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Evaluation of Cardiac Status in Thalassemic Children

KEYWORDS

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ABSTRACT *Background: Cardiac disease caused by anemia and transfusional iron overload remains the principal cause of death in patients with β-thalassemia major. Regular evaluation of cardiac function is recommended for all patients with thalassemia major and is now an integral part of their management*

Objective: The aim of this study is to evaluate cardiac status in thalassemic children by stress test and echocardiography

Methods: This is a prospective study including 20 patients with thalassemia major receiving regular blood transfusion and 20 age matched healthy children taken as controls. Baseline heart rate, blood pressures were taken and double product was calculated. Echocardiographic parameters at rest were measured. Study group was then subjected to exercise by Masters two step test. Post exercise heart rate and BP were taken and the changes in echocardiographic parameters were measured.

Results: Heart rate and systolic blood pressure response to exercise were significantly lower in cases compared to controls. Left ventricular end-diastolic and systolic dimensions and volumes as well as stroke volume at rest were significantly higher in cases compared to controls. After exercise, there was significant decrease in end diastolic volume in thalassemics indicating early diastolic dysfunction. However, there was no significant difference in stroke volume indicating that there was no significant left ventricular systolic dysfunction.

Conclusion: Left ventricular dysfunction in thalassemic patients may be due to chronic anaemia and iron overload. Regular assessment of cardiac function may help to improve the quality of life of these patients and may reduce the morbidity and mortality.

INTRODUCTION:

Beta (*ß*) thalassemia major is the most common type of haemolytic anaemia seen in children and adolescents. Previously, most patients with the disorder died from severe anaemia during the first decade, but with modern transfusion therapy many now survive beyond childhood. Cardiac disease is the major cause of death in these patients and even in the best centres, a third of patients die by the age of 35 years [1]. The deposition of iron in a thalassemics reduces the heart muscle capacity by affecting all the adaptive mechanisms at hand for responding to the demands of the body. The heart failure results from the combination of the interaction of cardiac dysfunction, hemodynamic overload and secondary compensatory morphofunctional abnormalities.

Patients remain asymptomatic with normal left ventricular function for a long period of time. Early identification of ventricular dysfunction, before the appearance of symptoms, can alter the prognosis of these patients because it reinforces the need to optimize the therapy with chelators. Echocardiography is a non-invasive technique that evaluates cardiac anatomy and function with images and recordings produced by sound energy. It has an established role in the assessment of left ventricular structure and performance.

Exercise intolerance and fatigue are common complaints in these patients. Exercise capacity is reduced and most studies have attributed these findings to a combination of anaemia and iron-mediated cardio toxicity [2, 3, 4]. Cardiopulmonary exercise function testing has been proposed as a non invasive test to detect early cardiac dysfunction [3]

We studied 20 β-thalassemia major patients in order to determine the effects of chronic anaemia and transfusional iron overload on the left ventricular function by echocardiography by comparing them to a healthy control group

Methodology:

It is a prospective study conducted on children with Thalassemia major with no symptoms of cardiac failure who regularly attended a tertiary care hospital for blood transfusion. Children with congenital heart disease, bronchial asthma and physical handicap were excluded from the study. Age matched healthy children were taken as controls. Ethical committee approval was taken and informed consent was obtained from parents. The study population was subjected to detailed history, examination, haemoglobin and ferritin estimation. They were then subjected to exercise testing by Masters two step test[5,6] The subject was made to climb up and down two steps ,each 9 inches high over one and half minute period. The following parameters were measured and studied before and after exercise - heart rate, systolic blood pressure and double product obtained by multiplying heart rate and systolic blood pressure. Echocardiographic parameters analyzed before and after exercise test were: Left Ventricular end-diastolic dimension, Left ventricular end systolic dimension, Fractional shortening, Left ventricular end diastolic volume, left ventricular end systolic volume, stroke volume and ejection fraction. The transverse dimensions of left ventricle at end diastole and systole were obtained with ultrasound beam passing though left ventricle slightly below the tips of mitral valve leaflets. The end-diastolic and systol-

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ic dimensions were taken as the maximum and minimum transverse dimensions respectively. Left ventricular end-diastolic dimension is the left ventricular internal diameter i.e. distance between the left septal surface of interventricular septum and posterior endocardial surface of left ventricle in the transverse plane, taken at the end diastole. Left ventricular systolic dimension is the left ventricular internal diameter taken at the peak of end systole-measured at the peak posterior motion of ventricular septum. Fractional shortening is the percentage shortening of left ventricular dimension .Ejection fraction is the percentage of end diastolic volume ejected in a single beat. Stroke volume is the amount of blood ejected from the ventricle per beat. Data were expressed as mean ± standard deviation.

RESULTS:

Study group consisted of 20 cases of Thalassemia children and 20 healthy age matched children as controls. 95% (19) of cases complained of fatigue. All the cases had pallor, hepatosplenomegaly and facial changes. Jaundice was noted in 7 cases and hyper pigmentation in 3 cases. Seventy percent of cases (14) were not on any chelation therapy due to financial constraints. The number of transfusions received were <100 transfusions in 10, 100-200 transfusions in 7 and >200 transfusions in 3 cases. Serum ferritin values were <500 ng/ml in 5 cases, 500-2500ng/ml in 6, 2500-5000ng/ml in 6 cases and was >5000 in 3 children.

Resting HR,Blood pressure and double product were not significantly different between cases and controls. The post exercise values and the gain in values were significantly higher in controls as compared to cases (Table 1)

Table 1:Value of selected parameters during exercise:

Parameter	Controls (n=20) Mean ± SD	Cases (n=20) Mean ± SD	P value
Heart rate(beats/min)			
Resting	87.95 ± 8.04	88.4 ± 17.15	0.669
Post exercise	137.6 ± 14.87	125.5 ± 18.3	0.027
Gain at exercise	49.65 ± 17.12	37.1 ± 17.69	0.028
Systolic Blood pressure(mmHg)			
Resting	99.5 ± 10.69	101.1 ± 9.11	0.614
Post exercise	120.6 ± 13.93	109.8 ± 14.63	0.022
Gain at exercise	21.1 ± 7.18	8.70 ± 10.56	0.000
Double product ($x10^3$ beats. mmHg)			
Resting	8.77 ± 1.35	8.98 ± 1.90	0.454
Post exercise	16.6 ± 3.00	13.78 ± 2.80	0.004
Gain at exercise	7.83 ± 2.41	4.80 ± 2.29	0.000

Table 2: Echocardiographic parameters during exercise

Parameter	Controls (n=20) Mean ± SD	Cases (n=20) Mean ± SD	P value
Left ventricular End-diastolic dimension (cm)			
Resting	3.46 ± 0.225	3.94 ± 0.52	0.002
Post exercise	3.45 ± 0.33	3.93 ± 0.55	0.011
Gain at exercise	-0.005 ± 0.26	-0.01 ± 0.33	0.894
Left ventricular systolic dimension(cm)			
Resting	2.16 ± 0.19	2.50 ± 0.37	0.001
Post exercise	1.92 ± 0.27	2.32 ± 0.42	0.001
Gain at exercise	-0.005 ± 0.26	-0.01 ± 0.33	0.959
Left ventricular end diastolic volume(ml)			
Resting	51.45± 10.72	69.65± 20.60	0.001
Post exercise	51.35 ± 12.10	69.00 ± 22.57	0.011
Gain at exercise	-0.10± 10.83	-0.65 ± 14.70	0.011
Left ventricular end systolic volume(ml)			
Resting	16.10 ± 4.5	24.55 ± 10.52	0.004
Post exercise	11.4±3.31	21.85 ± 12.81	0.001
Gain at exercise	-4.7± 4.98	-2.7±6.94	0.302
Stroke volume(ml)			
Resting	36.00 ± 8.81	44.63 ± 13.20	0.033
Post exercise	38.95± 10.39	49.94± 14.63	0.009
Gain at exercise	-4.7± 4.98	-2.7± 6.94	0.302
Fractional shortening(%)			
Resting	37.85± 3.57	36.05±5.29	0.215
Post exercise	44.55±5.39	40.3±5.67	0.020
Gain at exercise	6.75±5.03	4.25±6.59	0.195
Ejection fraction(%)			
Resting	68.95±5.04	66.42±6.49	0.178
Post exercise	77.15±6.20	72.65±6.49	0.031
Gain at exercise	8.20±6.76	6.22±7.28	0.380

Left ventricular end-diastolic and systolic dimensions at rest were significantly higher in cases compared to controls. However the change in dimensions following exercise was not significantly different.

The left ventricular end diastolic, systolic and stroke volumes were significantly higher in cases as compared to the controls .The change in end diastolic volume post exercise was significant. End systolic and stroke volume changes were not significantly different in two groups.

Fractional shortening and ejection fraction at rest and the change with exercise was not statistically different between the two groups.

There was no significant correlation between serum ferritin values, number of transfusions received and the echocardiographic parameters in the study.

Discussion:

In the present study, the heart rate and systolic blood

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pressure response to exercise were significantly lower in cases compared to controls. This can be explained by the diminished cardiac reserve in anaemic children. These findings are similar to the observations by Valder Cruz et al [7].

Myocardial oxygen uptake reflecting myocardial oxygen consumption can be estimated during exercise by the product of heart rate and systolic blood pressure i.e. the double product. In our study response was similar to the heart rate response. These findings are in agreement with the observations made by Kapoor et al in two different studies on anaemic children [8, 9].

There was significant increase in end diastolic and systolic dimensions at rest in thalassemic children indicating that left ventricular enlargement occurred in these children.

Left ventricular end diastolic and end systolic volumes were significantly higher in cases compared to controls .However overall stroke volumes also higher indicating that increased cardiac output in anaemia is mainly due to increased stroke volume. After exercise, there was significant decrease in end diastolic volume in thalassemics indicating early diastolic dysfunction in these patients. However, there was no significant difference in stroke volume indicating that there was no significant left ventricular systolic dysfunction in the cases. Study by Hyder SN on 50 thalassemic patients showed that 38% patients had LV dysfunction, of which isolated systolic dysfunction was in 4%, isolated diastolic dysfunction was in 30% and global dysfunction was in 4% patients [10]. According to literature [11], iron can affect all cardiac structures including papillary muscles, conduction system, and pericardium. The epicardial region of the left ventricular free wall is the most affected. Histological evaluation of individuals with iron overload has demonstrated myocyte hypertrophy with iron deposition in cytoplasm and macrophages. Diastolic dysfunction generally appears before systolic dysfunction in the natural history of ventricular dysfunction and can be explained by the initial phase of the structural heart alterations [12]

The main limiting factor in our study was smaller number of study subjects. Study on larger number of patients may yield higher conclusive results.

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