Ambulatory Blood Pressure Monitoring for Children With β–Thalassemia Major

A Preliminary Report

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Introduction. Heart disease is one of the most common reasons of death in β-thalassemia major. A few studies have been done in children about blood pressure changes. The aim of this study was to assess hemodynamic changes by ambulatory blood pressure monitoring (ABPM).

Materials and Methods. In this cross-sectional study, 30 patients with β-thalassemia major aged 5 to 18 years old were evaluated with 24-hour ABPM. The exclusion criteria were an ejection Fraction less than 50% and a glomerular filtration rate less than 90 mL/min/1.73 m^2. Hypertension was defined as a mean blood pressure index of 1 and greater with or without load blood pressure greater than 25%. Dipper status was defined as a 10% decrease in nighttime versus daytime mean arterial blood pressure.

Results. High blood pressure was detected in 16.7% of the patients. The whole-day ABPM showed hypertension in 6.7% of the children. During daytime measurements, systolic hypertension was seen in 3.3% (load 3.7%) and diastolic in 6.7% (load 3.3%). These figures for nighttime evaluation were 6.7% (load 3.3%) and 10.3% (load 6.9%), respectively. Nondipper status was detected in 56.7% of the children. There was no significant correlation between abnormal blood pressure and age, sex, body mass index, hemoglobin, number or rates of blood transfusion, or serum ferritin level.

Conclusions. The ABPM may be a useful instrument for early detection of hemodynamic changes in children with β-thalassemia major.

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INTRODUCTION

Left ventricular dysfunction, decreased stroke volume, myocarditis, and endothelial cell dysfunction have been reported in patient suffering from β-thalassemia major.[1-3] A retrospective study showed high rates of pulmonary hypertension among patients with β-thalassemia intermedia.[4] In contrast, β-thalassemia trait has been suggested as a protective factor against myocardial infarction and shows better ambulatory blood pressure monitoring (ABPM) profile compared to anemic and nonanemic patients with essential hypertension.[5-6] Heart Rate variability is secondary to changes in autonomic function and its influence on cardiovascular function. Heart rate variability decreases in β-thalassemia major, which might reflect cardiac autonomic neuropathy.[7]

Despite higher rates of cardiovascular morbidity in β-thalassemia major, there is no study about blood pressure measurements in this high risk

group. The aim of this study was to evaluate blood pressure abnormalities in children with β-thalassemia major by using ABPM.

MATERIALS AND METHODS

This was a cross-sectional study included patients with β-thalassemia major admitted between March 2011 to May 2012. The inclusion criteria were β-thalassemia major diagnosed by hemoglobin (Hb) electrophoresis (Hb F > 98% and Hb A2 > 5% at the time of diagnosis), age between 5 and 18 years old, ejection fraction greater than 50%, and glomerular filtration rate higher than 90 ml/min/1.73m^2. Informed consent was taken from the patient or parent. The study protocol followed the guidelines of the declaration of Helsinki and Tokyo for humans and was approved by the Institutional Human Experimentation Committee of Tehran University of Medical Sciences.

Demographic data, information about the amount and interval of blood transfusions, and level of serum ferritin were recorded. Then, blood pressure was measured manually by auscultatory method 3 times in a resting position with half-an-hour intervals, and the average of these measurements was considered as blood pressure. The last version of the Task Force table for age and height was applied to detect of hypertension, which was blood pressure equal or more than the 95th percentile.

All of the patients underwent 24-hour ABPM. All ABPMs were performed using validated device of Tiba Medical Ambluo 2400 Inc (Portland, Oregon, USA) with oscillometric monitor and actigraphy.[8] An appropriate cuff was used over the nondominant arm. The patient was requested to avoid excessive exercise and keep the arm still during measurements. The device was scheduled to measure blood pressure every 30 minutes for daytimes and ever hours for nighttimes. At least 35 correct measurements were considered sufficient. The mean systolic blood pressure (SBP), mean diastolic blood pressure (DBP), mean arterial pressure (MAP), SBP load, DBP load during 24 hours, daytime (8 AM to 10 PM), and nighttime (10 PM to 8 AM) were measured separately. We used normalized blood pressure references produced by the German Working Group for defining the 95th percentile of blood pressure.[9] Hypertension was defined as a mean blood pressure equal to or more than 95% for age, sex, and height with or without blood pressure load greater than 25%. Prehypertension was defined as a mean blood pressure equal to or more than 90% and less than 95% for age, sex, and height, or normal mean blood pressure with blood pressure load over 25%. White-coat hypertension was defined as a high office blood pressure measrement and normal ABPM. Masked hypertension was defined by normal office blood pressure and hypertension by ABPM. Dipper hypertension was defined by equal to or more than 10% drop of MAP level from day to night.

The Student *t* test, nonparametric Spearman correlation coefficient, and the chi-square test were used for comparisons and evaluations of correlations, where appropriate. A *P* value less than .05 was considered significant.

RESULTS

Thirty patents (18 girls and 12 boys) suffering from β-thalassemia major were included in the study. Their mean age was 13 years (range, 4.5 to 18 years). Table 1 shows the demographic data and laboratory parameters of the patients.

Serum ferritin level was between 1000 ng/mL and 2500 ng/mL in 11 patients (36.7%) and greater than 2500 ng/mL in 10 (33.3%). None of the patients had hypercholesterolemia and only 3 (10.0%) had a serum triglyceride level greater than 200 mg/dL. Blood transfusion had been done in 8 patients (26.7%) with an Hb level less than 8 mg/dL, in 17 (56.7%) with an Hb level of 8 mg/dL to 10 mg/dL, and in 5 (16.7%) with an Hb level greater than 10 mg/dL.

Table 1. Clinical and Hematologic Profile of Patients With β-Thalassemia Major

Characteristics	Values
Sex, n	
Female	18
Male	12
Age, y	13.0 ± 4.5
Body mass index, kg/m^2	17.5 ± 2.7
Transfusion Interval, wk	3 ± 1
Transfusion, bag per visit	1 ± 0
Hemoglobin, g/dL	8.7 ± 1.3
Serum ferritin, ng/mL	1928 ± 1599
Ejection fraction, %	67.7 ± 9.0
Manual systolic blood pressure, mm Hg	105.5 ± 11.6
Manual diastolic blood pressure, mm Hg	64.4 ± 9.0
Manuel heart rate, /min	86.4 ± 8.8

Table 2. Blood Pressure in 24-hour Ambulatory Blood Pressure Monitoring*

Blood Pressure Variable	24-hour	Daytime	Nighttime
Mean values			
SBP, mm Hg	97.41 ± 10.50	100.22 ± 9.90	118.30 ± 13.40
DBP, mm Hg	63.50 ± 6.40	65.06 ± 7.00	59.00 ± 6.70
Pulse rate, /min	83.51 ± 11.90	86.09 ± 12.10	77.30 ± 12.10
MAP, mm Hg	75.24 ± 8.20	76.96 ± 8.90	69.38 ± 6.70
Median values (range)			
SBP load, %	3.7 (0 to 85.4)	3.6 (0 to 97.1)	0 (0 to 85.7)
DBP load, %	2.7 (0 to 90.2)	4.4 (0 to 91.2)	0 (0 to 100)

*SBP indicates systolic blood pressure; DBP, diastolic blood pressure; and MAP, mean arterial pressure.

Table 3. Frequency of Hypertension According to 24-hour Ambulatory Blood Pressure Monitoring Data

Blood Pressure Variable	24-hour	Daytime	Nighttime	Dipper Status
SBP index >= 1	1 (3.3)	1 (3.3)	1 (3.4)	…
DBP index >= 1	2 (6.7)	2 (6.7)	3 (10.3)	…
MAP index >= 1	2 (6.7)	…	…	…
Pulse rate index >= 1	1 (3.3)	…	…	…
SBP load >= 25%	2 (6.7)	5 (16.7)	1 (3.3)	…
DBP load >= 25%	1 (3.3)	3 (10)	2 (6.9)	…
MAP nondipper	…	…	…	17 (56.7)
SBP nondipper	…	…	…	22 (75.9)
DBP nondipper	…	…	…	19 (65.5)
PR nondipper	…	…	…	18 (62.1)

*SBP indicates systolic blood pressure; DBP, diastolic blood pressure; and MAP, mean arterial pressure.

With auscultatory measurement of blood pressure, high blood pressure was detected in 2 patients (high SBP in 2 and high DBP in 1). By using the ABPM, it was found that these patients had white-coat hypertension. Table 2 depicts the average hemodynamic blood pressure measurements during the ABPM, and Table 3 presents the frequency of hypertension according the whole-day, day-time, and night-time blood pressure measurements. Systolic pre-hypertension was seen only in 1 patient. There was no correlation between the 24-hour ABPM with age, sex, weight, height, body mass index, blood transfusion intervals, hemoglobin level, and serum ferritin level. Five patients (16.7%) had a cardiac output less than 60%. The mean SBP index and DBP index were lower in patients with an ejection fraction less than 60% ($P < .05$). Considering all abnormal blood pressure measurements, except for nondipper status during whole-day, day-time, and night-time monitoring, 16.7% of the patients were hypertensive.

DISCUSSION

Detecting masked hypertension in 16.7% of apparently normotesnisve cases accompanied with a high rate of nondipping states were the major findings of the present study. There is a limited number of studies on the assessment of blood pressure in β-thalassemia major patients. Veglio and colleagues conducted a case-control study on a limited number of β-thalassemia major patients for blood pressure and heart rate variability. They found lower median blood pressure compared to controls, lower night-to-day time blood pressure differences, and lower norepinephrine levels.[10] In contrast to our study, Veglio and colleagues[10] did not look at the frequency of hypertension in the subjects by using the criteria for defining abnormal high blood pressure. Previous studies demonstrated proximal tubular dysfunction correlated with the degree of anemia.[11-13] Recent investigation showed lower creatinine clearance in patients on intensive transfusion policy.[5,14,15] None of these studies focused on blood pressure changes.

The ABPM of hypertensive β-thalassemia minor compared to patients with essential hypertension (anemic or nonanemic) showed better blood pressure profile in β-thalassemia minor; this is considered a protective factor for cardiovascular disease.[5] Heart rate variability is due to changes of autonomic

system that influence cardiovascular function. This variability is clearly decreased in β-thalassemia major that shows early autonomic neuropathy of the heart.[7] Arterial stiffness of β-thalassemia major is probably due to structural changes or endocardial cell dysfunction.[2,3] Therefore, one reason of increment of blood pressure in thalassemic patients might be secondary to volume overload due to blood transfusion. However, in this study, none of the patients were monitored during blood transfusion. Deposition of iron in myocardial cell that is accurately detected by magnetic resonance imaging and level of ferritin affects cardiac function. The present study showed no correlation between abnormal blood pressure and level of serum ferritin, Hb, or transfusion interval. Left ventricle dysfunction is well known in thalassemic patients. Even in patients who do not have clear symptoms of cardiac dysfunction, when dobutamin is infused, the sign of ventricular dysfunction will happen.[1] In this study, the mean blood pressure index was significantly lower in an ejection fraction less than 60%, that probably demonstrated ejection fraction primarily increased and consequently blood pressure rose, then ejection fraction and stroke volume gradually decreases lead to decline of blood pressure that represented the progression of cardiac dysfunction in this group.[4] Spirito and colleagues showed that in progressive stage of illness, systolic dysfunction accompanied by left ventricular dilation and decrease in ejection fraction.[16] The observation of high rates of nondipper status and diastolic hypertension was an important parameter of secondary causes of high blood pressure and is associated with poor cardiovascular outcome, and somehow it represents autonomic cardiac neuropathy.[10]

The limitation of the study was the low power, small sample size, and absence of a control group. A longitudinal ABPM study while considering associated kidney function, exact measurement of iron load of the heart is suggested for further evaluation.

CONCLUSIONS

This study showed that the 24-hour blood pressure and heart rate monitoring may be very important and useful in assessing the early stage of hypertension in hemodinamically stable thalassemic patients.

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CONFLICT OF INTEREST

None declared.

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