Short Communication

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Alteration of Heart Rate Variability in Patients of Depression

Physiology Section

DEEPTI JANGPANGI[1], SUNITA MONDAL[2], RAJIV BANDHU[3], DINESH KATARIA[4], ASHA GANDHI[5]

ABSTRACT

Introduction: Altered cardiac autonomic functions in form of reduced Heart Rate Variability (HRV) have been found to be associated with increased cardiovascular morbidity and mortality in depressive patients.

Aim: To investigate the relationship between HRV measures, which is a non-invasive marker of autonomic nervous system and depression.

Materials and Methods: The study included a convenient sample size of drug naive depressive patients (n=30) diagnosed on basis of ICD-10 and compared with age and gender matched healthy volunteers (n=30). Five minute ECG recording was done for HRV analysis and frequency domain measures like LF (Low Frequency), HF (High Frequency), LF/HF ratio as well as time domain measures like SDNN (Standard Deviation of all NN interval) and RMSSD (Root Mean Square of Successive differences of NN intervals) were obtained.

Results: In the frequency domain parameters, values of LF (nu) and LF/HF Ratio were found to be significantly higher ($p<0.001$) whereas, that of HF (nu) was significantly lower ($p<0.001$) in depression group as compared to control group. However, in the time domain parameters, no significant difference was observed in SDNN and RMSSD values in between the two groups.

Conclusion: HRV recordings showed significant changes in frequency domain parameters in the patients suffering from depression. Thus, it could be said from our study that autonomic imbalance reflecting enhanced sympathetic activation relative to parasympathetic component is associated with depression.

Keywords: Autonomic nervous system, Cardiovascular disease, Major depressive disorder

INTRODUCTION

Depression is assuming an importance globally, as it will become the second leading cause of disability worldwide by 2020 [1]. The implications of depression is not only limited to an impaired quality of life or occupational functioning but now it extends to various unfavourable health outcomes it may result in [2]. Most studies have now identified depression as a strong and independent risk factor for cardiovascular disease even in physically healthy individuals [3] and also for adverse cardiovascular outcomes such as mortality [4]. Although the underlying pathophysiological mechanism is yet to be elucidated, autonomic imbalance has been projected as one of the underlying mechanism [5]. Heart Rate Variability (HRV) is a useful non-invasive measure for assessing cardiac autonomic modulations. Autonomic nervous system acts through dynamic nature of the interplay between the sympathetic and parasympathetic branches and HRV reflects a balance between sympathetic and parasympathetic inputs to the cardiac pacemaker [6]. HRV is the variation over time of period between consecutive heart beats. Low HRV signifies increase in cardiac sympathetic modulation or relative decrease in cardiac parasympathetic modulation or both of heart rate [7].

Reduced HRV has been reported in several studies done in depressed patients both with and without cardiovascular diseases compared to non depressed subjects [8,9]. Although negative studies have been reported as well, which were unable to prove an association [10]. Most of the researches carried out to observe the association between HRV and depression have been done in individuals who were already either having Cardiovascular Disease (CVD) besides depression or were on medications [11]. These factors could have contributed to cause decreased HRV besides depression. Our study has attempted to investigate the cardiac autonomic functions using HRV analysis in drug naive depressive patients without any co-morbid diseases.

MATERIALS AND METHODS

The present study was a descriptive observational cross-sectional study conducted between November 2010-March 2012 and performed in Department of Physiology along with Department of Psychiatry, Lady Hardinge Medical College & Associated Hospitals, New Delhi. The study was approved by Institutional ethical committee of LHMC & associated hospitals.

Participants

Depression Group: The depression group comprised of a convenient sample size of 30 drug naïve patients of either gender in an age group of 20 – 45 years. Patients were diagnosed by an experienced psychiatrist according to ICD-10 (International Classification of Diseases-10) guidelines [12]. Patients suffering from any known organic diseases, or any other psychiatric disorders, substance dependence were excluded from the study.

Control Group: Thirty age and gender matched apparently healthy subjects were recruited. Body Mass Index (BMI) and socio-economic status was also duly matched. Subjects having any known organic diseases, psychiatric disorders, substance dependence were excluded. They were also screened with standardized Hindi version of Goldberg's General Health Questionnaire [13] for psychological well being. Those who were previously doing any form of yoga and physical training were also excluded from both the groups. All of the participants were also made to fill a semi-structured proforma with socio-demographic details. The objective of the study was explained to both the groups and a written informed consent was obtained prior to participate in the study.

In our study out of 30 depressive patients eight patients were suffering from mild depression, 16 patients were suffering from moderate depression and six patients were suffering from severe depression according to ICD-10.

The participants were instructed to come 2-4 hours after a light breakfast and to abstain from caffeine (tea/coffee) for at least 24 hours before recordings. The participants were familiarized with the laboratory settings and were informed about the procedures to be conducted. Recordings were taken in a silent room, maintained at a temperature of 22-26^0 Celsius. The physiological parameters and HRV recordings were carried out in between 9 am to 12 noon to obviate any diurnal influences. Body Mass Index (BMI) was computed by body weight in kilograms divided by the square of standing heights in meters (kg/m^2). Blood pressure (SBP/DBP) was measured as per following the American Heart Association guidelines [14].

HRV Recording: Five minutes recording was taken after 15 minutes of supine rest using lead II ECG. HRV was recorded by autonomic neuropathy analyser RMS supplied by Recorders and Medicare systems, Chandigarh, India. The data was stored in computer and analysed as per the guidelines of task force of European society of cardiology and the Northern American society of pacing electrophysiology (1996) [7]. The data was analysed using a computer programme developed by the RD of Recorders and Medicare system, Chandigarh, India to obtain the frequency domain and time domain parameters. Fast Fourier transformation was used to determine HRV components.

Frequency Domain Measures

LF (nu): Low frequency; 0.04 to 0.15 Hz- reflects both sympathetic and parasympathetic modulations of heart rate.

HF(nu): high frequency; 0.15 to 0.4 Hz- primarily reflects parasympathetic activity of heart rate.

LF:HF Ratio: Signifies sympathovagal balance and thus sympathetic modulations.

Time Domain Measures

SDNN: Standard deviation of all N-N intervals-reflects both sympathetic and parasympathetic influences.

RMSSD: Root mean square of successive differences of NN intervals-primarily reflects parasympathetic influences on heart rate.

STATISTICAL ANALYSIS

The parameters are presented as Mean±Standard error of mean. The Kolmogorov-Smirnov (KS) normality test was used for data. Comparisons between depressed and control groups were made, using unpaired students t-test for normally distributed data. Chi-square test was employed to compare categorical variables. GraphPad prism software version 5 (Graph Pad Software Inc., San Diego, CA, USA) was used for statistical evaluation.

RESULTS

[Table/Fig-1] illustrates the socio-demographic characteristics of two groups. No significant difference was observed in age, gender, BMI, SBP/DBP in between the two groups. The socio-economic status was also non significant in between the two groups. In the comparison of HRV measures in between the two groups, values of LF (nu) ($p<0.001$), LF:HF Ratio ($p<0.001$) were significantly higher and HF (nu) ($p<0.001$) parameter was significantly lower in depression group compared to controls [Table/Fig-2]. While no significant difference was obtained in SDNN and RMSSD parameters [Table/Fig-2].

Parameters	Normal Controls (n = 30)	Depression Patients (n = 30)	p-value
Age (years)	29.80±1.13	30.33±1.27	0.755†
Sex (M:F)	14 : 16	14 : 16	1.00‡
BMI (kg/m^2)	22.57±0.35	22.93±0.32	0.447†
SBP (mm of Hg)	113.3±1.12	110.50±1.55	0.139†
DBP (mm of Hg)	69.8±1.29	69.20±1.37	0.750†
Socio-economic status	Upper – 2 Middle – 20 Lower – 8	Upper – 2 Middle – 20 Lower – 8	1.00‡

[Table/Fig-1]: Socio-demographic parameters between depression patients and normal controls.
BMI: Body Mass Index, Data expressed in Mean and Standard error of mean, $p>0.05$ is considered as not significant, *$p<0.05$ is considered as significant, †Unpaired t-test, ‡Chi-square test.

Parameters	Normal Controls (n = 30)	Depression Patients (n = 30)	p-value
LF (normalized units)	68.82±1.54	76.13±0.55	†$p<0.001$***
HF (normalized units)	31.26±1.54	24.09±0.57	†$p<0.001$***
LF:HF Ratio	2.41±0.15	3.23±0.09	† $p<0.001$***
SDNN (ms)	50.90±5.12	58.70±6.40	0.345†
RMSSD (ms)	35.40±2.55	35.40±2.80	0.999†

[Table/Fig-2]: Comparison of HRV measures low frequency (LF), High frequency (HF), LF: HF Ratio, SDNN and RMSSD. Data expressed in Mean and Standard error of mean,***$p<0.001$ is considered as very highly significant, $p>0.05$ is considered as not significant, †Unpaired t-test.

DISCUSSION

In this study, we found a statistically significant association between LF, HF, LF:HF ratio and depression. The LF and LF:HF Ratio was statistically significantly higher in depression group compared to control group. This is indicative of enhanced sympathetic activity. The HF parameter which is a measure of parasympathetic activity was found to be significantly lower in depression group. The findings of our frequency domain measures of HRV in depression patients corroborates with previous studies such as that of Udupa et al., who studied drug naïve Major Depressive Disorder (MDD) patients without any co-morbidity and reported significantly higher LF:HF ratio and lower HF (nu) in MDD group compared to control. However LF, SDNN and RMSSD showed no significant difference between two groups [15]. A meta-analysis done by Kemp et al., in depression patients without cardiovascular diseases also reported the association between reduced HRV and depression and was found to be more in severely depressed individuals [16].

In addition, Agelink et al., showed the inverse correlation of parasympathetic HRV values with the severity of depression [17]. In a recent study Wang et al., also observed higher LF, LF:HF Ratio and lower SDNN, RMSSD and HF values in depression group compared to control group [18]. In the present study we did not find any significant differences in RMSSD and SDNN parameters in between the two groups. Similar findings were reported by Sayar et al., as no significant differences in any of the time-domain measures in between major depressive and healthy control group could be ascertained [19]. Although most of the studies have consistently found the association between HRV and depression, few studies have failed to elucidate such results. The inconsistencies observed in some studies could be attributable to heterogeneity of diseases, medication confounds and methodological differences in studies [10].

The results of the present study support the hypothesis that depression involves alteration in autonomic regulation of heart, which is a state of more sympathetic activation and less parasympathetic activation. Though the underlying mechanism by which HRV is altered in depression cannot be deciphered from our study but reduced HRV seen in depression could be partially explained by polyvagal theory. Polyvagal theory states that vagus helps to promote social engagement and flexible adjustments to environmental demands. It also exerts regulatory control upon functions of emotion, attention, communication which are found to be compromised in depression; it could be due to impairments of low vagal tone [20].

The strength of our study lies in study population, which was drug naive, without any cardiovascular risk factors or co-morbid diseases besides depression which could confound the results.

LIMITATION

The first limitation of our study was sample size which may not be sufficient to detect an association between SDNN, RMSSD and depression. The second limitation was the cross-sectional nature of our study, which limits us to draw any causal inference.

CONCLUSION

It can be concluded from our study that alteration in HRV is present in patients of depression, in accordance with what most of the prior studies have suggested. Thus it would be beneficial to detect such vulnerable individuals early, among depression patients and by lifestyle changes, targeting regulation of autonomic control could help in reducing biological dysregulation often found to be present in depression, further assisting in reducing the future adverse cardiovascular risk associated with depression in them.

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PARTICULARS OF CONTRIBUTORS:
1. Senior Resident, Department of Physiology, Lady Hardinge Medical College and Associated Hospitals, New Delhi, India.
2. Director Professor and Head, Department of Physiology, Lady Hardinge Medical College and Associated Hospitals, New Delhi, India.
3. Professor, Department of Physiology, Lady Hardinge Medical College and Associated Hospitals, New Delhi, India.
4. Head of Department and Director Professor, Department of Psychiatry, Lady Hardinge Medical College and Associated Hospitals, New Delhi, India.
5. Director Professor, Department of Physiology, Lady Hardinge Medical College and Associated Hospitals, New Delhi, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Deepti Jangpangi,
C-2/11, Flat No-3, First Floor, IGNOU Road, Saidula-Jab Ext, New Delhi-110030, India.
E-mail: drdeeptijangpangi@gmail.com

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