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Research Article

IMPACT OF PHARMACOLOGICAL TREATMENT ON CARDIOVASCULAR AUTONOMIC FUNCTION TESTS IN PATIENTS OF OCD AND ITS CLINICAL RELEVANCE: A FOLLOW-UP STUDY

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ABSTRACT

Objectives: Obsessive-compulsive disorder (OCD) is associated with increased mortality due to coronary artery disease. Autonomic dysfunction has been associated with an increased risk of developing cardiovascular illness. Thus, this study examined that autonomic dysfunction is inherent in the disease process and it improves with early initiation of treatment.

Methods: A total of 50 drug-naive patients meeting the ICD-10 criteria for OCD were subjected to autonomic function tests at baseline and then follow-up assessments were done at the 3rd and 6th month of treatment. The follow-up parameters were compared statistically with the baseline parameters.

Results: Difference of time domain parameters of heart rate variability at baseline and second follow-up were statistically significant ($p<0.05$). Difference of frequency domain parameters of HRV at baseline and second follow-up were also statistically significant ($p=0.000$).

Conclusion: OCD is characterized by inherent autonomic dysfunction. Thus, physicians should carefully monitor metabolic and cardiovascular health in patients with OCD early in the course of the disorder and early initiation of treatment can further prevent these cardiovascular events.

Keywords: Autonomic function test, Heart rate variability, Obsessive-compulsive disorder.

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INTRODUCTION

Patients who have anxiety disorders, and Obsessive-compulsive disorder (OCD) in particular, are more likely to get cardiovascular problems [1]. A mechanism has been suggested that is autonomic dysfunction. For the human autonomic nervous system (ANS) to function properly, the sympathetic and parasympathetic nervous systems must function in harmony. Heart rate variability (HRV) can be used to gauge this equilibrium. Since anxiety disorders are linked to reduced HRV, which measures the beat-to-beat change in the heart rate (HR) across time, cardiovascular disease risk is increased. Greater HR variability guards against harmful cardiovascular events. The technique section provides a detailed description of HRV [2,3]. Obsessive-compulsive disorder patients are characterized by intrusive thoughts and strong cravings to engage in ritualized behaviors. Anxiety is reportedly experienced by patients who struggle to regulate these urges and thoughts. Anxiety is linked to distinct physiological traits such as higher somatic arousal and autonomic reactions [4]. OCD and autonomic functions have been the subject of some systematic research. Slaap *et al*. conducted a sitting-position HRV and conducted a spectral analysis to analyze frequency-domain HRV parameters. They found no evidence that OCD patients had a decreased HRV [5]. Pittig *et al*. found that OCD patients had lower baseline high frequency (HF) than controls for the frequency-domain characteristics of HRV [6]. Methodological issues in the studies could be the cause of the conflicting outcomes. Therefore, it was intended for the current study to analyze HRV, which will reveal information about these patients' cardiovascular risk. In addition, it will offer direction to health-care professionals when they are thinking about therapies that could further lower the risk of cardiovascular disease and other physical health issues in these population. This has contributed to the growing need to comprehend how the ANS works in OCD.

METHODS

Study setting

The present study was a prospective study in the Department of Psychiatry along with the Department of Physiology, GGSMCH.

Ethical considerations

This study was approved by the Institutional Ethical Committee.

Sampling technique

Subjects were included by purposive sampling technique.

Study population

Fifty consecutive drug naïve subjects in the year 2019-2020 fulfilling the inclusion and exclusion criteria were included in the study.

Inclusion criteria

a. Subjects should be drug naïve
b. Providing written informed consent, being between age from 18 to 45 years
c. Matching the ICD-10 criteria for OCD
d. Participants with severe cardio-respiratory disease, intellectual disability, head injury, neurological sickness, or other medical conditions were disqualified.

Methodology

The inclusion and exclusion criteria were compared to the patients who had been enrolled. Using a psychiatric thesis pro forma, the patients were assessed for sociodemographic and health-related factors including primary complaints, history of current or prior disease, duration/course, and mental state examination. To unbiasedly gauge the severity of the disease, YBOCS was used on the patients. The consultant validated the diagnosis using the ICD-10. To support inclusion/exclusion criteria, the patients underwent the necessary examinations. Before beginning

treatment, the enrolled patients underwent an autonomic function test that comprised a resting state HRV assessment. At 3 months and 6 months after the treatment, two follow-up evaluations were conducted. The second follow-up parameters were then compared statistically with the baseline parameters. HRV test was done using Digital Polygraph Physio Pac software version 1, Medicaid systems, Chandigarh. 5 min ECG recordings (lead II) were done during resting state. ECG was analyzed during computer software to calculate HRV in two different domains, that is.

Time domain and frequency domain

Time domain variables that were calculated included the mean R-R, a standard deviation of normal-to-normal interval (SDNN), NN50 (mean number of times an hour in which change in normal sinus intervals exceeds 50 Ms), PNN50 (the proportion of nn50 divided by total numbers of NNs at different interval sand square root of the mean squared differences of successive normal-to-normal intervals (RMSSD) of HRV.

Frequency domain variables that were calculated included low frequency (LF) component, LF expressed as normalized unit (LF nu), HF component, HF expressed as normalized units (HF nu), and LF/HF ratio.

In healthy individuals, HF constitutes about 60%, and LF constitutes 40% of the total power (TP) of the HRV. Therefore, an LF-HF ratio of less than 1 indicates good cardiovascular health. However, the LF-HF ratio in a normal population varies from 0.5 to 1.5. The sympathovagal balance was assessed by the LF-HF ratio.

Statistical analysis

The data pertaining to sociodemographic and other clinical variables was entered as a data matrix in Microsoft® Excel® and analyzed using IBM® SPSS® software version 20.0.0 in the light of suitable statistical tests. To represent the data, tables, and columns diagrams were used.

RESULTS

The demographic data is presented in Table 1.

Table 2 shows that the mean scores of SDNN, RMSSD, and NN50 at baseline were low and their values increased at subsequent follow-ups. Mean value of the RR interval was decreased on subsequent follow-ups. This indicates lesser parasympathetic control in OCD patients at baseline.

Table 3 shows the mean score of frequency domain parameters of HRV at different visits. An increase in HF nu from baseline to second follow-up represented increased vagal drive. The LF component of HRV value decreased from baseline to subsequent follow-ups. This indicated a decrease in sympathetic drive with treatment.

Table 4 shows a comparison of the mean score of time domain parameters at baseline and second follow-up. Differences were statistically significant ($p<0.05$) among mean RR ($p=0.014$), mean RMSSD, and mean PNN50 ($p=0.000$, $p=0.004$, respectively).

Table 5 shows a comparison of the mean score of frequency domain parameters at baseline and second follow-up. Differences were statistically significant ($p=0.000$) among LF and HF parameters.

Fig. 1 depicted a comparison of mean scores of the LF: HF ratio at different visits. The mean score of LF: HF, however, remained in the normal range even at baseline but decreased over subsequent follow-ups indicating the increase in parasympathetic and a decrease in sympathetic activity.

DISCUSSION

The mean R-R, SDNN interval, NN50 (mean number of times per hour when change in normal sinus intervals exceeds 50 Ms), PNN50 (proportion of nn50 divided by total numbers of NNs at different intervals), and the square root of the mean squared differences of successive normal to normal intervals (RMSSD) were the time domain measures of HRV used in our study. For treatment-related follow-ups, mean R-R interval values fell from baseline values, indicating an increase in parasympathetic activity. A statistically significant difference existed ($p=0.014$). For treatment follow-ups, the value of RMSSD and PNN50 rose in comparison to the baseline. Indicating an increase in parasympathetic activity, the difference was statistically significant ($p=0.000$, $p=0.004$, respectively).

The outcomes were consistent with impaired parasympathetic modulation seen in mental diseases that are closely related to one another, such as generalized anxiety disorders [6], schizophrenia [7], depression, and bipolar mania [8]. They are probably linked to the illness's underlying traits, separate from the effects of psychiatric drugs. Hoehn-Saric *et al.*'s study was unable to identify a baseline difference in mean R-R between OCD patients and controls [8]. Our result is

Table 1: Distribution of sample according to demographic profile

S. No.	Parameter	Categories	Number of subjects n=50	Percentage
1	Age of presentation	18–25	11	22
		26–35	24	48
		35–45	15	30
		Total	50	100
2	Gender	Males	31	62
		Females	19	38
		Total	50	100
3	Residence	Rural	27	54
		Urban	23	46
		Total	50	100
4	Education	Illiterate	1	2
		Primary	3	6
		Middle	6	12
		High School	29	58
		Intermediate	1	2
		Graduate	6	12
		Professional	4	8
		Total	50	100
5	Occupation	Unemployed	5	10
		Homemaker	16	32
		Student	7	14
		Daily wager	2	4
		Farmer	7	14
		Govt. job	4	8
		Private job	9	18
		Total	50	100
6	Family history	Absent	44	88
		Present	6	12
		Total	50	100
7	Religion	Sikh	34	68
		Hindu	16	32
		Others	0	0
		Total	50	100
8	Monthly Income	<10,001	3	6
		10,002–29972	21	42
		29973–49961	19	38
		49962–74755	6	12
		>74755	1	2
		Total	50	100
9	Family structure	Nuclear	30	60
		Joint	17	34
		3-Gen	3	6
		Total	50	100
10	Marital status	Married	34	68

HRV: Time-domain parameters

supported by Hu finding that persons with anxiety had significant low reactivity of HR and RMSSD [9].

An examination of the HRV's frequency domains revealed that, during the course of OCD treatment, the HF HRV values steadily rose. It was discovered that there was a statistically significant difference in the mean HRV HF domain scores at baseline and the second follow-up (p=0.000). Therefore, this suggested that vagal drive had grown over follow-ups. In a 1995 study, Klein *et al*. found that people with anxiety disorders exhibit lower HF HRV at rest or in reaction to anxiety-provoking stimuli than non-anxious controls [10]. In addition, a study by Chalmers *et al*. revealed that, regardless of the precise diagnosis, the HF domain of HRV was decreased in people with anxiety disorders relative to healthy controls; however, the results for OCD and specific phobia were all non-significant [11].

Table 2: Time domain parameters in OCD patients at different visits

Parameters	Mean score	SD
Mean R-R		
Baseline	0.861	0.198
1st follow-up	0.811	0.172
2nd Follow-up	0.794	0.165
Mean SDNN		
Baseline	54.3	15.7
1st follow-up	55.8	17.06
2nd follow-up	57.5	17.8
Mean RMSSD		
Baseline	34.1	11.7
1st follow-up	37.63	8.89
2nd Follow-up	40.00	6.43
Mean NN50		
Baseline	129.34	45.492
1st Follow-up	130.42	46.912
2nd follow-up	137.72	37.602

HRV: Frequency-domain parameters

Table 3: Frequency domain parameters in OCD patients at different visits

Parameters	Mean score low frequency (nu)	Mean score high frequency (nu)
Baseline	49.83±11.2	43.12±16.6
1st follow-up	42.22±10.8	43.9±15.3
1nd follow-up	37.9±10.6	47.8±13.8

The HRV's low-frequency component mostly reflects a person's heart sympathetic drive. In our investigation, we discovered that there was a statistically significant difference between the mean scores of the LF domain of HRV at baseline and second follow-up (p=0.000). Consequently, the sympathetic drive's decline following treatment was shown. The mean LF: HF score, on the other hand, stayed within the normal range even at baseline but fell with time, showing that following therapy, parasympathetic activity increased and sympathetic activity reduced in OCD patients. However, LF HRV did not differ between people with any anxiety illness and controls, according to research by Chalmers *et al*. [11].

However, the authors did not analyze time-domain factors; they only looked at HF-HRV. Our findings differ from those of Slaap *et al*., who looked at the ANS function in 53 patients with panic disorder, 54 patients with OCD, and 24 age-matched healthy controls. The researchers examined frequency-domain characteristics (TP, LF, HF, and LF/HF) and discovered that OCD patients do not have worse HRV than healthy controls. Time-domain and non-linear HRV characteristics were not examined [5].

It should be mentioned that our patients were drug-free when they first joined the program. According to a prior study, OCD and reduced HRV are related, and the effects of psychotropic medicines are mostly responsible for this link [6]. Similar findings were made in a study on the HRV in people with panic disorder, obsessive-compulsive disorder, and healthy volunteers by Slaap *et al*. In his study, OCD patients had a mean LF: HF ratio of 1.8, which was higher than that of the control group, which was 1.5 [5]. Contrary to Kemp *et al*.'s findings, which demonstrated that there was no change in HRV between pre- and post-treatment comparisons that collapsed across a number of therapies, including TCAs, our study's results showed a difference in HRV [12].

The interpretation of our results should consider some limitations. Our study followed the patients for only 6 months duration. Further, follow-ups of more extended periods are required to assess the effects of treatment on autonomic functions to get more reliable data. The sample size was 50. If the same study would have been conducted on a larger number of subjects, the probability of generalizing the results of the study shall increase.

To address the cumulative effect or clarify whether OCD patients with comorbid depression have unique neurocardiac characteristics compared to non-comorbid patients, future studies should include patients with comorbidities.

Table 4: Comparison of mean score of time domain variables at baseline and second follow-up

Parameters	Mean score		Mean difference	Standard Deviation	t-value	p-value
	Baseline	2nd follow-up				
Mean RR	0.861	0.794	0.06	0.18	2.53	0.014*
Mean SDNN	54.3	57.5	3.2	11.39	1.94	0.057
Mean RMSSD	34.1	40.00	5.87	7.26	5.71	0.000**
Mean NN50	129.34	137.72	8.380	46.672	1.270	0.210
Mean PNN50	20.17	22.83	2.66	6.16	3.050	0.004*

*p<0.05=Significant, **p<0.001=Highly significant, *P*>0.05=Non-significant

Table 5: Comparison of mean score of frequency domain variables at baseline and second follow-up

Parameters	Mean score		Mean difference	Standard deviation	t value	p-value
	Baseline	2nd follow-up				
Low frequency	49.83	37.9	11.87	14.46	5.804	0.000**
High frequency	43.12	47.8	−4.710	8.82	−3.772	0.000**
LF: HF Ratio	1.4	0.88	0.59	0.72	5.76	0.000**

*p<0.05=Significant **p<0.001=Highly significant *P*>0.05=Non-significant

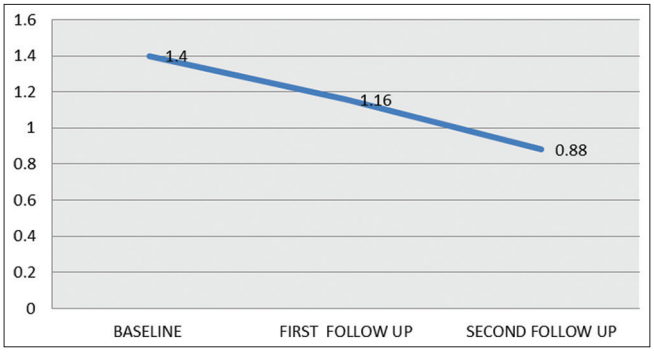

Fig. 1: Comparison of mean score of low frequency: high frequency ratio at different visits

CONCLUSION

In summary, OCD is a prevalent mental illness that can lead to serious disability and an increased risk of cardiovascular disease. Independent of the effects of psychotropic drugs, this elevated risk is most likely due to the disease's fundamental traits. Furthermore, our findings highlight the importance of early OCD treatment in preventing these cardiovascular events in OCD patients.

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AUTHORS CONTRIBUTION

Each author has contributed significantly to all of the following: (1) the idea and design of the study, or the collection, analysis, and interpretation of data; (2) writing the article or critically revising it for important intellectual content; (3) final approval of the version to be submitted; and (4) agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated.

CONFLICT OF INTEREST

Nil.

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