results between the Groups were investigated with the Mann Whitney U test and student t test.

Nonparametric Mann Whitney U test was used for comparing data for age, BNP and S velocity at Group 1 and Group 2 also for subGroups of Group 1.

Comparison for other parameters between Group 1 and Group 2 was performed by student t test.

In both Groups, all subjects were examined for the correlation between systolic and diastolic dysfunctions and serum BNP levels. The correlations between the Groups regarding serum BNP levels, M-Mode values and tissue Doppler results was determined using the Spearman correlation analysis.

RESULTS

Demographic data, serum BNP levels and pulsed wave tissue Doppler values of Group 1 and 2 are presented in Table 1, 2 and 3. There were no dif-

TABLE 1: Age, body weight, diagnosis, and serum BNP levels of the cases in Group 1.

No	Age	Weight (kg)	Diagnosis	BNP (pg/mL)
1	4 months	3.66	VSD (PM), Sec. ASD	3270
2	11 years	42	MI 2º, MVP	9
3	7 months	5.5	CoA, PDA	148
4	2 months	4.2	DCMP, MI 1º	198
5	13 months	7	VSD (Multiple), Sec. ASD	1550
6	33 months	9.4	AS	340
7	1.75 months	3.74	AS, MI 2º	1650
8	7 months	5.4	Cor Triatriatum	897
9	10 years	31	VSD, CoA, AS, AVP	200
10	2 years	11	AS, DCMP	2300
11	3.5 days	0.8	PM, PDA, CHF	1390
12	11 years	45	Constructive Pericarditis	401
13	6 months	5	Down Syndrome, AVSD	137
14	2 years	9	SIT, VSD, R-AVV Deficiency	5000
15	15 years	15	Congenital Myopathy, LV systolic dysfunction	86
16	1.5 months	5	Down Syndrome, AVSD	165
17	15.3 years	36	VSD, Operated CoA	5
18	10 months	6	DCMP, MI 1º	594
19	15 months	8	VSD (Perimembraneous)	192
20	12 months	8	CoA, PDA	160
21	15 months	10	VSD	1080
22	10 months	6	DCMP, MI 1º	406
23	9 months	6	VSD	340
24	3 months	4	Down Syndrome, VSD (Multiple), Sec. ASD	62
25	1 months	3	VSD, PFO	1800
26	5 years	22	Operated AVSD, MI 3º-4º	133
27	5.5 months	3.9	VSD, PFO, PDA	4390
28	12 months	8.3	DCMP	1770
29	2 years	8	DCMP, MI 2º	600
30	7 years	18	VSD	18
31	5.5 months	6	DCMP	2800
32	2.5 years	12.4	DCMP	1580
33	5.5 months	5	CoA, DCMP, MI 1º	880
34	4.5 years	11	Operated TOF+Sec. ASD,VSD (Residuel)	1100

VSD: Ventricular septal defect, Sec. ASD: Secundum ASD, MI: Mitral insufficiency, MVP: Mitral valve prolapse, CoA, Coarctation of the aorta, PDA: Patent ductus arteriosus, DCMP: Dilated cardiomyopathy, AS: Aortic stenosis, AVP: Aortic valve prolapse, PM: Prematurity, CHF: Congestive heart failure, AVSD: Atrioventricular septal defect, SIT: Situs inversus totalis, R-AVV: Right atrioventricular valve, LV: Left ventricle, PFO: Patent foramen ovale, TOF: Tetralogy of Fallot

TABLE 2: Age, body weight, diagnosis, and serum BNP levels of the cases in group 2.

No	Age	Weight	Diagnosis	BNP
1	7 years	23	VSD (Restrictive)	15
2	4 years	16	VSD (Restrictive)	22
3	10 years	25	VSD (Restrictive)	28
4	6 years	18	AS (Mild-Moderate)	88
5	4 years	13	Sec. ASD (Small)	38
6	5 years	12	Sec. ASD (Small)	22
7	12 years	39	PFO	11
8	7 years	21	Sec. ASD (Small)	27
9	3 years	15	PDA (Restrictive)	8
10	8 years	23	VSD (Restrictive)	59
11	6 years	17	Sec. ASD (Small)	43
12	6 years	24	Sec. ASD (Small)	50
13	8 years	28	VSD (Restrictive)	72
14	6 years	20	VSD (Restrictive)	43
15	7 years	17	PDA (Restrictive)	6
16	5 months	6	PS (Mild)	12
17	7 years	20	PS (Mild-Moderate)	18
18	8 years	25	PFO	7
19	10 years	30	VSD (Restrictive)	78
20	3 years	12	VSD (Restrictive)	22

PS: Pulmonary stenosis.

Serum BNP levels, echocardiographic M MODE values, and findings from pulsed wave tissue Doppler evaluation of the sub-Groups of Group 1 are shown in Table 4.

In Group 1 patients with hemodynamically significant heart disease, 70.6% of the subjects had CHF findings during physical examination (Table 4). Furthermore, a majority of these subjects were diagnosed as dilated cardiomyopathy (DCMP; n = 9; 37.5%), in seven of whom it was isolated and in two of them it was associated with severe aortic valvular stenosis and severe discrete coarctation of the aorta. In 20 cases (57.1%) of the Group 1, LVEDd was within the normal range with respect to age, while in 14 cases LVEDd was found to be higher than upper normal limit (mean:11 ± 7.6 mm, range: 0.1-22.9, $p< 0.05$, Table 4). In all cases with DCMP, LVEDd was found to be above the upper limits of normal. In Group 1, only a seven month-old case with cor triatriatum manifested pressure and volume loading of the right ventricle (Table-1). Serum BNP level of this case was measured as 897 pg/mL.

In the Group 2, most of the cases had a restrictive VSD (n = 8; 40%, Table 2). Using M-Mode echocardiography LVEd measurements were found to be within normal range in all cases of the Group 2. Of the M-mode echocardiographic measurements, IVSd, LVEDd and LVPWDd values were higher in Group 1 compared to Group 2, except for

TABLE 3: Mean or median and interquartile ranges of age, body weight, serum BNP levels, M MODE, and pulsed wave tissue Doppler results of all cases

	Group 1 Mean ± Standard deviations or Median (Interquartile range) Values	Group 2 Mean ± Standard deviations or Median (Interquartile range) Values	p
Age (month)	12.0 (32.7)	42.0 (67.00)	>0.05*
Body weight (kg)	11.3 ± 11.1	12.9 ± 6.8	>0.05* *
Serum BNP (pg/mL)	500.0 (1440.5)	24.5 (35.50)	<0.05*
IVSd (cm)	0.59 ± 0.18	0.59 ± 0.11	>0.05* *
LVEDd (cm)	3.35 ± 1.19	3.06 ± 0.83	>0.05* *
LVPWd (cm)	0.62 ± 0.17	0.58 ± 0.19	>0.05* *
FS (%)	29.9 ± 11.9	34.1 ± 4.8	>0.05* *
EF (%)	56.4 ± 17.8	65.2 ± 6.5	>0.05* *
S velocity (m/sec)	0.166 (0.02)	0.115 (0.02)	<0.05*
E' velocity (m/sec)	0.18 ± 0.04	0.19 ± 0.05	>0.05* *
A' velocity (m/sec)	0.14 ± 0.04	0.10 ± 0.01	<0.05* *
E'/A'	1.32 ± 0.3	1.88 ± 0.4	<0.05* *
IVRT (msec)	51.9 ± 8.7	47.6 ± 3.7	<0.05* *
ICT (msec)	57.9 ± 16.3	54.4 ± 8.6	>0.05* *
ET (msec)	254.7 ± 21.8	249.3 ± 21.4	>0.05* *

P<0.05: statistically significant, p>0.05: statistically insignificant

- *non-parametric Mann Whitney u test
- * * independent samples t test

IVSd: End-diastolic interventricular septum thickness, LVEDd: Left ventricular end-diastolic diameter, LVPWDd: Left ventricular posterior wall thickness at end-diastole, FS: Fractional shortening, EF: Ejection Fraction, S: Tissue Doppler imaging (TDI) peak systolic wave velocity, E': TDI peak early diastolic wave velocity, A': TDI peak late diastolic wave velocity, IVRT: ısovolumic relaxation time, ICT: Isovolumic contraction time, ET: Ejection time.

TABLE 4: Medians and interquartile ranges of serum BNP levels, M MODE values, and pulsed wave tissue Doppler results of the cases in Group 1's subgroups

	Group 1A	Group 1B		Group 1C	Group 1D	
	Median (IQR)*	Median (IQR)*	p	Median (IQR)*	Median (IQR)*	p
BNP (pg/mL)	600.0 (1382.0)	340.0 (1513.0)	0.425	740.0 (1400.7)	270.0 (1710.7)	0.047
LVEDd (cm)	4.8 (1.5)	2.70 (1.0)	0.00	3.0 (2.0)	3.0 (2.1)	0.009
FS (%)	21.0 (18.0)	32.0 (10.0)	0.012	30.5 (15.7)	31.5 (23.5)	0.00
EF (%)	44.0 (30.0)	64.0 (15.0)	0.004	62.0 (24.7)	59.0 (33.0)	0.00
S velocity (m/sec)	0.1 (0.03)	0.1 (0.02)	0.294	0.1 (0.02)	0.1 (0.02)	0.745
E' velocity (m/sec)	0.1 (0.05)	0.1 (0.08)	0.184	0.1 (0.04)	0.1 (0.08)	0.505
A' velocity (m/sec)	0.1 (0.08)	0.1 (0.07)	0.535	0.1 (0.07)	0.1 (0.07)	0.271
E'/A'	1.2 (0.4)	1.4 (0.30)	0.039	1.2 (0.3)	1.4 (0.5)	0.017
IVRT (msec)	52.0 (14.0)	53.7 (10.9)	0.645	52.1 (15.0)	52.8 (10.4)	0.403
ET (msec)	249.4 (23.6)	255.7 (23.3)	0.845	256.2 (23.5)	252.3 (21.5)	0.885
ICT (msec)	46.7 (35.7)	58.8 (22.1)	0.501	55.4 (22.5)	53.1 (28.7)	0.829

*median(ınterquartile range)

FS and EF. On the other hand, there was no statistical significant difference between the M-mode echocardiographic values of Group 1 and Group 2 ($p>0.05$; Table 3).

Median serum BNP level was found to be 740 pg/mL in Group 1-C and 270 pg/mL in Group 1-D (Interquartile ranges 1400.75 and 1710.75, respectively) and difference was not statistically significant ($p> 0.05$; Table 4). However, mean serum BNP level was significantly higher in Group 1-C and in Group 1-D when compared to Group 2 ($p< 0.05$). Mean serum BNP level was 1667±1369.3 pg/mL in patients with DCMP. The difference between median serum BNP level of Group 1-A (600 pg/mL, interquartile range: 1382) and Group 1-B (340 pg/mL, interquartile range: 1513) was insignificant ($p> 0.05$,Table 4). On the other hand, mean serum BNP level were found to be significantly higher in Group 1-B and Group 1-A when compared to Group 2 ($p< 0.05$).

Mean LVEDd was measured as 2.55±0.67 cm in Group 1-B, 4.36 ± 0.9 cm in Group 1-A, 3.34±1.21 cm in Group 1-C, and 3.38 ± 1.2 cm in Group 1-D**.** Although, mean LVEDd was higher in Group 1-A (4.36 ± 0.9) when compared to Group 1-B (2.55 ± 0.67, $p< 0.05$), there was no statistically significant difference between Groups 1-C (3.34 ± 1.2 cm) and 1-D (3.38 ± 1.2 cm, $p> 0.05$, Table 4).

FS was found to be lower in Group 1-A when compared to Group 1-B, and in Group 1-C when compared to Group 1-B ($p< 0.05$ and $p> 0.05$, respectively; Table 4).

EF was found to be lower in Group 1-A when compared to Group 1-B and in Group 1-C when compared to Group 1-D. These differences were found to be significant in terms of LVEDd and non-significant in terms of the presence of CHF ($p<0.05$ and $p>0.05$, respectively; Table 4).

Median S wave velocity was lower in Group 1 compared to Group 2 ($p< 0.05$, Table 3). In addition, A' wave velocity was higher in Group 1 compared to Group 2 ($p< 0.05$; Table 3). There were no significant differences between the two Groups regarding E' velocity values ($p> 0.05$; Table 3). In Group 2, E'/A' value was within the normal range whereas in Group 1 it was below normal, and this difference was found to be statistically significant ($p< 0.05$, Table 3). IVRT was found to be longer in Group 1 when compared to Group 2 ($p> 0.05$, Table 3). Mean ET and ICT were not different significantly between the two Groups ($p> 0.05$; Table 3). Pulsed wave tissue Doppler values were not significantly different between Group 1-B and Group 1-A, and between Group 1-C and 1-D ($p>0,05$, $p> 0.05$, respectively, Table 4).

No statistically significant difference was found regarding pulsed wave tissue Doppler imaging in patients with CHF findings and normal FS-EF-LVEDd values when compared to the cases without any hemodynamically significant cardiac lesions who were included in Group 2.

In the Group with CHF findings and without suspected clear systolic dysfunction, mean serum BNP levels were 825.9 ± 1162.3 pg/mL which was

significantly higher when compared to Group 2 ($p< 0.05$).

In Group 1-C, FS-EF values were below normal and/or they had larger LVEDd than normal. A' wave velocity was higher (0.13 ± 0.01 m/sn and 0.10 ± 0.01 m/sn, respectively; $p< 0.05$) and E'/A' value was lower (1.17 ± 0.4 and 1.88 ± 0.4, respectively; $p< 0.05$) when compared to Group 2. Mean serum BNP levels of cases with CHF findings and left ventricular dysfunction and/or with LVEDd above normal were found as 1640 ± 1245.2 pg/mL,which was 2-fold higher when compared to the Group with CHF findings but without left ventricular systolic or diastolic dysfunction ($p< 0.05$). Other pulsed wave tissue Doppler results of these two Groups with CHF did not show any statistically significant difference ($p>0.05$).

In Group 1, a poor, positive and, non-significant correlation was found between these cases' serum BNP levels and S and E' wave velocities (r: 0.024 and 0.04, respectively), whereas a non-significant correlation was found between these cases' serum BNP levels and A' wave velocities. A non-significant correlation was found between serum BNP levels and E'/A' values, whereas a non-significant correlation was found between serum BNP levels and time intervals. When M MODE values and serum BNP levels of the Group 1 were evaluated, a moderate, negative, and significant correlation was established between serum BNP levels and IVSD and FS values (r: -0.44 and -0.42, respectively) whereas a non-significant correlation with LVEDd and EF and a non-significant correlation with LWPWd was determined. There was no statistically significant correlation between serum BNP levels and age, body weight, M MODE values, and pulsed wave tissue Doppler results of the cases in Group 2.

DISCUSSION

BNP and the N-terminal segment of its pro-hormone (NT-proBNP) is considered as a strong biomarker in determining the diagnosis and prognosis of heart diseases.[2]

BNP limit value is suggested to be at 100 pg/mL in the diagnosis of heart failure. This value is 95% specific for HF diagnosis and has a sensitivity of 82% for all HF cases and, according to New York Heart Association (NYHA), and a sensitivity of 99% for class IV cases. Studies show that this value is more dependable than all of the other parameters. In addition, the negative predictive value is too high under 100 pg/ml, whereas this value is approximately 96%[2] under 50 pg/mL. In our study, 70.6% of the cases in Group 1 classified as hemodynamically significant had congenital heart disease findings on their physical examinations. The majority of these cases were diagnosed as DCMP. Mean serum BNP levels of patients with CHF and without CHF were approximately 27 and 32 times more than the cases in Group 2 ($p< 0.05$). Mean serum BNP level of all DCMP cases with CHF findings, significant left ventricular systolic dysfunction and bigger LVEDd were significantly high.

BNP release is regulated by blood pressure and volume load. A correlation was found between left ventricular chamber volume, left ventricular end-diastolic pressure, and plasma BNP concentration was found.[9] However, BNP also increases in diseases effecting the right ventricule, such as pulmonary embolism, primary pulmonary hypertension, cor pulmonale and arrhythmogenic right ventricular dysplasia. However, this increase is smaller when compared to cases with left ventricular dysfunction.[2] In case 1 of Group 1 who was diagnosed as cor triatriatum, serum BNP level was measured as 897 pg/mL; This value was smaller than the average value of Group 1 and it was considerably higher than the mean value of Group 2.

Diastolic dysfunction, a drop in S wave velocity, E' wave velocity, E'/A' value, and an increase in IVRT are found in diastolic dysfunction by pulsed wave tissue Doppler imaging.[13] BNP has been shown to increase in diseases leading to LV diastolic dysfunction, such as aortic stenosis, hypertrophic cardiomyopathy, hypertension, and restrictive cardiomyopathy. However, this increase is smaller when compared to the one in systolic dysfunction. BNP levels have been shown to increase linearly with the severity of the diastolic dysfunction.[14,15] In accordance to previous reports, average S wave velocity was found to be lower in

Group 1 as compared to Group 2, whereas mean A' velocity was detected higher in Group 1. The E'/A' value was found lower than normal in Group 1 and normal in Group 2. IVRT was detected to be longer in Group 1 as compared with Group 2. However, to regards to E' wave velocity values, a statistically significant difference was detected between the two Groups.

Some studies suggest that CNH assays, in particular a BNP assay, may be useful for the diagnosis of left ventricular diastolic dysfunction. In a study performed on 34 patients, no significant correlation was found between a CNH assay and decreased diastolic function attributable to doxorubicin-induced cardiotoxicity in children with cancer. The reason for some of these conflicting results may be different causes and/or mechanisms responsible for cardiac dysfunction.[16]

The value of BNP in the diagnosis of isolated diastolic dysfunction is similar to that of in systolic dysfunction. In the exclusion of clinically significant left ventricular diastolic dysfunction (LVDD), BNP values lower than 57 pg/ml have a 100% negative predictive value. In patients clinically diagnosed with HF and with normal LV function, BNP has been found to be the strongest predictor of LVDD.[2] In this study, a significant correlation was not detected between tissue Doppler parameters and serum BNP levels.

In the study, the mean serum BNP level of cases with CHF along with systolic dysfunction and/or whose LVEDd are higher than normal, and also who were found to have diastolic dysfunction findings in pulsed tissue Doppler imaging were found to be approximately two times higher as compared to the Group that has CHF findings but no left ventricular systolic or diastolic dysfunction, and this finding was statistically significant.

Although brain natriuretic peptide test cannot discriminate systolic and diastolic dysfunction on its own, in situations where systolic functions are found normal with echocardiography, low BNP levels rejects LVDD possibility clinically.[2] In our study, LVDD was not detected in any one of the cases of which serum BNP levels were low. As LVDD is detected in all of the cases with CHF accompanied with systolic dysfunction and/or in cases with higher than normal, LVEDd the reason for the higher mean serum BNP levels detected in these cases may be emanating from systolic dysfunction only, diastolic dysfunction might be contributing to this high level as well. On the other hand, as a significant diastolic dysfunction was not detected either in the comparison of the cases in Group 1 with CHF findings and without any systolic dysfunction and with normal LVEDd with Group 2, it was found that the serum BNP level in these cases increased without echocardiographic systolic or diastolic dysfunction findings.

CONCLUSION

BNP is an important diagnostic marker of hemodynamically significant ventricular cardiomyopathies, especially the ones leading to volume and pressure elevation in left ventricle.

In these types of cardiac diseases serum BNP levels increase without a significant systolic or diastolic dysfunction. BNP can be used as a screening test. It allows early diagnosis of the CHF. It must be remembered that effective clinical management is available when medical therapy is administered early.

Since BNP levels are higher in cases with significant systolic and diastolic dysfunction when compared to the cases without, it is useful in the classification of CHF. It can even be used as a guiding parameter in referring the cases with an indication for early operation or, in contrast, it can contribute reducing the interventions, such as cardiac catheterization and early operations (on the condition that other indication-generating parameters are considered as well). All of these results prove the usability of BNP in diagnosis and follow-up in pediatric cardiology.

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