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PARASYMPATHETIC FUNCTION TESTS IN BETA THALASSEMIA MAJOR PATIENTS

Physiology

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ABSTRACT

Background : The incidence of β - thalassemia in different regions of India varies from 3% to 17%, with a mean prevalence of 4%. Heart disease is the most important complication of longstanding blood transfusion. This study was designed to evaluate early cardiovascular dysfunction in Beta thalassemia major patients by assessing parasympathetic activity between study group and control group.

Materials & methods : Present study was a cross sectional type of study and consisted of 50 normal subjects (control group) and 50 patients of beta thalassemia major (study group). Two parasympathetic function tests i.e. Deep breathing test (DBT) and Lying to standing (30:15) ratio were included in the study. After the recording of data, statistical analysis of observations was done using Z test.

Result : There was decreased 30:15 ratio as well as a decrease in deep breathing difference in the study group as compared to control group and the difference was statistically significant.

Conclusion : Decreased 30:15 ratio and deep breathing difference in study group shows impaired vagal activity suggesting parasympathetic dysfunction in beta thalassemia major patients.

KEYWORDS

Beta Thalassemia Major, Deep Breathing Test, Lying To Standing Ratio

INTRODUCTION

10% of the total world thalassemics are born in India every year. [1] Thalassemia major is severe, develops during the first year of life, and requires life-long transfusion therapy for survival.[2] A few studies have documented initial cardiovascular dysfunction in thalassemia major patients even without clinical manifestation of heart failure. [3,4]

Cardiovascular Autonomic reactivity refers to cardiovascular responses to potential stimuli, which are essentially reflexive in nature indicating cardiovascular tolerance and adaptation. [5,6] In their study Elefterios et al showed subclinical autonomic dysfunction in beta-thalassemia major patients.[7]

In most autonomic disorders, parasympathetic function is affected before sympathetic function, so Deep breathing test (DBT) provides a sensitive screening measure for parasympathetic dysfunction in many autonomic disorders. [8] On changing the posture from supine to standing, the heart rate increases immediately, usually by 10 to 20 beats per minute. On standing HR increases until it reaches maximum at about the 15th beat, after which it slows down to a stable state at about 30th beat. The ratio of R-R intervals corresponding to the 30:15 heart beat is called as 30:15 ratio which is a measure of parasympathetic function.

MATERIALS AND METHODS

The present study was a cross sectional type of study conducted in the Department of Physiology and Department of Paediatric Medicine, Grant Government Medical College, Mumbai and in the Thalassemia unit of St. George Hospital, Mumbai. Before commencement of the project, approval was taken from the Institutional Ethical Committee.

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. with concomitant sickle cell anaemia or with associated congenital or acquired heart disease or any other endocrionological disorders were excluded from the study. Written informed consent was taken before the clinical examination of the subject. The subject was allowed to relax on a bed in supine position for 10 minutes and then parasympathetic function tests were performed after initial 1-2 sessions of practice.

Parasympathetic function test

1. Deep breathing test (DBT)

First baseline ECG was recorded for 1 minute in supine position. During DBT subject was asked to do maximal inspiration for 5 seconds and maximal expiration for 5 seconds for 6 cycles per minute. Difference between maximum heart rate during inspiration & minimum heart rate during expiration averaged over 6 cycles & Deep Breathing Difference (DBD) was calculated.

2. Lying to standing ratio (30:15)

The test was conducted after 10 minutes of supine rest. Baseline ECG was recorded for 1 minute and then subject was asked to attain the standing posture within 3 seconds without any support. 30:15 ratio, which is the ratio of longest R-R interval around 30th beat divided by shortest R-R interval around 15th beat after standing was calculated.

RESULTS

The mean Body mass index (BMI) was 17.01±3.21 and 18.05±3.74 kg/m² in the study and control group respectively.

Table no. 1 : Comparison of Deep Breathing Difference of subjects & Statistical analysis using 'Z' test

	Study group MEAN±S.D	Control group MEAN±S.D	P VALUE	Z TEST
DBD(bpm)	16.04±5.68	27.92±5.97	<0.0001	Statistically significant

(DBD – Deep Breathing Difference)

Table no. 2 : Comparison of 30:15 ratio of subjects & Statistical analysis using 'Z' test

	Study group MEAN±S.D	Control group MEAN±S.D	P Value	Z Test
30:15 Ratio	1.107±0.072	1.3±0.19	<0.0001	Statistically significant

DISCUSSION

The mean difference in the heart rate during DBT in study and control groups was 16.04±5.68 and 27.92±5.97 respectively. (Table no. 1) The findings were statistically significant showing reduced reactivity of study group to DBT. Decrease in deep breathing difference in this study is probably mainly due to decreased vagal tone indicating abnormal parasympathetic function in beta thalassemia major patients.

Studies have suggested that the orthostatic response consists of three phases. [9,10,11] These consist of the initial response (during the first 30 seconds), the early "steady state" alteration (at 1-2 minutes) and lastly the prolonged orthostatic period (at least five minutes upright). The early steady state adjustments to upright posture consist of an increase in heart rate of roughly 10 to 15 beats per minute, an increase in diastolic pressure of around 10 mmHg and little or no change in the systolic blood pressure. At this point, as compared to the supine position, the blood volume of the thoracic area is reduced by approximately 30%, the total cardiac output is

decreased by 30%, and the average heart rate is increased by 10 to 15 beats per minute.

In the present study mean 30:15 ratio of study and control groups was 1.1±0.07 and 1.3±0.19 respectively and the difference was statistically significant. (Table no. 2) 30:15 ratio is used commonly to assess the damage of afferent or efferent limb of cardiovascular reflexes. Although both sympathetic and parasympathetic fibres participate in the changes of R-R interval after this procedure, this test is mainly used to assess the integrity of the parasympathetic fibres participating in the autonomic control of the heart. [12,13] In this study decreased 30:15 ratio may be due decreased parasympathetic activity.

The present study is in accrodance with Elefterios Stamboulis et al who electrophysiologically evaluated the autonomic function in a consecutive series of patients with beta-thalassemia major and in normal individuals. [7] The prevalence of impaired autonomic function was higher in beta-thalassemia patients (13%, n = 5) than in control subjects (0%, n = 0; p = 0.026). They concluded that subclinical autonomic dysfunction appeared to be more prevalent in beta-thalassemia patients compared to controls.

The findings of this study can be correlated with other studies to extrapolate possible mechanisms for our findings. Brinda Venkatraman et al proposed that blunting of baroreceptors and chemoreceptors due to chronic hypoxia may be the root cause of dysfunction of parasympathetic reflex arc in chronic iron deficiency anemia even though they could not point out the exact site of the lesion in the parasympathetic reflex arc or the sympathetic reflex arc. [14]

This may also be due to chronic anemia which may lead to a persistent sustained decrease in autonomic fluctuations as shown by Franzoni el al. [15] Repeated hypoxemic episodes, as in sickle cell anemia patients may increase sympathetic activity and decrease parasympathetic activity. [16]

Studies in rats shows that chronic intermittent hypoxia results in a significant cell loss in the nucleus ambiguous, [17] which give rise to several vagal efferent axons that innervate ganglionated plexuses in the dorsal surface of cardiac atria, which in turn may have different functional roles in cardiac regulation. [18] In addition, chronic intermittent hypoxia alters the structure of cardiac ganglia and results in reorganized vagal efferent projections to cardiac ganglia. [19] Also chronic and repeated hypoxic episodes in sickle cell anemia may lead to alterations in parasympathetic responses by autonomic hypersensitivity. [20] Thus long standing hypoxia due to chronic anemia may be the cause of parasympathetic dysfunction in patients of beta thalassemia major patients.

CONCLUSION

Decreased 30:15 ratio and deep breathing difference in the study group shows impaired vagal activity in beta thalassemia major patients. This could be due to chronic hypoxia secondary to chronic anemia. Thus there was early cardiovascular dysfunction in beta thalassemia major patients in pre-clinical phase of heart disease.

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