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Original Article

Effect of Slow Breathing Exercise on Time Domain Heart Rate Variability in Transfusion Dependent Thalassemic Patients

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Abstract:

Time domain measure of heart rate variability (HRV) is a newersystem to seek out any alteration in cardiac autonomic nerve function (CANF) in transfusion dependent thalassemic (TDT) patients. Slow breathing exercise (SBE) plays important role in improvement of HRV in health and various diseases.This research aims to observe the effect of slow breathing exercise (SBE) on time domain measures of HRV in TDT patients. This prospective interventional study was done in the Department of Physiology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka in 2018 on 60 male TDT patients aged 15-30 years. Thirty patients received conventional treatment and 30 patients performed slow breathing exercise along with the conventional treatment for 3 months. Age and sex matched healthy control were taken to compare. All subjects were followed up at baseline and after 3 months. Time domain HRV parameters were recorded by Power Lab 8/35. For statistical analysis paired sample 't' test and independent sample 't' test were done. Mean RR interval, Mean SD, RMSSD and pRR50% were found significantly lower in TDT patients compared to healthy control at baseline and on the other hand mean heart rate was significantly higher in this group of patients. After 3 months of slow breathing exercise, significant decrement of mean heart rate and significant increment of others parameters occurred with trend of improvement in cardiac autonomic nerve function in TDT patients. In conclusion slow breathing exercise may improve cardiac autonomic nerve function and sympathovagal balance in transfusion dependent thalassemic patients.

Key words: Transfusion, Thalassaemia, Heart Rate, Breathing Exercise.

Introduction:

Thalassemia is one of the commonest genetic blood diseases in the world. Worldwide, approximately 150 million people carry the thalassemia gene[1]. Every year in Bangladesh among the born children nearly 6000 are affected with this inherited disease[2,3]. Due to ineffective erythropoies and extramedullary hemolysis anemia remains the predominant clinical feature of thalassemic patients. These patients become transfusion dependent thalassemic patients (TDT) as they require regular blood transfusion to sustain their life[4,5]. Repeated blood transfusion is the primart therapy, but this therapy causes the major problem iron overload in patients[6]. Iron deposition in heart leads to cardiotoxicity that result in cardiomyopathy and becomes the main reason for death among these patients[7,8]. Depressed heart rate variability (HRV) is linked to higher risk of arrhythmias after myocardial infarction and heart failure in TDT patients[9]. Some researchers assessed cardiac autonomic nerve function in thalassemic patient and found depressed HRV in them[10].

HRV is a newer and broadly used method for evaluating cardiac autonomic tone in diabetes and other cardiovascular disease that records beat to beat variation of heart rate or RR interval[11-14].

Variability in heart rate is influenced by the parasympathetic nerves, which decrease heart rate and the sympathetic nerves, which accelarates it. Higher variability of HRV was observed in physically active young healthy subject whereas low variability was found in acute MI, Left ventricular hypertrophy due to hypertension or aortic valve disease which is linked to greater risk of adverse cardiac event & sudden death[12-16]. In addition, Low HRV is a strong and independent predictor of bad prognosis both in heart disease patients and general population[16-18].

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Time domain includes both simple and statistical complex measures of RR interval of normal beats such as mean heart rate, mean of successive RR interval, standard deviation of the difference between successive RR intervals (SDSD), root of the mean squared differences of successive RR intervals (RMSSD), the number of interval differences of successive RR intervals greater than 50 ms (RR50) and the proportion derived by dividing RR50 by the total number of RR intervals (PRR50%)[12]. As this recording was done in resting condition, therefore this value represents the variability of cardiac vagal tonic discharge, in other words cardiac vagal modulation during the period of recording[19-20].

Among the different types of Yoga SBE is one where controlled regulation of breathing through alternate nostrils is done in order to regulate rhythmical respiration and to keep the mind calm. SBE has important role on autonomic balance by increasing parasympathetic activity and decreasing sympathetic activity[21]. This exercise improve CANF by increasing parasympathetic activity or decreasing sympathetic activity in some diseases and also in normal healthy person[22,23]. Though several studies investigated SBE on autonomic function in other diseases but there is no published report investigating the effect of SBE on nonlinear measures of HRV in TDT patients. Therefore this study aimed to observe the effect of SBE on time domain measures of HRV in TDT patients so that SBE can be used in adjunct to conventional treatment and improve CANF as well as reduce the cardiovascular complications.

Materials and Methods:

This prospective interventional study was carried out in the year 2018 at the Department of Physiology, BSMMU, Shahbag, Dhaka to observe the cardiac autonomic nerve function by assessing time domain parameters of HRV in 60 male diagnosed TDT patients, aged 15-30 years. These patients were subdivided equally into 30 patients assigned with slow breathing exercise and 30 patients without slow breathing exercise in addition to conventional treatment. For comparison 30 apparently healthy subjects were taken as control.

The patients were enrolled from the outpatient department of Transfusion Medicine and Hematology, BSMMU by purposive sampling and the controls were selected from community of Dhaka city. The protocol of this study was approved by the Institutional Review Board of BSMMU. All patients were studied at baseline before intervention and same patients were studied after 3 months assigned with or without SBE. Similarly healthy subjects were studied at baseline and after 3 months. All the subjects were free from respiratory disease, renal disease, diabetes mellitus, thyroid disorder and other hematological diseases. After explaining informed written consent was taken from each subject.

After enrollment the subjects were advised to follow some instructions in the previous night of HRV test day. They were advised to finish their meal by 9:00 pm on previous night, to remain free from any type of stress, not to take sedative hypnotic medication. They were requested to take light breakfast without tea and coffee and to attend the autonomic nerve function test laboratory in the department of Physiology, BSMMU between 8:00 am to 10:00 am on the test day. A through physical examinations including pulse, BP, height, weight were measured and BMI was calculated. The subject was advised to take rest for 15-20 minutes in controlled laboratory environment. During this period he was not allowed to talk, eat or drink, to perform physical or mental activity, even sleep. ECG was recorded on lead II for 5 minutes by data acquisition device Power Lab 8/35 (AD instrument, Australia). HRV recording was analyzed by Lab chart software. Patients weretrained with the steps of slow breathing exercise and advised to exercise slow breathing in a sitting position daily in themorning and eveningfor half an hour for consecutive three months. For recording the exercise, a diary with time schedules including the figures and rules of SBE in Bangla were provided. Patient was monitored by frequent home visits if possible, during their appointment in the hospital for blood transfusionand also was communicated 3-5 times per week via telephone calls. Patient was advised to come for follow up assessment after 3 months in the same department.

Data were expressed as Mean ± SE and percentage. Statistical analysis was done using SPSS version 16 and Microsoft Excel 2007. Paired sample 't' test and independent sample 't' test were done, p value of < 0.05 was considered as statistically significant.

Results:

In this study, all TDT patients were similar to healthy control by age and waist hip ratio but not by BMI, MUAC. But all these parameters were similar in SBE and non SBE patients (Table I). In this study, at baseline, pulse rate and mean heart rate was significantly ($p<0.001$) higher and SBP, DBP, mean RR interval, SD, RMSSD and PRR 50% were significantly ($p<0.001$) lower in TDT of both groups compared to control. Again no significant differences in all these parameters were observed between SBE and non SBE patients at baseline (Table II).

After 3 months follow up, TDT patients without SBE had similar pattern of these parameters when compared to their baseline values, whereas after three months of SBE, mean value of pulse rate and mean heart rate significantly (P<0.01) decreasedbut mean RR interval, SD, RMSSD and PRR 50% significantly (p<0.001, P<0.01 and P<0.001 respectively) increased in these patients (Table III). Again post intervention values of all these parameters showed different trends in SBE group compared to their non SBE counterparts and it was statistically significant. Though the values of mean RR interval, SD, RMSSD and PRR 50% in SBE group after 3 months were significantly increased and mean heart rate significantly decreased but did not reach close to control (Table IV).

Table I: Age, BMI, Waist Hip ratio and MUAC (n=70)

Parameter	Control (n=24)	Non SBE (n= 22)	SBE (n=24)
Age (years)	18.75±0.84	19.4±0.88	18.75±0.81
BMI(kg/m^2)	19.53±0.47	15.89±0.39***	15.87±0.37***
Waist Hip ratio	0.86±0.02	0.86±0.02	0.86±0.01
MUAC(cm)	25.54±0.47	20.36±0.61***	20.20±0.51***

Data were expressed as mean ± SE. Statistical analysis was done by independent sample t test. BMI=Body mass index, MUAC= mid upper arm circumference. ***p<0.001 (*non SBE and SBE TDT baseline vs Control baseline).

Table II: Baseline values of pulse rate, blood pressure (BP) and time domain measures in different groups (n=70)

Parameter	Control (n=24)	Non SBE (n= 22)	SBE (n=24)
Pulse rate(beats/min)	70.00±1.69	90.09±2.17***	87.9±2.31***
SBP(mm of Hg)	116.75±1.06	101.55±1.74***	100.58±1.9***
DBP(mm of Hg)	74.58±1.15	63.45±1.08***	62.92± 1.84***
Mean heart rate	70.58±1.78	90.74±2.2***	89.4±2.7***
Mean RR interval	866.17±22.18	670.16±16.34***	675.7±15.9***
SD	49.16±4.77	15.9±2.2***	16.41±1.82***
RMSSD	49.11±4.77	15.89±2.2***	16.4±1.82***
pRR50%	28.29±4.09	2.61±1.04***	1.9±0.75***

Data were expressed as mean ± SE. Statistical analysis was done by independent sample t test. SBP = Systolic blood pressure, DBP = Diastolic blood pressure, SD = Standard deviation of successive RRinterval differences between adjacent RR intervals, RMSSD = Square root of mean of squared differences of successive RR interval, PRR 50% = Percentage of R-R interval differingby >50ms from adjacent intervals. ***p<0.001(*non SBE and SBE TDT baseline vs Control baseline).

Table III: Pre and post intervention values of pulse rate and blood pressure (BP) and time domain measures in different groups (n=46)

Parameter	Non SBE (n= 22)		SBE(n=24)	
	Pre	Post	Pre	Post
Pulse rate(beats/min)	90.09±2.17	90.82±2.2	87.9±2.31	82.42±2.1**
SBP(mm of Hg)	101.55±1.74	102.82±1.21	100.58±1.9	101.25±1.91
DBP(mm of Hg)	63.45±1.08	64.36±0.91	62.92±1.84	63.08±1.79
Mean heart rate (beats/min)	28.6±2.62	27.95±2.54	89.4±2.7	83.76±2.12**
Mean RR interval (ms)	670.16±16.34	664.27±15.04	675.7±15.9	727.67±16.24***
SD (ms)	15.9±2.2	15.55±2.1	16.41±1.82	24.97±2.8***
RMSSD	15.89±2.2	15.56±2.09	16.4±1.82	24.95±2.28**
PRR 50%	2.61±1.04	1.74±0.68	1.9±0.75	5.09±1.3***

Data were expressed as mean ± SE. Statistical analysis was done by paired sample t test. SBP= Systolic blood pressure, DBP = Diastolic blood pressure, SD = Standard deviation of successive R Rinterval differences between adjacent RR intervals, RMSSD = Square root of mean of squared differences of successive RR interval, PRR 50% = Percentage of RR interval differingby >50ms from adjacent intervals. ***p<0.001,**p<0.01 (Post SBE vs Pre SBE).

Table IV: Post follow up values of pulse rate, blood pressure (BP) and time domain measures in different groups (n=70)

Parameter	Control (n=24)	Non SBE (n= 22)	SBE(n=24)
Pulse rate(beats/min)	69.83±1.8	90.82±2.2	82.42±2.1**###
SBP(mm of Hg)	117.33±0.75	102.82±1.21	101.25±1.91###
DBP(mm of Hg)	74.00±1.00	64.36±0.91	63.08±1.79###
Mean heart rate (beats/min)	71.49±1.87	91.41±2.08	83.76±2.12*###
Mean RR interval (ms)	855.66±22.46	664.27±15.04	727.67±16.24**###
SD	48.02±4.26	15.55±2.1	24.97±2.28**###
RMSSD	47.97±4.26	15.56±2.09	24.95±2.28*###
PRR 50%	28.07±3.98	1.74±0.68	5.09±1.3*

Data were expressed as mean ± SE. Statistical analysis was done by independent sample t test. SBP = Systolic blood pressure, DBP = Diastolic blood pressure, SD = Standard deviation of successive RR interval differences between adjacent RR intervals, RMSSD =

Square root of mean of squared differences of successive RR interval, PRR 50% = Percentage of RR interval differingby >50ms from adjacent intervals. **p<0.01, *p<0.05(*SBE vs non SBE); ###p<0.001 (#SBE vs Control).

Discussion:

The present study assessed cardiac autonomic nerve function in diagnosed Transfusion Dependent Thalassemic (TDT) patients before and after slow breathing exercise with conventional treatment for 3 months by analysis of time domain measures of HRV and compared these results with control.

Data of this study showed lower MUAC and BMI in TDT patient groups compared to control but similar in both patients group resemble to the observation in a similar study[24]. They concluded that the low BMI and MUAC represents growth deficiencies in these group of patient compared to their healthy counterpart might be related to toxic effect of iron chelation therapy, low hemoglobin and high ferritin level.

In this study, significantly higher resting pulse rate, lower SBP and DBP in patient groups compared to control group agree to other investigators reporting similar observation[9,25]. In patients with thalassemia cardiac output is increased as they suffer from chronic anemia which is attributed to increased cardiac dimension and heart rate. Moreover, increased blood volume at the time of blood transfusion may cause uncontrolled stimulation of cardiac receptors with sympathetic afferents and vagal with drawa land consequently impaired cardiac autonomic tone. Though cardiac output is increased but due to low peripheral resistance, blood pressure is decreased in these patients[26-27].

After practicing slow breathing exercise for 3 months, the significant decrement of pulse rate in patients suggests improvement of CANF. In contrast sustained higher pulse rate in patients without SBE indicate no improvement in CANF after 3 months. Thus these results obviously suggest that SBE is effective to improve CANF, but the post intervention heart rate of SBE group was not close to normal which suggests that 3 months of SBE in TDT patients could not restore parasympathetic activity enough to normal. On the other hand, there were no significant changes in SBP and DBP were found after SBE in patients group. This fact might be due to small duration of SBE.

Significantly higher mean heart rate and lower mean RR interval, SD, RMSSD and PRR50 % in both TDT patients group compared to healthy counterpart before intervention is suggestive of impaired autonomic harmony in these patients.

Moreover, after three months performance of SBE, there was significant decrement of mean heart rate and increment of these parameters in these patients, which pointwards improvement of autonomic harmony has been achieved by SBE.

On the other hand, no significant change was observed in these parameters in the patients not performing SBE which imply continued autonomic disharmony in absence of intervention. Though the values of mean RR interval, SD, RMSSD and PRR 50% in SBE group after 3 months were significantly increased and that of mean heart rate significantly decreased but did not reach close to control. These observations provide strong support for good effect of SBE on mean heart rate, mean RR interval, SD, RMSSD and PRR 50% in TDT patients.

Improvement of sympathovagal balance by SBE has been proved in many other investigations mostly in healthy subjects and also in some diseased condition. The improvement achieved by SBE might have been related to the fact that SBE improves peripheral oxygen consumption, neuronal oxygen usage and thus improved autonomic balance. This method causes increased tidal volume in lungs that trigger the inhibitory reflex by the stretch receptor located in the wall of this organ and increases parasympathetic activity. SBE also improves sympathovagal balance by enhancing central inhibitory rhythm[18,28-30].

Conclusion:

Based on the results of this study it can be concluded that slow breathing exercise may improve impaired autonomic function in TDT patients by increasing parasympathetic while decreasing sympathetic activity with the autonomic balance more parasympathetic dominance in the TDT patients.

So, SBE is an effective measure to reduce the risk of cardiovascular disease in TDT patients. Therefore, SBE can be recommended for thalassemic patients as a part of complementary medicine to protect these patients from cardiovascular morbidity.

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