Kocaeli Med J 2018;7; 1:47-51

Beta Talesemi Major Tanılı Çocuk Hastalarda Kardiyak Fonksiyonların Değerlendirilmesi

Assessment of Cardiac Functions in Pediatric Patients with Beta Thalassemia Majör

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ÖZ

GİRİŞ ve AMAÇ: *Talasemiler, globulin zincir sentezinde defektler sonucu oluşan kalıtsal hastalıklardır. Bu hastalarda, şelasyon tedavisine rağmen demir birikimi sonucu oluşan kardiyak disfonksiyon önemli mortalite ve morbidite nedenidir. Kardiyak disfonksiyonun nedenleri kronik hemolitik anemi ilişkili ventrikül kaslıma disfonksiyonu ve kardiyak output artışı ile birlikte ventriküler dilatasyon ve demir birikimidir. Bu çalışmanın amacı oral şelasyon tedavisi alan beta talasemi majör tanılı hastalarda kardiyak fonksiyonların Doppler ekokardiyografi ile incelenmesidir.*

YÖNTEM ve GEREÇLER: *Bu çalışmada, Ocak-Eylül 2014 tarihleri arasında, beta talasemi major tanılı, 2-16 yaş arasında 49 hasta ve kontrol grubu olarak da aynı sayıda 49 sağlıklı hasta incelendi. Tüm hastalara ayrıntılı fizik muayane sonrasında elektrokardiyografik ve ekokardiyografik inceleme uygulandı.*

BULGULAR: *Hasta grubunun ortalama ferritin değeri 1275+904 ng/ml idi. Grupların ekokardiyografik bulguları karşılaştırıldığında, hasta grubunda miyokardiyal performans indeksi istatistiksel olarak yüksek bulundu (p=0.017). Ek olarak, hasta grubunda sol ventrikülde tip 1 diyastolik disfonksiyon saptanırken, sol ventrikül sistolik, sağ ventrikül sistolik ve diyastolik disfonksiyon görülmedi.*

TARTIŞMA ve SONUÇ: *Talasemi majör tanılı hastalarda başta kardiyovaskuler sistem olmak üzere birçok sistemde demir birikimi toksik etki göstermektedir. Demir şelasyon tedavisi ile hastalığın prognozu düzelse de yüksek moratalite ve morbidite halen önemli bir problem olarak kalmaktadır. Çalışmamız beta talasemi majorlu hastalarda erken dönemde subklinik sol ventrikül diyastolik disfonksiyonu geliştiğini, buna karşın sağ ventrikül fonksiyonlarının ve sol ventrikül sistolik fonksiyonlarının bozulmadığını göstermektedir.*

Anahtar Kelimeler: *Beta talasemi major, miyokardiyal performans indeks, diyastolik disfonksiyon*

ABSTRACT

INTRODUCTION: *Thalassemias are hereditary diseases caused by defects in the globulin chain synthesis with variable clinical severity. Cardiac dysfunction related to iron loading despite chelation treatment is a major cause of morbidity and mortality in these patients. The aim of this study is the evaluation of cardiac functions in beta thalassemia major diagnosed patients receiving oral chelation treatment*

METHODS: *This study was performed on 49 cases between 2-16 years followed due to the diagnosis of beta thalassemia major in outpatient clinic between the dates of January-September 2014. 49 cases with similar age, gender, height and weight with the study group were selected as the control group. All cases underwent regular outpatient examination (physical examination, electrocardiography and echocardiography). Systolic and diastolic functions of the study and control groups were evaluated with echocardiography.*

RESULTS: *Average ferritin value of the study group was found to be 1275+904 ng/ml. In comparison of echocardiographic findings of the study group and control group, myocardial performance index was found to be significantly high in the study group (0.32 versus 0.43, p=0.017). In addition, left ventricular type 1 diastolic dysfunction was detected in the study group. No statistically significant difference was detected between two groups in terms of the left ventricular systolic, right ventricular systolic and diastolic functions.*

DISCUSSION and CONCLUSION: *Our study indicates in patients diagnosed with beta thalassemia major that left ventricular diastolic dysfunction occurs at early age and the left ventricular systolic, right ventricular systolic and diastolic functions are not affected in early stage.*

Keywords:*Beta thalassemia major, myocardial performance index, diastolic dysfunction*

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Başvuru Tarihi: 26.12.2017
Kabul Tarihi:28.01.2018

INTRODUCTION

Beta thalassemia is an autosomal recessive disease characterized by hemolytic anemia resulting from decrease in one or more globulin chain production in hemoglobin tetramer. Transfusion is the basis of supportive treatment in these patients (1). Hemolysis, increase in intestinal absorption and iron loading in the organs as a result of intense transfusions organ are observed in thalassemia syndromes.

Transfusions and chelation programs have been successful in the treatment of these patients, but especially due to cardiac complications, morbidity and mortality rate is still high (2). The reasons of cardiac dysfunctions are ventricular contractility related to chronic hemolytic anemia and increase in cardiac output, ventricular dilatation and iron loading (3).

The purpose of this study is to evaluate cardiac functions in patients receiving blood transfusions and oral chelation treatments due to thalassemia major without heart failure.

MATERIAL AND METHODS

This study was performed on 49 patients between 2-16 years followed due to the diagnosis of beta thalassemia major by Van Yüzüncü Yıl University Faculty of Medicine Pediatric Hematology Outpatient Clinic between the dates of January-September 2014. 49 cases with similar age, gender, height and weight with study group were selected as the control group. All cases underwent regular outpatient examination (physical examination, electrocardiography and echocardiography). Serum ferritin level was studied in the study group.

Echocardiographic examinations were performed by using standard imaging techniques. Interventricular septum and posterior wall diastolic thicknesses were measured with the left ventricular end-systolic and end-diastolic diameter from parasternal long-axis images with M-mode method. Left ventricular ejection fraction and shortening fraction were automatically determined using M-mode. Pulse Doppler recordings were obtained by placing on the point matching up with mitral valve ends which are 1 cm above sample volume annular line in mitral valve. For the measurement of deceleration time, the time between the highest point and the point descending to baseline of E (early diastolic flow velocity) was measured. E/A ratio was calculated by finding the highest values of mitral valve E and A (late diastolic flow velocity). For the measurement of aortic ejection time, isovolumetric relaxation and contraction time, after placing sample volume in the manner of matching up with mitral valves, transducer was directed towards the left ventricle outflow tract. When aortic Doppler flow was observed, by measuring the endpoint of aortic flow and the starting point of mitral flow, isovolumetric relaxation time (IVRT) and by measuring the endpoint of mitral flow and the starting point of aortic flow, isovolumetric contraction time (IVCT) were found and myocardial performance index (MPI) was calculated. Sample volume was placed in tricuspid valve region for the right ventricle. Deceleration time was measured in the apical 4-chamber position as in E and A mitral valve. Then by placing sample volume to right ventricular outflow tract in parasternal short axis position, to just below the pulmonary valves, pulmonary ejection time, IVRT and IVCT were measured, MPI was calculated 4.5.This study was performed in accordance with Decleration of Helsinki 2008.

STATISTICAL ANALYSIS

Descriptive statistics in terms of features elaborated in the statistical analysis; were stated as average+standard deviation. In terms of these features, ANOVA test was performed in comparison of the groups. In order to determine the relationships among the features; Pearson correlation coefficient was calculated in groups separately. Statistical significance level was considered as 5% in the calculations and SPSS 16.0 statistical software package was used. Before starting to this study, consent of Yüzüncü Yıl University Faculty of Medicine Chairman of the ethics committee of non-invasive clinical research was obtained.

RESULTS

The average age of the study group was 9.32+3.40 (3-16 years), the average age of the control group was 8.90+3.23 (2-15 years). No statistically significant difference was detected between the study group and the control group in terms of age, height, weight average (p>0.05) (Table 1).

Table 1. Demographic characteristics of all cases

	Study Group	Control Group	P
Age (year)	9.32±3.40	8.90±3.23	p>0.05
Height (cm)	122,07±17.54	123,13±18.20	p>0.05
Weight (kg)	24.78±8.24	25.13±9.23	p>0.05

Average serum ferritin level of the study group was 1275+904 ng/mL (290-2160). In comparison of echocardiographic measurements of the study group with control group, mitral E, mitral E/A ratio was detected to be statistically significant low in the study group (respectively p=0.031 and p=0.021). Left atrial diameter, left ventricular end-diastolic diameter, mitral A, mitral deceleration time, mitral IVRT and mitral MPI in the study group was found to be statistically significant higher than the control group (p=0.041, p=0.044, p=0.032, p=0.024, p=0.031, p=0.017, respectively). In comparison of the left ventricular ejection and shortening fractions of the study group with control group, no statistically significant difference was detected (p>0.05) (Table 2).

In comparison of tricuspid flow velocity, E /A ratio, deceleration time, IVRT and MPI values of the study group with control group, no statistically significant difference was detected (p>0.05) (Table 3).

Type 1 diastolic dysfunction was detected in 9 out of 49 patients in the study group (E/A<1, deceleration time and elongation at IVRT).

Table 2. Left ventricle M mode and mitral valve Doppler echocardiographic measurements of the study and control group

	Study group	Control group	p
Aortic diameter (mm)	21.11±3.18	20.43±3.42	0,237
Left atrial diameter (mm)	26.70±3.28	24.26±4.11	**0.041***
LVEDD (mm)	38.82±4.72	36.39±4.84	**0.044***
LVESD (mm)	23.41±3.72	22.56±3.54	0.357
IVSD (mm)	7.57±1.22	7.07±1.25	0.110
PW (mm)	7.80±1.17	7.44±0.96	0.115
Ejection fraction	72.02±6.71	73.91±3.96	0.243
Shortening fraction	34.37±4.34	34.48±3.53	0.274
Mitral E (cm/sec)	80,02±18,37	87,20±15,16	**0.031***
Mitral A (cm/sec)	62,52±21,93	57,57±11,45	**0.032***
Mitral E/A ratio	1,26±0,48	1,51±0,30	**0.021***
Mitral deceleration time	176,11±24,77	152,61±22,57	**0.024***
Mitral IVRT	70,02±15,84	53,15±15,52	**0.031***
Mitral MPI	0,43±0,15	0,32±0,06	**0.017***

Statistically significant (p<0.05), data are presented as average ± standard deviation LVEDD: Left ventricular end-diastolic diameter, LVESD: Left ventricular end-systolic diameter, IVSD: interventricular septum diastolic diameter, PW: Left ventricular posterior wall diameter, E: Early diastolic flow velocity, A: late diastolic flow velocity, IVRT: Isovolumetric relaxation time, MPI: Myocardial performance index

Table 3. Tricuspid valve Doppler echocardiographic measurements of the study and control group

	Study group	Control group	p
Tricuspid E (cm/sec)	70,87±17,08	69,80±13,46	0.741
Tricuspid A (cm/sec)	63,57±13,70	60.52±14,58	0,854
Tricuspid E/A ratio	1,15±0,30	1.27±0.33	0.066
Tricuspid deceleration time	155.91±18.73	157.89±22.51	0.648
Tricuspid IVRT	52.89±15.96	51.54±14.88	0,676
Tricuspid MPİ	0.32±0.073	0.32±0.098	0.897

*: Statistically significant (p<0.05), data are presented as average ± standard deviation, E: Early diastolic flow velocity, A: late diastolic flow velocity, IVRT: Isovolumetric relaxation time, MPI: Myocardial performance index

DISCUSSION

In patients with beta thalassemia major, iron loading is known to be toxic on several systems, particularly in cardiovascular system. Even prognosis of the disease gets better with chelation treatment, high morbidity and mortality rates are still observed (1,2). Oztarhan et al. found the left ventricular end-diastolic diameter significantly high in thalassemia major diagnosed pediatric patients when compared to the control group in their study6. In the study we performed, as compatible with literature, left ventricular end-diastolic diameter and the left atrial diameter being an indicator of diastolic dysfunction were detected to be large in thalassemia major diagnosed patients when compared to the control group ($p<0.05$). Pennell et al. detected the values of the ejection fraction significantly low in thalassemia major diagnosed patients when compared to the control group in their study (7). In comparison of the left ventricular ejection and shortening fractions of the study group with control group, no statistically significant difference was detected in our study ($p>0.05$). The reason of the absence of significant difference in the left ventricular ejection and shortening fraction values in our study may be related to the early stage of beta thalassemia major diagnosed patients taken into the study.

Systolic and diastolic functions of the ventricles can be demonstrated globally with MPI. MPI is an easily applicable, reproducible, non-invasive and irresponsive to heart rate method8. Noori et al. found left ventricular MPI significantly high in the sick group when compared to the control group in the study they performed in beta thalassemia major diagnosed patients and reported that early systolic and diastolic dysfunction developed in beta thalassemia major diagnosed patients under the age of 10 (9). In our study, MPI was detected to be significantly high in the study group when compared to the control group (0.32+0.06 versus 0.43+0.15, $p=0.017$). When the right ventricle MPI values were compared, statistically significant difference between the study and control groups was not detected.

Restrictive cardiomyopathy and decrease in ventricular relaxation in the heart caused by iron loading was reported in the previous studies. It was demonstrated that myocardial damage affected diastolic functions earlier than systolic functions in beta thalassemia major diagnosed patients. In these patients, the major cardiac abnormalities are the left ventricular systolic and diastolic dysfunction, pulmonary hypertension, valvulopathies, arrhythmias and pericarditis (9,10). Gharzuddine et al. have found systolic functions normal in all cases in the study which they compared thalassemia major, thalassemia intermedia and normal individuals. They detected IVRT significantly high in thalassemia major diagnosed group when compared to the other two groups, E/A ratio significantly low (11). Decrease in mitral E, increase in A, decrease of E/A ratio below 1, elongation in IVRT and deceleration time and IRT were observed in Type 1 diastolic dysfunction (12). In our study, type 1 diastolic dysfunction was detected in 9 patients in the study group. These results were found to be consistent with the left ventricular MPI values. Increase in the left ventricular MPI values in the group of the beta thalassemia major diagnosed patients were considered to be a result of diastolic dysfunction since systolic functions were normal.

The limitations of the study; One limitation of the study is only the evaluation of cardiac functions by echocardiography, but no comparison with cardiac MRI (T2 star) findings. The studies with more cases and the examinations of cardiac MRI studies may give useful additional information about cardiac functions in these patients. Another limitation is that long term follow up of cardiac functions in these patients was unfortunately not available.

In conclusion with the era of the result of this study is that, although the normal detection of systolic functions in beta thalassemia major diagnosed patients, the left ventricular diastolic function may deteriorate at early age and the right ventricular diastolic function do not seems to be affected in early stage.

Disclosure statement: All authors declare that there are no conflicts of interest.

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