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TIME DOMAIN INDICES OF HEART RATE VARIABILITY IN BETA THALASSEMIA MAJOR PATIENTS

Physiology

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ABSTRACT

Background :Thalassemia is one of the common genetic disorders requiring lifelong blood transfusions for survival which results inaccumulationof iron in the body which is toxic to many tissues, including heart. The present study was undertaken to determine the Heart Rate Variability (HRV) in beta thalassemia major patients and to compare the mean values of time domain indices of HRV in study and control group. **Materials & methods :**The present cross sectional study consisted of 50 normal subjects (control group) and 50 patients of beta thalassemia major (study group). HRV was recorded in both the groups with Medicaid Physiopac and HRV analysis was done using Kubois software version 2.1 **Result :** Time domain parameters were decreased in study groupas compared to control group and the difference was statistically significant (Z test). **Conclusion :**The reduced levels of HRV could possibly be as a result of chronic anaemia and cardiac autonomic dysfunction secondary to iron overload cardiomyopathy due to repeated blood transfusion.

KEYWORDS

Beta thalassemia major, Heart rate variability, Time domain indices

INTRODUCTION

Beta -Thalassemia major (BTM) is caused by the reduced synthesis of β - globin chains, which leaves an erythrocyte excess of unopposed α - chains; the resulting ineffective erythropoiesis leads to chronic haemolytic anaemia.1BTM patients may need to have repeated blood transfusions throughout their life for survival, which leads to so many complications such as transfusion related infections, sensitization, iron-overload related cardiac, endocrine and liver disturbances and toxicities of iron chelators.2Heart disease is the most important complication and the main determinant of survival.[3]

Heart rate variability (HRV) is a non-invasive tool for the assessment of cardiac autonomic control.4Power spectrum analysis of HRV can quantify the sympathovagal balance modulating the sinus node pacemaker.5Time domain indices of HRV analysis are derived from either direct RR interval measurements or the differences between successive RR intervals.6Parameters of time-domain analysis include:RR – time interval between two successive heart beats, RMSSD - the square root of the mean squared differences of the successive NN intervals, NN50 - Number of intervals greater than 50 ms, pNN50 - Proportion of differences in consecutive NN interval, TINN - Triangular interpolation of RR intervals,all reflecting parasympathetic activity.

Franzoni et al first proposed that HRV was depressed in BTM patients.7Also Dolunay et al have shown that time domain parameters were significantly lower in BTM patients than in the control group.8 Whereas no correlation between HRV parameters and cardiac function in BTM patients has been shown by De Chiara B et al.9

Although analysis of HRV is currently used to investigate the mechanism responsible for cardiovascular control in normal and pathophysiologic conditions,10 there have been few studies about HRV in BTM patients.11Thus the present study was designed to detect relationship between time domain indices ofHRV and BTM patients receiving regular blood transfusion.

MATERIALS AND METHODS

The present study was a cross sectional type of study conducted in the Department of Physiology and Paediatric Medicine, Grant Medical College and in the Thalassemia unit of St. George Hospital, Mumbai.

The study design involved 100 individuals who were divided into two groups of 50 normal subjects (control group) and 50 patients of beta thalassemia major (study group) receiving regular blood transfusions between the age group of 8 to 20 years involving both, males and females. Patients with concomitant sickle cell anaemia or with associated heart disease were excluded from the study.

The subjects were asked to report in the lab after an adequate night's sleep. ECG recording was done for 5 minutes in supine position after 10 minutes of rest using "Medicaid Physiopac" and it was analysed by Kubois software, Version 2.1. Statistical analysis was done using Z test.

RESULTS

Table 1 shows general growth parameters between study group and control.

Table 1 : General growth parameters

	Study group (MEAN±S.D)	Control group (MEAN±S.D)
Mean age (yrs)	13.42±4.43	14.84±3.92
Mean height (cm)	133.45±16.27	148.61±18.05
Mean weight (kg)	31.05±10.9	41.1±13.89
Mean BMI (kg/m2)	17.01±3.21	18.05±3.74

As shown in table 2 there was decrease in time domain indices of HRV in study group compared to control group and the difference was statistically significant.

Table 2 : Comparison of Time Domain Indices of HRV of subjects and statistical analysis with Z test

	Study group MEAN±S.D	Control group MEAN±S.D	P VALUE	Z TEST
MEAN RR(ms)	604.5±77.18	732.18±102.44	<0.0001	Statistically significant
RMSSD (ms)	10.28±3.73	32.54±21.35	<0.0001	Statistically significant
NN50 (count)	1.42±2.32	15.36735±14.02	<0.0001	Statistically significant
pNN50(%)	0.6±0.98	8.51±6.67	<0.0001	Statistically significant
TINN	84.84±24.74	184.18±118.66	<0.0001	Statistically significant

As shown in table 3, there was decrease in haemoglobin levels in study group compared to control group and the difference is statistically found to be Statistically Significant.

Table no. 3 : Comparison of haemoglobin levels of subjectsand statistical analysis with Z test

	Study Group MEAN±S.D	Control Group MEAN±S.D	P VALUE	Z TEST
Haemoglobin (gm/dl)	7.51±1.01	13.64±1.69	<0.0001	Statistically significant

DISCUSSION

The present study shows that time domain parameters were

significantly reduced in thalassemics. Our findings are in accordance with the findings of Jyotsna Et al who had shown time domain parameters viz SDNN, RMSSD, PNN50 were significantly reduced in thalassemics.12 Our study is also in correlation with study done by Silvilairat Set al who showed that all time domain parameters were significantly lower in patients with cardiac T2* $\leq$ 20 ms and in those with cardiac T2* > 20 ms than in the control group.[13]

Reduced HRV predicts increased risk for subsequent cardiac events.9The reduced levels of HRV could possibly be as a result of chronic anemia. In present study hemoglobin levels of study group were significantly lower than control group.Association of changes in HRV indices with various types of anemia like iron deficiency anemia,14 vitamin B12 deficiency,15 etc. has been studied previously. The study results of Gehi A et al have proved that in anemic patients with stable coronary heart disease, each 1 g/dL decrease in hemoglobin was associated with increased odds of having low HRV, which puts the anemics at greater cardiac risk.[16]

Similar findings were shown by Yokusoglu et al, who detected impairment of global indices of HRV that might be caused by increased sympathetic and decreased parasympathetic activity in patients of iron deficiency anemia.14 They proposed that low oxygen tension in tissues might be the cause of altered autonomic function in iron deficiency anemia. So it can be concluded that anemia is associated with low HRV and puts the anemic patients at higher risk of sudden death especially if concomitant heart disease exists.[16]

In contrast the study done by Gehlot et al found that there is no statistically significant relation between haemoglobin concentration and HRV in mild to moderate anaemia,17 and going further Agrawal K et al, revealed no significant correlations between HRV and blood parameters indicating, mild and moderate anemia may not have effect on cardiac autonomic modulation.[18]

Apart from chronic anemia this may also be due to transfusional iron overload. Iron overload cardiomyopathy results from the accumulation of iron in the myocardium, and it is the leading cause of death in patients receiving chronic blood transfusion therapy.19 Jyotsna Shukla et al have shown that patients who received inadequate or no iron chelation therapy, had more reduced HRV parameters.20 According to Adriana et al the most frequent cause of death in thalassemia major patients was cardiopathy (69%), followed by infections (14%), malignancy (5%), renal failure (5%), thrombosis (5%) and chronic liver disease (2%).21Despite the advances in therapeutic management of thalassemia major and the resulting substantial improvement of patient's survival, heart disease always represented and still remains the primary cause of mortality and a major cause of morbidity.[22]

Thus Low HRV may actually represent an early feature of cardiac disease in thalassemic patients with no evidence of ventricular dysfunction at routine evaluation.[10]

CONCLUSION

The present study shows that there is reduced HRV in BTM patients as compared to control group. This may be because of chronic anemia and cardiac autonomic dysfunction secondary to iron overload cardiomyopathy due to repeated blood transfusion which remains the main stay of treatment in these patients.Thus analysis of HRV may be useful for early detection of cardiac complications in beta Thalassemia especially in the preclinical stage of cardiac involvement.

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