

Parasympathetic Nerve Function Status in Major Depressive Disorder Patients and Its Correlation with Duration of Disease

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Abstract

Introduction: Cardiovascular (CV) morbidity is a major problem in patients suffering from depression. Greater CV mortality is found in cardiac patients with depression than without depression. Depressive disorder can cause altered autonomic nerve function. This study design to assess autonomic nerve function activity by heart rate variability analysis in patients with major depressive disorder and its correlation with duration of disease. **Materials and Methods:** This case study was conducted in the Department of Physiology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbag, Dhaka in 2011. 60 patients of both sexes with major depressive disorder (MDD) aged from 20-50 years were included in the study group (Group B). The patients were selected from out and inpatient Department of Psychiatry in Bangabandhu Sheik Mujib Medical University (BSMMU). Group B were divided into B-1 consisting of 30 drug naive MDD patients & B-2 consisting of 30 medicated MDD patients. For comparison age and sex matched 30 apparently healthy subjects (Group A) were also studied. The HRV parameters were recorded by 4 active channels, Polyrite-D machine. For statistical analysis ANOVA, independent sample t-test, chi-square test and Pearson's correlation coefficient test were performed by using SPSS for windows version-16 as applicable. **Results:** Mean resting pulse rate, mean heart rate, systolic blood pressure were significantly higher in drug naive and medicated MDD patients in comparison with that of healthy control. Mean R-R interval, Max/Min R-R interval, SDNN, RMSSD, PNN50%, NN50% were significantly lower in this groups of patients. Correlation analysis showed negative correlations of SDNN, RMSSD, PNN50%, NN50% with disease duration which was statistically significant only for SDNN. **Conclusion:** Sympathovagal imbalance may occur in both drug naive and medicated MDD patients which is associated with higher sympathetic and lower vagal modulation of the heart rate. In addition, parasympathetic nerve function parameters show negative relationship with the duration of disease.

Keywords: HRV, MDD, SDNN, RMSSD.

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Introduction

Depression is one of the most common disorders that present with depressed mood, sadness, indifference, apathy or irritability and is usually associated with changes in sleep patterns, appetite and weight, motor agitation or retardation, fatigue, impaired concentration and decision making, feeling of guilt and thoughts of death or dying¹. Depression is one of the leading causes of disability and global burden of disease². About 14.4 million people of United States are believed to suffer from Depression. Women are affected 2 to 3 times more often than men¹. The prevalence of depression in Bangladesh is 2.9% for males and 11.6% in females and the male-female ratio is 1:2.63³. Depression is multi factorial in origin. It has been observed that there is a genetic predisposition to depression especially in its early onset. Depressive episodes are often triggered by stressful life events⁴. The epidemiological study found greater cardiovascular mortality in cardiac patients with depression than without depression because of altered Autonomic nervous system (ANS) activity in depressive disorders⁵. ANS modulates the electrical and contractile activity of the myocardium through the involvement of sympathetic and parasympathetic outflow. ANS alteration includes increased sympathetic and reduced vagal activity which is strongly involved in the pathophysiology of arrhythmogenesis, sudden cardiac death, myocardial infarction, congestive cardiac failure and diabetic neuropathy⁶.

Heart rate variability (HRV) is a sensitive non invasive method used to study intrinsic cardiac autonomic activity as well as sympathovagal balance between cardiac sympathetic and parasympathetic activity⁷. Time domain variables of HRV such as include mean R-R interval and mean heart rate, the standard deviation of the NN interval(SDNN), the square root of the mean squared difference of successive NN interval (RMSSD), NN50% and PNN50% in general reflect cardiac vagal activity⁷. Lower Mean R-R interval and higher heart rate were observed in MDD patients compared to that of healthy control⁸⁻¹³. Whereas some investigators reported lower heart rate in MDD patients in comparison to controls¹⁴. Because of conflicts in result this study aimed to evaluate the impact of depression on cardiac autonomic nerve function by measuring time domain variable of HRV in MDD patient and relation of these parameter with disease duration.

Materials and Methods

This cross sectional study was carried out to observe the HRV by time domain method in 60 major depressive patients (group B) with age ranged from 20-50 years in the Department of Physiology, Bangabandhu Sheikh Mujib Medical University (BSMMU) from 1st January to 31st December 2011. For comparison 30 age and sex matched healthy subjects (Group- A) were also studied. MDD patients were further subdivided according to treatment into B-1 drug naive MDD patients, B-2 treated MDD patients. The patients were selected from the Department of Psychiatry, BSMMU and the controls were selected from community of Dhaka city. All the subjects were free from heart disease, hypertension, diabetes mellitus, chronic kidney disease, psychic disorders, and smoking. After selection, informed written consent was taken from them. Then the subject was interviewed and detail history regarding personal history, drug history, past medical history was taken to exclude exclusion criteria. Then thorough physical examinations and anthropometric measurement including height, weight, BMI were recorded in a prefixed questionnaire. The subject was kept in complete bed rest in supine position for 15-20 minutes in a cool and calm environment. During this period subject was advised not to talk, eat or drink and also not to perform physical or any mental activity, even sleep. Then all preparations for recording of the Heart rate variability parameters were made by connecting the channels of ECG and 5 minutes recording was taken in supine position. Data were obtained by software analysis of the power spectral band of the HRV. Data were expressed as mean \pm SE. As test of significance one way ANOVA, chi square test, student's unpaired t-test, Pearson's correlation coefficient test were employed as applicable.

Results

In drug naive and treated MDD patients the mean resting pulse rate, SBP & DBP were significantly ($p < 0.001$) higher in comparison to control. No difference in these parameters were found between drug naive and treated patients (Table-I). Mean values of R-R interval SDNN, RMSSD, NN50%, PNN50% were significantly ($p < 0.001$) lower but mean heart rate was ($p < 0.001$) higher in MDD patients in both drug naive and medicated patient than control. Again, no significance difference were observed when compared all these parameters between two groups of patients (Table II). Correlation analysis showed significant negative correlation between SDNN and duration of depression in study group (Figure 1). This study also showed negative correlation of RMSSD (Figure 2), PNN50% (Figure 3) NN50% (Figure 4) with duration of disease in study group.

Table-I: Resting Pulse rate and BP in different groups (n=90).

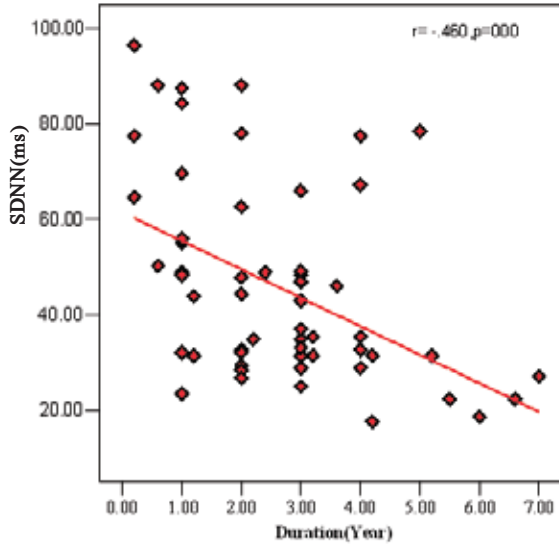
Variables	Control (n=30)	Drug naive MDD (n=30)	Treated MDD (n=30)
Pulse (beat/min)	74 \pm 1.42 (60-90)	86 \pm 1.25*** (70-100)	85 \pm 1.17*** (72-98)
SBP (mm of Hg)	112 \pm 1.91 (95-135)	122 \pm 1.77*** (100-135)	120 \pm 2.00*** (100-140)
DBP (mm of Hg)	70 \pm 1.49 (60-90)	76 \pm 1.27** (60-90)	74 \pm 1.16ns (60-85)

Data were expressed as Mean \pm SE. Statistical analysis were done by One-way ANOVA^a and Independent sample t-test^b. *** = $p < 0.001$ ** = $p < 0.01$, ns = non significant ($p > 0.05$) control vs patients.

Table-II: Time domain measures of HRV in different groups (n=90).

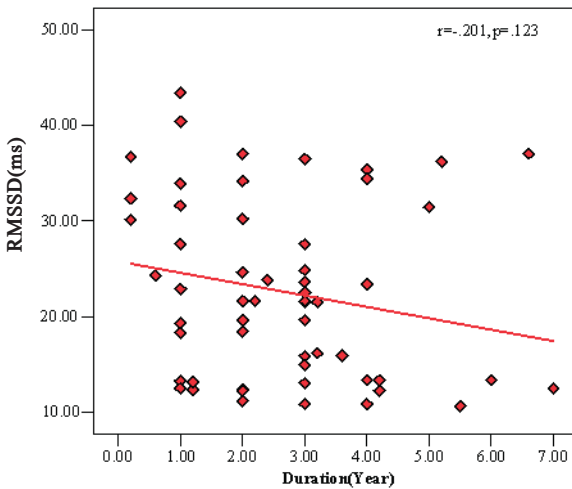
Groups	Control (n=30)	Drug naive MDD (n=30)	Treated MDD (n=30)
Mean heart rate (beat/min)	76 \pm 1.17 (65-88)	87 \pm 2.29*** (62-110)	86 \pm 1.81*** (68-100)
Mean R-R interval(sec)	0.79 \pm 0.01 (0.68-0.91)	0.71 \pm 0.02** (0.55-0.97)	0.71 \pm .01*** (0.60-0.88)
SDNN (ms)	77.28 \pm 2.59 (47.4-97.4)	47.22 \pm 3.88*** (22.3-96.49)	44.54 \pm 3.59*** (17.51-87.47)
RMSSD (ms)	34.30 \pm 0.8 (22.54-40.23)	21.35 \pm 2.05*** (10.65-40.39)	24.08 \pm 2.27*** (12.26-43.44)
NN50 (%)	72 \pm 5.44 (20-138)	34 \pm 6.6*** (1-153)	23 \pm 5.5*** (1-123)
PNN50 (%)	23.0 \pm 2.48 (7.9-50.4)	10.2 \pm 2.18*** (.02-28.4)	11.49 \pm 1.39** (0.9-28.8)

Data were expressed as Mean ± SE. Statistical analysis were done by One-way ANOVA^a and Independent sample t-test^b. ms= millisecond .*** = p<0.001 ** = p<0.01, ns = non significant (p>0.05) control vs patients.



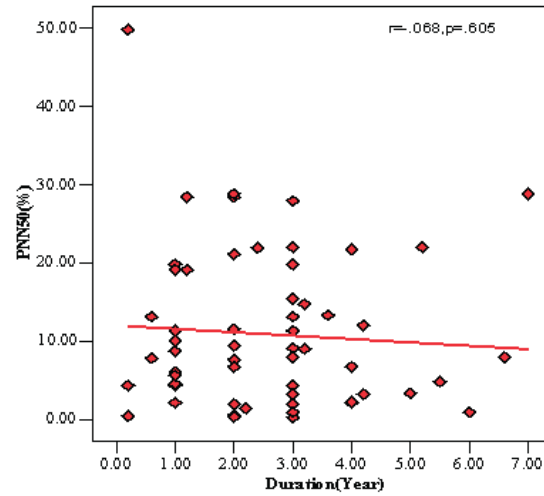
Statistical analysis was done by Pearson's correlation-coefficient (r) test.
SDNN: Standard deviation of NN interval

Figure 1: Correlation of SDNN with duration of disease.



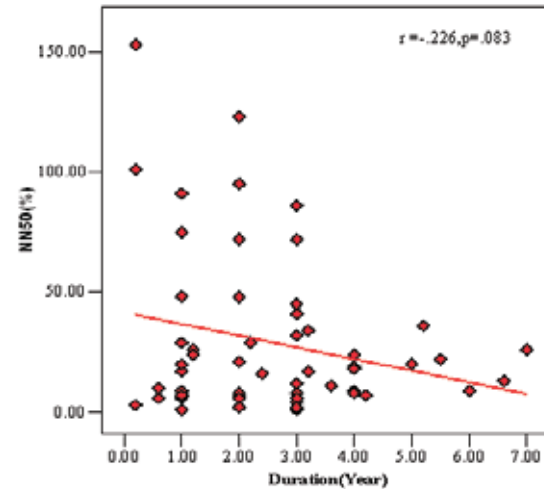
RMSSD: Square root of mean squared differences between adjacent NN intervals

Figure 2: Correlation of RMSSD with duration of disease



PNN50%: number of R-R interval differing by >50 ms from adjacent interval divided by the total number of all R-R interval

Figure 3: Correlation of PNN50% with duration of disease



NN50%: = number of interval differences of successive NN intervals greater than 50 m

Figure 4: Correlation of NN50% with duration of disease

Discussion

In the present study, the time domain parameters of HRV in patients with Major Depressive Disorder were analyzed to access their cardiac autonomic activity and the effect of treatment with anti depressive medication. In addition to HRV resting pulse rate, systolic blood pressure (SBP) and diastolic blood pressure (DBP) were also recorded. Moreover correlations of some parameters of HRV with duration of disease were also studied in order to observe any change with duration. In this study the resting pulse rate, SBP, DBP were significantly higher in both drug naive and medicated MDD patients. DBP was higher but not statistically significant in treated patients when compared with control. These findings consistent to some researchers⁸, whereas opposite results were reported by some other groups^{9,15}.

Significantly higher mean heart rate, lower mean R-R interval SDNN, RMSSD, PNN50%, NN50% were found in all MDD patients compared to control. Several investigators reported similar results^{8-13,15,16}. Again some researchers found similar trends but it was not statistically significant^{8,14,17}. In the present analysis no significant difference in HRV parameters were found between drug naive and treated patients of MDD. In the present study significant negative correlation of SDNN with disease duration suggest strong relationship between altered vagal activity with duration of disease. RMSSD, NN50% and PNN50% also showed negative correlations with disease duration. All the relationships were statistically not significant. The observation of present analysis suggest that cardiac vagal tone was decreased in MDD patients. In addition, effect of anti depressive medication is not apparent on compromised cardiac autonomic function in MDD patients. Moreover, cardiac autonomic activity gradually decreased with duration of disease. Literatures on reduced HRV in MDD patients suggested that, vagus acts as control center for attention, co-ordination, emotion, communication which are altered in depression¹⁸. Some researchers have identified elevated concentrations of corticotrophin releasing hormone (CRH) in cerebrospinal fluid and it has also been suggested that hyperactivity of CRH containing neuron in hypothalamus stimulates several autonomic centers which are concerned with the regulation of peripheral sympathetic activity¹⁹. It has been also suggested that reduced monoamine in CNS lead to decreased central nor epinephrine (NE) level in depression. Therefore, low CNS NE activity would cause withdrawal of α^2 receptor mediated inhibitory effect on peripheral sympathetic outflow¹⁹. The exact mechanism of poor vagal activity in MDD patients is not evident. Moreover, anti depressive medication mostly affect the serotonergic system and which has no association with vagal center. Therefore this treatment may not improve cardiac parasympathetic function.

Conclusion

In the present study, it has been observed that impairment of cardiac autonomic nerve function activity in both drug naive and medicated MDD patients. It has been shown that markedly decreased parasympathetic with increased sympathetic activities were found in this patients. Antidepressant treatment failed to improve impaired autonomic function and cardiac autonomic activity gradually decreased with duration of disease.

Conflict of Interest: None.

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