Original Article

P-wave Dispersion in Patients with Major Thalassemia

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Abstract

Background

Prolonged P-wave duration and P-wave dispersion indicate interatrial conduction disturbance and early predict arrhythmia especially atrial fibrillation. Iron deposition in the atrial tissue might prolonged the atrial conduction time, and this study evaluated the P-wave prolongation and increased P-Wave dispersion in these patients.

Materials and Methods

Fifty patients with major thalassemia and fifty healthy controls were studied, which age and sex matched between cases and controls. All patients and the controls were examined and had an ECG. The P-wave dispersion defined as the difference between the maximum and minimum P-wave duration. P-wave dispersion was compared between two groups. student's T-test and pearson's correlation were used as needed.

Results

There was a significant difference between the P-wave dispersion of the 2 groups (P=0.019). Maximum P-wave duration and P-wave dispersion in patients had strong correlation with age (disease duration). P-wave duration and P-wave dispersion had no correlation with regularity or irregularity of desferal use.

Conclusion

Maximum P-wave duration and P-wave dispersion were seen in older cases, which significantly get prolonged. This could show that the myocardial involvement and dysfunction was probably more in the older patients.

Key words

Arrhythmias, Cardiac, beta-Thalassemia; Atrial Fibrillation

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Introduction

Thalassemia major is an inherited hemoglobin disorder resulting in chronic hemolytic anemia and requires frequent blood transfusions (1). Disease prognosis has been modified with regular blood transfusions and iron chelation therapy with deferoxamine. Transfusion therapy, together with elevated gastrointestinal absorption of iron, determines iron overload which causes most of the mortality and morbidity associated with the disease (2).

Cardiac failure and sudden death, the latter probably is due to arrhythmias, remain the major causes of death in β-thalassemia major (TM). Iron toxicity in biological systems is believed to be associated with its ability to catalyze the generation of free radicals (3). The incidence of iron-overload cardiomyo-pathy ranges between 11.4 and 15.1% in β-TM patients (2).

Iron-overload cardiomyopathy is associated with a four- to six-fold increase in the risk of developing atrial fibrillation (AF). At this stage; patients are usually asymptomatic (4). Several noninvasive electrocardiographic (ECG) parameters have been suggested to predict AF. Depression of intra-atrial conduction causes a lengthening of P-wave (5).

P-wave parameters including maximal P-wave duration (P max) and P-wave dispersion (Pd) (6). P-wave dispersion (PD) is difference from the minimum (P min) and maximum (P max) P-wave duration on standard 12-lead electrocardiogram (ECG) and is considered as an index of the discontinuous and an inhomogeneous and anisotropic distribution of connections between myocardial fibers in atrial tissues (7). A reliable test is necessary for the presymptomatic identification of cardiomyo-pathy thus this study was set up to evaluate P-wave measurements (especially P min, P max and PD) in patients with β-TM.

Materials and Methods

The present cross-sectional and case-control study was conducted at the Cardiac Department, Alzahra Hospital, in Shiraz, Iran. Fifty consecutive patients with thalassemia major who were in normal sinus rhythm and a group of fifty healthy age and sex matched subjects were taken under investigation. There were 23 females and 27 males with an age range of 2- 31 years in each group without clinically apparent cardiovascular disease by physical examination, electrocardiography and echocardiography. Included patients gave their verbal and written consent for participation in the study. The patients had been regularly transfused (every 3-4 weeks), and everyone received chronic chelation therapy. Patients with diabetes mellitus, hypertension (systolic and diastolic blood pressure (140/90 mmHg), hepatic, renal, thyroid diseases, valvular heart disease, ventricular preexcitation , and atrioventri-cular conduction abnormalities were excluded from the study.

All subjects underwent a routine standard 12-lead body surface ECG recorded at a paper speed of 50 mm/s and gain of 10 mm/mv in the supine position. At the time of electrocardiographic recording, all subjects were in sinus rhythm and none were taking any type of antiarrhythmic agent. All ECG's were scanned through cannon scanner and subsequently analyzed electronically after 400% magnification by adobe Photoshop software. The analysis was performed by one investigator who was blinded to the participants' clinical status. Three consecutive ECG complexes were analyzed and given averaged measures for each lead. The offset of the P-wave was defined as the junction between the end of the P-wave deflection and the isoelectric line (8, 9). The P max was defined as the longest atrial conduction time measured from the 12

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leads and P min, as the shortest atrial conduction time. The difference between P max and P min was calculated and defined as Pd (Pd=P max-P min).

Statistical Analysis

Analysis was performed using Student's t test. P values ≤0.05 were considered to be statistically significant. Correlations were performed using Pearson's correlation analysis.

Results

The study group was composed of 50 β-TM patients (27 boys and 23 girls) aged between 2 and 31 years, and the control group was composed of 50 healthy age and sex matched subjects.

Table 1 summarizes the electrocardiographic characteristics of the study population. Table-1showed that there was a significant difference between the P-wave dispersion of two groups (P=0.019). Maximum P-wave duration and P-wave dispersion in patients had strong correlation with age or disease duration (Figure-1). Maximum P-wave duration and P-wave dispersion in patients with age of 16-31 years old was higher than 2-16 years old. (P=0.004 and P=0.04 respectively). P-wave duration and P-wave dispersion had no correlation with regularity or irregularity of desferal use.

Table 1. Maximum and minimum P-wave Duration and P-wave Dispersion in patients and controls

	Patients(N=50)	Controls(N=50)	
	Mean±SD	Mean±SD	P-value
Max P-wave Duration*	110±19.88	107.96±15.64	0.57
Min P-wave Duration*	62.8±11.04	52.4±10.3	0.001
P-wave Dispersion*	47.2±18.35	55.56±16.55	0.019

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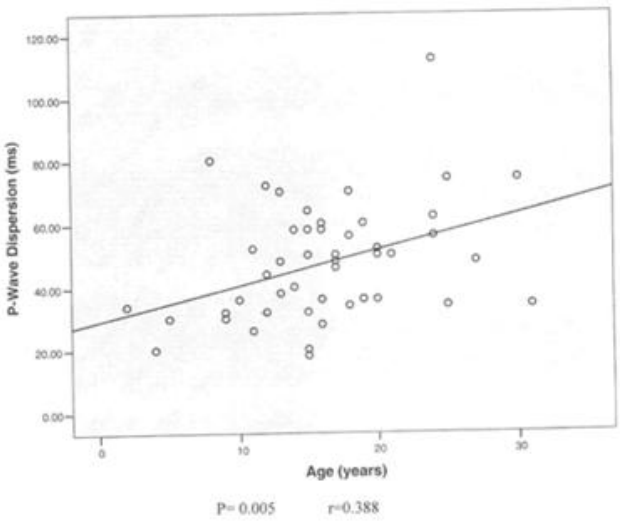

Figure 1.Correation between age (disease duration) and P-wave dispersion in thalassemia major patients

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Discussion

Beta-thalassemia major (β-TM) is a hereditary hemoglobinopathy caused by reduced synthesis of β-globin chain and requires frequent blood transfusions. Myocardial iron heart failure secondary to overload is the most common cause of death in this disease. In homogeneous propagation of sinus impulses and the prolongation of atrial conduction time and site-dependent inhomogeneous atrial conduction may result in a highly variable P-wave duration. P-wave dispersion is a reliable test for the presymptomatic identification of cardiomyo-pathy and has predictive value especially for paroxysmal trial fibrillation. Pd values of >40 ms of duration were found to be correlated with AF, with a sensitivity of 74–83%and specificity of 81–85% (10,11).But recent study by Nussinovitch suggested that Pd, Pmax, and Pmin span a wide range of values in healthy individuals. Gender and age have no significant effects on P-wave parameters (12) .Pd has been studied in some other cardiac conditions such as atrial enlargement, obesity, hypertension, atrial septal defect, pulmonary stenosis, and dilated cardiomyopathy(13,14). One study reported that increased sympathetic activity leads to a significant elevation in Pd (15). In our study we compared P min, P max and Pd in β-TM patients and control group. It was found that P min was significantly prolonged in the β-TM group but Pd was not prolonged. These findings did not suggest the hypothesis that iron overload toxicity might be related to depression of intra-atrial conduction and increase Pd in our β-TM patients.

This is similar to study of Acar et al. On 22 β-TM patients and 22 age- and gender-matched healthy controls, P max, P min were significantly prolonged in the β-TM group compared to the healthy controls (p=0.005, p=0.01, respectively). Pd was found similar between groups (p=0.46). They speculated that it is difficult to claim, based on P-wave parameters, that β-TM patients have an increased risk of AF development (16).

In contrast Nisli et al, on 81 children with β-TM; and 74 healthy children (control group) without clinically apparent cardiovascular disease, found that Maximum P-wave duration and Pd were significantly higher in β-TM patients than in control subjects (17). In another study conducted by Russo et al. on 40 b-TM patients (age37.5 ± 10.2; 33 M) and 40 healthy subjects used as controls, matched for age and gender, β-TM group presented increased values of the Pd (40.1 ± 12.9 vs. 24 ± 7 ms; P=0.004).They showed a significant increase in P max and Pd in β-TM patients with conserved systolic and diastolic cardiac functions, compared to sex- and age-matched normal controls (18).

Although there was no significant between increased age and Pd values,(12) in this study the maximum and minimum P-wave duration and Pd in patient group had strong correlation with age (disease duration). Thus a prolonged duration of the disease may affect P-wave measurements and risk of AF development. This is similar to study performed by Acar et al (15).

The small number of cases included is certainly a limitation, and large randomized studies are needed to determine the role of individual P-wave parameters in predicting AF development. PD measurement errors done with manual evaluation may be a potential bias for observed results although, according to Dilaveris et al (11), scanning and digitizing ECG signals from paper records using anoptical scanner is a feasible and accurate method for measuring P-wave duration. P-wave measurements of β-TM patients with sinus rhythm were performed using the 12-lead ECG; however, rhythm Holter monitoring and an event recorder were not performed in study participants to eliminate paroxysmal AF .

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In conclusion, our study showed that the risk of AF development should not be based on the P-wave measurements in patients with β-TM. Other hand with advancing age or disease duration, maximum P-wave duration and P-wave dispersion significantly get prolonged. This may indirectly show that the myocardial involvement and dysfunction was probably more than in the older patients.

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Conflict of Interest

None declared.

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