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EVALUATION OF CARDIOVASCULAR AUTONOMIC FUNCTIONS IN MIGRAINE INDIVIDUALS IN TERTIARY CARE HOSPITAL

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Abstract

Introduction: *Migraine is a chronic neurological disorder characterized by recurrent disabling attacks of a headache with heterogeneous characterized by headache and hypersensitivity to sensory stimuli. Migraine attacks can depend upon from multitude of causative factors like diet, stress, fatigue, environmental changes and hormonal changes among others. It causes painful condition where individuals suffer from recurrent episodes of headache, which could be very severe. Pain sensations are discerned at various levels of the nervous system. Migraine as one of the top 20 leading neurological causes of disability according to WHO. About 12% of world's population suffers from migraine and in India about of 1200 million populations there are 150-200 million migraineurs under treatment. About 20% in females and 6% in males has prevalence of migraine. Migraine is define as a heterogeneous disorder where there is variation in attacks in duration, frequency, severity, character and associated with physical and emotional disability. There is anxiety and panic disorder with sympathetic over activity with stress being the most important triggering factor. Migraine is also associated with ischemic stroke. Autonomic nervous system (ANS) plays central role in the cascade of events leading to migraine attack.*

Aim: *The main aim of this study is to testing migraine on cardiac autonomic functions and finding the sympathetic or parasympathetic dysfunction in the heart that relates with the pathogenesis of migraine.*

Material and methods: *This study was carried out in the Dept. of Physiology at Chandulal Chandrakar Memorial Medical College Kachandur, Durg.. In this study total 60 individuals were included from ages 20 to 50 years with 30 in each group. Two groups were included in this study. Migraine fulfilling International Headache Society (IHS) criteria for migraine consists of newly diagnosed cases were included in this study. Participant's individuals were instructed about various manoeuvres that would be employed and allowed to practice these manoeuvres. ECG was acquired by continuous recording for 5 min (320 s) which is needed for short term ECG analysis. Mean respiratory rate (RR), mean HR, total power, low frequency (LF), high frequency (HF), and LF/HF were estimated as proposed by Wang and Mishra(2006). Both the sympathetic and parasympathetic reactivity of ANS test were done with Orthostatic standing test (OST) as well as deep breathing (DB) which tests the intactness of parasympathetic function were performed after giving enough rest in between the tests. Isometric handgrip (IHG) test and cold pressor (CP) test were also performing for evaluating the sympathetic reactivity.*

Result: *Total 30 patients were include in each group with mean age of control group 33.3 ± 5.6 and mean age of case group 30.9 ± 8.6. 24 cases in controls and 26 in cases group there is Female dominant which shown females are more prone to migraine. While compares the resting HR, diastolic blood pressure (DBP) and systolic blood pressure (SBP), between the cases and controls as shown in table no 1. There was not significant between Mean value for HR and mean value of DBP between cases and control. However mean value of SBP showed a P = 0.001 which was highly significant. The mean value of HR, RR interval and total power were also not statistically significant as P > 0.05.*

Conclusion: *Evaluation of cardiovascular functions in migraine reveals sympathetic hypofunction with an intact parasympathetic activity which as indicated by a significant reduction of sympathetic modulation of RR intervals. Better understanding of the role of sympathetic function and its dysfunction may help to prevent or successfully treat migraine and other headaches.*

Keywords: *Migraine, Autonomic function, Sympathetic activity, Headache*

Introduction

Migraine is a chronic neurological disorder with heterogeneous characterized by headache and hypersensitivity to sensory stimuli[i]. According to World health organization (WHO) it is ranked as 7 th most disability causing disorder characterized by chronic neurological disorder associated with autonomic dysfunction[ii,iii]. Migraine attacks can depend upon from multitude of causative factors like diet, stress, fatigue, environmental changes and hormonal changes among others. It causes painful condition where individuals suffer from recurrent episodes of headache, which could be very severe[iv].

Pain sensations are discerned at various levels of the nervous system[v]. Autonomic nervous system (ANS) and nociceptive are two components of an integrated central network which are critical for adaptation and survival in response to internal or external challenges. in brain stem there are various areas like the adrenergic neurons of the rostral ventrolateral medulla, the noradrenergic cell groups of the caudal ventrolateral medulla, ventrolateral pons and locus ceruleus region and periaqueductal gray mater (PAG) which are involved in autonomic, antinociceptive, endocrine and behavioral controls in response to nociceptive inputs[vi].

Migraine as one of the top 20 leading neurological causes of disability according to WHO. About 12% of world's population suffers from migraine and in India about of 1200 million populations there are 150-200 million migraineurs under treatment. About 20% in females and 6% in males has prevalence of migraine[vii]. Migraine is define as a heterogeneous disorder where there is variation in attacks in duration, frequency, severity, character and associated with physical and emotional disability. There is anxiety and panic disorder with sympathetic over activity with stress being the most important triggering factor. Migraine is also associated with ischemic stroke[viii].

Heart rate variability (HRV) is sensitive and non invasive tool capable of assessing individual sympathetic and parasympathetic activity. HRV analysis is used for the evaluation of autonomic regulation of cardiovascular function[ix]. Autonomic nervous system (ANS) plays central role in the cascade of events leading to migraine attack. The main aim of this study is to testing migraine on cardiac autonomic functions and finding the sympathetic or parasympathetic dysfunction in the heart that relates with the pathogenesis of migraine.

Material and Methods:

This study was carried out in the Dept. of Physiology at Chandulal Chandrakar Memorial Medical College Kachandur, Durg. In this study total 60 individuals were included from ages 20 to 50 years with 30 in each group. Two groups were included in this study. Migraine fulfilling International Headache Society (IHS) criteria for migraine consists of newly diagnosed cases were included in this study. In this study participants population were not on any medication for a headache as well as they were screened for normal cardiac, respiratory, renal and hepatic functions. Patients with other causes of a headache, hypertension, diabetes, ischemic heart disease, and neuromuscular disorder were excluded from this study.

Study population were asked ANS questionnaire to assess the autonomic dysfunction. In each group 30 individuals were subjected to autonomic function tests along with resting heart rate (HR) variability as described by Ewing et al[x]. Participant's individuals were instructed about various manoeuvres that would be employed and allowed to practice these manoeuvres. ECG was acquired by continuous recording for 5 min (320 s) which is needed for short term ECG analysis. Mean respiratory rate (RR), mean HR, total power, low frequency (LF), high frequency (HF), and LF/HF were estimated as proposed by Wang and Mishra(2006). Both the sympathetic and parasympathetic reactivity of ANS test were done with Orthostatic standing test (OST) as well as deep breathing (DB) which tests the intactness of parasympathetic function were performed after giving enough rest in between the tests. Isometric handgrip (IHG) test and cold pressor (CP) test were also performing for evaluating the sympathetic reactivity.

Observations and Results:

Total 30 patients were include in each group with mean age of control group 33.3 ± 5.6 and mean age of case group 30.9 ± 8.6. 24 cases in controls and 26 in cases group there is Female dominant which shown females are more prone to migraine. While compares the resting HR, diastolic blood pressure (DBP) and systolic blood pressure (SBP), between the cases and controls as shown in table no 1. There was not significant between Mean value for HR and mean value of DBP between cases and control. However mean value of SBP showed a P = 0.001 which was highly significant. The mean value of HR, RR interval and total power were also not statistically significant as P > 0.05.

Table 1: Comparison of all parameters of case and control (n=30)

Parameters	Controls	Cases	P value
HR/min	78.3±5.9	77.6±7.7	0.808
SBP mmHg	121.9±4.7	111.8±12.7	0.001
DBP mmHg	76.6±4.9	74.1±8.4	0.142
LF	44.1±10.0	40.7±15.2	0.316
HF	55.7±10.3	60.3±15.2	0.293
LF/HF	0.8±0.4	0.8±0.6	0.803
HR mean	78.2±7.7	76.7±10.8	0.562
RR mean	0.8±0.1	0.8±0.1	0.148
Total power	2538.8±1686.7	3019.9±9292.8	0.781

Note: HR: Heart rate, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, LF: Low frequency, HF: High frequency, RR: Respiratory rate.

Table 2 shows comparing increase in HR above the resting value in cases and controls. The P value was highly significant (P = 0.001). There was also an increase

in DPB above the resting value during IHG test which was highly significant (P = 0.010).

Table 2: Comparison of HR and DBP changes during isometric hand grip test between cases and controls

Vitals	Controls	Cases	P value
HR/min	12.2±1.7	8.3±5.4	0.001
DBP mmHg (1 min)	7.8±2.3	6.0±2.7	0.01

Note: HR: Heart rate, DBP: Diastolic blood pressure, SD: Standard deviation

Table 3 shows comparing increase in HR and DPB above the resting value during CP Test in cases and controls. The P value was very highly significant for the increase in HR. therefore increase in DPB above the resting value during CP test was also highly significant (P = 0.004).

Table 3: Comparison of DBP changes during cold pressor test between cases and controls

Vitals	Controls	Cases	P value
HR/min	11.0±1.8	8.2±2.9	<0.0001
DBP mmHg (1 min)	9.7±2.0	7.1±2.8	0.004

HR: Heart rate, DBP: Diastolic blood pressure

Table 4 showing the comparison of parameters obtained in OST namely 30/15 ratio, SPB, DBP difference from the resting value in cases and control. The 30/15 ratio was highly significant (P < 0.01). The SBP and DBP changes during OSTs were also highly significant. Therefore comparison of E/I ratio during DB and SB between cases and control, P value was not statistically significant (P = 0.422).

Table 4: Orthostatic standing test: Comparison of 30/15 ratio, changes in SBP and DBP between cases and controls

Characteristics	Controls	Cases	P value
30/15 ratio	1.1±0.05	1.2±0.3	0.039
SBP mmHg	−2.8±5.5	7.4±4.6	0.001
DBP mmHg	3.8±3.3	−2.3±4.6	<0.0001

SBP: Systolic blood pressure, DBP: Diastolic blood pressure

Discussion:

ANS is strongly influenced by sympathetic and parasympathetic divisions. Dysfunction of autonomic nervous system in migraine has been a subject of considerable interest. Based on vasomotor reactions to temperature changes, cardiovascular tests and responses to pharmacological tests as well as hypo- hyper functioning of both the sympathetic and parasympathetic nervous system have been suggested[5]. There are various studies showing migraine patients generally suggest sympathetic hypo function of sympathetic nervus system with denervation super sensitivity though it. Sympathetic dysfunction plays a major role in the etiopathogenesis of migraine.

Some evidence suggesting that a mild parasympathetic hypo function with denervation super sensitivity may be present in migraineurs [xi]. In comparison to control group Basal heart rate variability (BHRV) was found to be more in migrainous group although statistically non-significant. Increased HRV indicates parasympathetic hyper function or it may be due to a low sympathetic outflow in the pain patients. But 30:15 ratios showed increased values in controls than in migraineurs which suggests a parasympathetic hyperfunction. Therefore all three tests are indicative of the integrity of parasympathetic nervous system[xii,xiii] whereas this study shows a higher parasympathetic tone in migraine patients.

The resting HR measurement signifies the autonomic tone at rest while, the cardiovascular response by stressors which is essentially reflexive in nature, signifies the autonomic reactivity[xiv]. ANS functions providing information on both sympathetic and parasympathetic functions Spectral analysis applied to inter beat interval (HR variability) has been considered as a useful parameter. They give frequency specific contribution to HR power spectrum can be evaluated by FFT. According to study of Mikamo et al[xv] the sympathetic hypofunction by measuring the low concentration of norepinephrine levels among the migraineurs.

However there was no significant change in mean HR and mean RR, when compared to the control groups, in the time domain analysis. This study shows reflex which withdraws parasympathetic and increases sympathetic activity failed to respond decrease in DPB and HR when compared to the controls which is similar to the studied done by Havanka-Kanniainen et al[xvi], Pogacnik et al[xvii] and Mosek et al[10] showed a smaller sympathetic activation in response to stressor. Another physiological stress test which assesses the efferent sympathetic outflow in CP test statistically significant decrease in DPB and the failure to increase the HR. a studied of Rubin et[xviii] al shows no significant difference between migraineurs and controls in response to CP test. Sympathetic dysfunctional in migraineurs is because of decreased norepinephrine (NE) concentration leading to subsequent increase in the co transmitters like dopamine (immediate precursor of NE) prostaglandins, neuropeptide Y and adenosine from the sympathetic neurons. Clinical symptoms of migraine can be linked to these co transmitters[xix,xx].

Conclusion:

Evaluation of cardiovascular functions in migraine reveals sympathetic hypo function with an intact parasympathetic activity which as indicated by a significant reduction of sympathetic modulation of RR intervals. Increases in HF power an indicator of parasympathetic activity that reveals a parasympathetic dominance. Better understanding of the role of sympathetic function and its dysfunction may help to prevent or successfully treat migraine and other headaches.

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