

Major Beta-thalassemia: Protective or predisposing Factor for Cardiovascular Diseases

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Abstract

Introduction: Cardiac dysfunctions have been well known in patients with Major thalassemia. Some studies have focused on differences in blood pressure and heart rate between these patients and normal population, while this view has not been proven in other studies. Given the importance of hemodynamic factors in the health of these individuals, we intend to test the hypothesis as to whether or not hemodynamic factors of these patients differ from normal subjects.

Methods: Patients were selected from among the thalassemic patients referred to a blood clinic of one of the third-level hospitals in Tehran. Finally, 50 patients and 50 normal subjects were studied in two groups. All subjects have been assessed using Holter monitoring. Mean average systolic blood pressure and heart rate of subjects were recorded for a period of 24 hours.

In addition, demographic data on the subjects, and some laboratory tests (such as serum lipid profile and glucose levels of the patients) were also determined and compared between the two groups.

Results: 100 people were evaluated in two groups, including 50 patients with thalassemia major and 50 normal subjects, matched by age and gender. The mean age of the subjects was 16.3 ± 6.7 years; and there is no significant difference in mean age of both groups. 23 female patients (46%) were in the case group, and 21 female patients (42%) were in the healthy group, the ratio for which there is no statistically significant difference between the two groups ($P > 0.05$). The average level of serum glucose, lipid profiles, as well as none of the hemodynamic factors had no statistically significant difference in the two groups. Only the mean systolic blood pressure was significantly lower in male patients than among men without the disease.

Discussion: Despite the lack of difference in blood pressure between the case group and others, it seems that gender could play a protective role against cardiovascular diseases in men with thalassemia major.

Keywords: beta-thalassemia, Cardiovascular diseases, hemodynamic, blood pressure

Introduction

Left ventricular dysfunctions are well known in patients with thalassemia minor.(1, 2) In patients with obvious symptoms of cardiovascular dysfunctions, reducing the LV (left ventricle) distance as well as reducing the stroke volume are among the identified defects in this group.(1, 2) Even patients who have not shown clear symptoms of cardiovascular dysfunctions manifest signs of ventricular dysfunction after dobutamine injection. Coronary failure also shows itself simultaneous with deficiency of ventricles.(3) On the other hand, the left ventricular contractile dysfunctions and change in myocardial iron structure have also been reported in these patients, which along with

myocarditis are among the involvements of these patients, resulting in the cardiovascular complications in these patients.(4, 5) Some studies show that, probably, arteries in these patients become hard due to a structural change or impairment of endocarditic cells; and so arterial load will increase and impose more pressure to the left ventricle.(6-8) Some studies have also shown that high blood pressure and heart rate in these patients are lower than that in normal population; so thalassemia major is regarded as a protective factor against cardiovascular diseases.(9, 11)

Although research in this area is very young and the results have not been confirmed yet, various studies have a lot of difference in their opinions, and do not

confirm the results of each other. For example, some studies have reported no difference in hemodynamic parameters in both groups.(11) Some studies regard the underlying factors (like gender) as a factor influencing this difference;(11) and some also consider beta-thalassemia as an independent factor in the protection of these patients from cardiovascular complications.(11) In this regard, there is no consensus yet on current research. So in this study, we intend to examine the hemodynamic variables (such as blood pressure and heart rate) depending on the patients' background variables. In previous studies, only the moment blood pressure of the patients is highlighted, while the blood pressure in the study subjects using Holter monitoring and recording blood pressure and heart rate were measured in this study; and the hemodynamic changes have been investigated for the underlying factors (such as gender, age and history of the underlying disease) as separated.

Patients and Methods

Patients were selected from among thalassemic patients referring to a blood clinic of one of the third-level hospitals in Tehran. The condition for entering patients older than 12 years was the consent of the legal guardian of the patient as well as no history of proven heart disease until starting time of the study. Those without the disease that have no history of cardiovascular disease and whose age and sex match with those in these patients, were used as control group in proportion to the number of patients. Finally, 50 patients and 50 normal subjects were entered into this study. All subjects were assessed using Holter monitoring. Mean systolic blood pressure and heart rate of subjects were recorded for a period of 24 hours. Their mean systolic blood pressure as well as average heart rate were examined.

In addition, demographics on subjects and some laboratory tests (such as serum lipids and sugar levels) were determined; and hemodynamic changes were evaluated according to background variables.

Mean, median, range, standard deviation, frequency and frequency percentage were determined using statistical software SPSS V.19 and using descriptive analyses. For comparison of qualitative averages, independent T test was used after the normal distribution of data was tested to determine whether it is followed by 1-sample KS; and k.s-Ttest-Chisquare statistical test was used for the comparison of qualitative ratios. In all tests,

significance level was considered as two tails, and $P < 0.05$.

Results

100 people were evaluated in two groups, including 50 patients with thalassemia major and 50 normal subjects. Mean age of the subjects was 16.3 ± 6.7 years; and average age in each group is given and compared as separate in table- 1.

23 female patients (46%) were in the case group versus 21 female (42%) in healthy group, the ratio for which there is no significant difference between the two groups ($P > 0.05$).

Plasma levels of fasting glucose, High density lipoprotein (HDL), Low density lipoprotein (LDL) and Triglyceride (TG), were measured in both groups, which are given and compared as separate in Table 1.; there is no significant difference between any of the cases above ($P > 0.05$).

Mean average systolic blood pressure in the case group was 118.8 ± 8.7 mm Hg. The average was 124.6 ± 9.1 mm Hg in those without the disease. Comparison of the two means (Independent T-test) indicates no significant difference between them ($P = 0.31$). Average diastolic blood pressure in the case group was 78.8 ± 5.6 mm Hg. The average was 79.4 ± 5.1 mm Hg in those without the disease. Comparison of the two means (Independent T-test) indicates no significant difference between them ($P = 0.42$). Overall mean 24-hour blood pressure measured with Holter monitoring in the case group was 100 ± 6.6 mm Hg. It was 109.4 ± 7.1 mm Hg another group. Comparison of these two averages (Independent T-test) indicates no significant difference ($p = 0.42$). Average heart rate is given in Table 1 as separated; and two separate groups had no statistically significant difference ($P = 0.07$). After considering the factor of gender, mean average systolic blood pressure in male patients was significantly less than healthy men (122.6 ± 7.9 vs. 131.8 ± 8.8 , $P = 0.02$).

Table- 1. Statistical comparison of the measured variables

Variable	Thalassemic	Healthy	P value
Age	16.8±2.9	16.6±3.1	0.12
fasting glucose	109.4±12.5	107.3±11.1	0.78
TG	171±16.6	168±18	0.8
LDL	121.7±17.3	119.8±12.6	0.93
HDL	37.6±3.3	38.9±2.8	0.46
Systolic blood	124.6±9.1	118.8±8.7	0.31
Diastolic blood	79.4±5.1	78.8±5.6	0.67
Mean blood	109.4±7.1	100±6.6	0.42
Heartbeat	77.6±6.8	84.8±8.9	0.07

High density lipoprotein= HDL, Low density lipoprotein= LDL, Triglyceride= TG

Discussion

There has been much discussion for several years on whether thalassemia major creates a background to affect the cardiovascular diseases; and it is almost seen as an established subject, showing that thalassemia is associated with heart diseases and poor functioning of ventricles, regardless of the details.

In some previous research, it has been suggested that patients with thalassemia are faced with increased blood pressure and heart rate; however, it has shown in some studies that there is no difference between people with and without the disease in this regard.

Some studies are based on the fact that in addition to cardiac complications (such as iron deposition in myocytes), this disease probably has a protective role against heart diseases by lowering blood pressure.(9, 11)

Since the studies in this regard were limited in number, we tried to test this hypothesis in this study with a slightly different approach by using Holter monitoring method.

Our results showed that there is no significant difference in blood pressure (systolic, diastolic, and mean 24-hour) between patients and normal subjects, the opinion which has been confirmed in some previous studies (11) and the opposite result is obtained in some studies.(9, 10)

Vyssoulis et al. in Greece began to study about 8,861 non-diabetic patients with hypertension: the patients were divided into three groups, whose mean average systolic blood pressure of midnight and midday were compared.

The results suggest that the mean systolic blood pressure in patients with thalassemia major was lower compared to other two groups, the difference which was statistically significant.

They also compared the effects of the altering factors (such as age, body mass index (BMI), dyslipidemia) with the difference in systolic blood pressure of midnight and midday. The results indicate statistically significant differences between the groups above, and showed that systolic blood pressure in the case group is still lower than those without the disease despite taking the above cases; and this difference is statistically significant. The researchers confirmed the theory according to which beta thalassemia major may protect the patients from cardiovascular diseases such as heart attacks.(9)

Veglio et al. studied 18 patients with thalassemia major, and compared them with 9 normal subjects as control group. They found that the average heart

rate of patients with thalassemia major during the night were significantly higher than that in the control group. They also showed that the mean average systolic blood pressure and diastolic blood pressure in patients with thalassemia major were significantly lower than that of the opposite group. This blood pressure is related to how the patients are positioned.

Norepinephrine levels in blood of patients with thalassemia major were also significantly lower than control group. The researchers above believe that the main reason for this hemodynamic difference is related to different activity of the sympathetic nervous system in these patients.(10) The results of our study are more consistent with those in the study of Karimi et al.

They examined the effects of beta thalassemia on blood pressure in young patients. 408 patients referred for screening for beta-thalassemia were entered in this study. The blood pressure of patients was measured twice at an interval of 20 minutes. 208 patients with beta thalassemia were compared with 200 normal subjects.

They showed that the mean average systolic blood pressure is almost identical in both groups; and they have no significant difference. The simultaneous analysis of blood pressure and gender showed that men with beta-thalassemia have a lower mean average systolic blood pressure (as much as 10 mm Hg) than control group. Finally, the researchers concluded in their study that beta thalassemia in young men has protective effects against the development of high blood pressure.(11)

Our study is also among the first studies examining the protective effects of beta-thalassemia against heart disease in the presence of gender. As this study was done on Iranian population, further attempts in this field seem to be necessary in order to confirm these results in other races.

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