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A study of cardiovascular reflex tests in adults with chronic migraine and chronic tension-type headache

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ABSTRACT

Background: Autonomic function tests can be used by patients with chronic migraine and chronic tension-type headaches (TTH) as a non-invasive, sensitive, and reliable marker for evaluating heart function. Studies have demonstrated sympathetic and parasympathetic dysfunction. Patients with migraines experience sympathetic and parasympathetic nervous system hyperfunction, while tension headache sufferers experience the opposite. **Aims and Objectives:** Parasympathetic reactivity tests will be used in the current study to evaluate the cardiac autonomic functioning in patients with chronic migraine and chronic TTH in the adult age group. **Materials and Methods:** Two groups of headache patients were enrolled: Those with chronic migraine (n=25) and those with chronic TTH (n=25). To conduct statistical analyses, SPSS version 21 was used. For parameters with normal and abnormal distributions, the unpaired t-test and Mann–Whitney *U*-test, respectively, were employed. **Results:** Out of 25 subjects, parasympathetic reactivity tests such as Valsalva ratio (1.38±0.10 vs. 1.49±0.19, P=0.022*) and expiratory-inspiratory ratio (1.18±0.03 vs. 1.25±0.77, P=0.000*) in chronic migraine were significantly decreased as compared to chronic TTH. Lying to standing 30:15 ratio (1.15±0.08 vs. 1.19±0.10, P=0.090) and delta heart rate (14.56±1.39 vs. 14.96±1.43, P=0.320) was decreased in chronic migraine as compared to chronic TTH but was not significant. **Conclusions:** In contrast to the chronic TTH group, the chronic migraine group's total parasympathetic tone was reduced. We therefore draw the conclusion from the findings that regular monitoring of the parasympathetic reactivity can be very helpful in predicting cardiovascular risk for these patients in addition to advising the treatment practices for chronic migraine and chronic TTH, which include regular exercise and medication.

Key words: Cardiac autonomic functions; Sympathetic tone; Parasympathetic tone; Chronic migraine; Chronic tension-type headache; Parasympathetic reactivity; Autonomic nervous system; Autonomic functions; Cardiovascular reflex tests; Autonomic dysfunction

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INTRODUCTION

Millions of individuals worldwide suffer from migraine, a common neurological illness, and chronic tension-type headaches (TTH), whose lifetime frequency in the general population has been shown to vary from 30% to 78% in different studies. Both of these illnesses have been associated with autonomic symptoms.[1] While TTH is often bilateral with an oppressive or tense feel and typically mild to moderate severity that lasts hours to days without remission, migraines are intrinsically unilateral and pulsatile.[1] Although the specific etiology of migraines and tension headaches is unclear, both forms of headache are impacted by a variety of different variables, including bad

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lifestyle choices, stress, and extreme exhaustion. Despite the fact that the specific origin of each form of headache is uncertain, stress is the fundamental cause of both types of headaches. Although a migraine complication has been associated with ischemic stroke,[2] and some studies have shown that migraineurs have a greater risk of stroke and coronary artery disease than healthy people. The relationship between migraines and tension headaches is still mainly unknown.

Since the regulation of the sympathetic and parasympathetic nervous systems is largely unknown, it is still uncertain if the autonomic nervous system (ANS) is involved in migraines or chronic TTH.[3] The development of chronic migraine and chronic tension headache (TTH) is reportedly influenced by both underactive sympathetic and overactive parasympathetic reactivity, as well as tension headaches, according to a small number of case–control studies of cardiovascular function in migraineurs.[4-9] Effective diagnosis, prevention, and/or treatment of migraine and tension headache patients may be accomplished with better knowledge of the sympathetic dysfunction connected to these headache forms. A fundamental phase in the development of migraines is the activation of the trigeminovascular system, which comprises the meningeal vessels, somatic and autonomic nerves, and both.[10]

Although the autonomic functioning of migraineurs and TTH patients was the topic of several investigations, the conclusions were debated and confusing. The major purpose of this research is to determine the kind of dysautonomia by analyzing the status of autonomic control with a cardiovascular reflex test. A number of studies have demonstrated a substantial relationship between unfavorable cardiac events and ANS dysfunction.[11] It is a well-known fact that the balance between sympathetic and parasympathetic activity produces normal heart rate fluctuations. High parasympathetic reactivity is an indication of high adaptation, which shows that the autonomic control systems are operating appropriately. Conversely, low variability suggests aberrant and inadequate flexibility in the ANS.[11] According to the study, the probability of adverse occurrences in individuals with a range of medical disorders has been demonstrated to be highly connected with lower parasympathetic drive. Analyzing parasympathetic reactivity tests is a valuable, reliable, and non-invasive way of diagnosing early autonomic deficits and offers a superior quantitative and qualitative evaluation when compared to traditional examinations. At rest, time and frequency domain indices predominantly reflect vagal modulation, according to the research, which also implies that sympathovagal regulation of cardiovascular function relies on the interplay between the sympathetic and parasympathetic branches of the ANS.[12]

The cause of this autonomic dysfunction is postulated to be activation of the trigeminovascular system, therefore, alleviation of this permanent state of autonomic dysregulation is the primary objective of current treatment strategies for patients with migraine. Migraine leads this state of autonomic dysregulation and restoring parasympathetic reactivity improves autonomic functions. Thus, ruling out autonomic dysfunctions in these patients by cardiovascular reflex tests will helpful in improving parasympathetic tone that might have beneficial effects on recovery of autonomic balance in trigeminovascular system.

In our knowledge, there are few studies that have investigated autonomic dysfunction by standard cardiovascular reflex test in patients of migraine and chronic tension-type headache.

Aims and objectives

Aim of the study is to evaluate the dysfunctions autonomic nervous system in Chronic Migraine and Chronic Tension Type Headache.

The objective of the study was to use Parasympathetic reactivity tests was used to evaluate the cardiac autonomic functioning in patients with chronic migraine and chronic tension-type headache (TTH) in the adult age group.

MATERIALS AND METHODS

After receiving ethical permission from the institutional ethical committee of Naraina Medical College, Kanpur, this cross-sectional research was carried out. December 2022 to March 2023 was the time period for the conduction of study. Before each patient's assessment, a written waiver was obtained from them. Both sexes and adults between the ages of 25 and 45 were represented in this research by 25 patients with chronic migraine and 25 people with chronic TTH. Patients with a history of autoimmune disorders, uncontrolled high blood pressure, diabetes mellitus, heart failure, congenital heart abnormalities, arrhythmias, valvular heart disease, neuropsychiatric illnesses, and other medical comorbidities were excluded from this study.

Study design

Cardiovascular reflex tests - Tests of parasympathetic cardiovascular reflexes

Deep breathing test (DBT) (expiratory-inspiratory [E: I] ratio and delta heart rate [ΔHR])

The basis for this test is the respiratory sinus arrhythmia phenomenon, which is most pronounced at a respiration rate of six breaths per minute. The subject exhales and inhales for 5 s each during each cycle of breathing, and the ratio of the maximum to minimum R-R interval in expiration and inspiration, respectively, is calculated for each cycle. The E: I ratio is the average of these ratios. The E: I ratio for adolescents is ≥1.21.[13]

For an average of six cycles, the ΔHR is recorded for each cycle. The average value is >15 bpm. Age reduces respiratory arrhythmias.[13]

Valsalva manoeuver

The Valsalva maneuver assesses the baroreceptors' performance. Forced expiration against resistance results in an increase in transthoracic pressure, which briefly raises blood pressure (Phase 1). This causes bradycardia, which in turn decreases venous return to the heart, decreasing stroke volume, lowering blood pressure, and triggering a reflex tachycardia (Phase 2). When the maneuver is stopped (Phase 3), there is a further drop in blood pressure because the expansion of the pulmonary vasculature causes an increase in heart rate. Phase 4 baroreceptor activation causes the blood pressure to rise along with bradycardia. By dividing the longest RR interval in Phase 4 by the shortest RR interval in Phase II, the Valsalva ratio (VR) is calculated. Typical ratio is ≥1.21.[13]

Active standing (orthostatic test - 30:15)

Here, the effects of active standing on reflex cardiac autonomic changes are examined. The subject is forced to lie face down. When one immediately assumes an upright position, there is a significant redistribution of blood to the lower limbs, which lowers venous return and stroke volume. In the first 30 s, there is a sudden drop in systolic and diastolic blood pressure as a result of a physiological compensatory response, and the heart rate increases. The response stabilizes after 1–2 min.

The minimum RR interval near the fifteenth beat is equal to the maximum RR interval at around the 30th heartbeat. This is a 30:15 ratio, so the value should be ≥1.04.[13]

Statistical analysis

Data were collected, processed, and analyzed using licensed SPSS version 21.0 statistical software. The data were presented as mean±SD. Statistical significance of the differences was carried out in two different groups of headache patients by unpaired t-test or Mann–Whitney test. For qualitative data, Chi-square test will be applied and Pearson/Spearman correlation will be done. The significance level was set at P<0.05.

RESULTS

This study included 25 patients with chronic migraine and 25 patients of chronic TTH of both sexes aged 25–45 years. The mean age of chronic migraine group was 30.79±3.52 years, whereas the mean age of chronic TTH group was 32.72±5.35 years as shown in Table 1 and Figure 1. The mean BMI of chronic migraine group was 25.10±1.86 kg/m^2, whereas mean BMI of chronic TTH group was 25.19±2.27 kg/m^2 as shown in Table 1.

Table 1: Comparison of basal parameters in chronic migraine and chronic TTH patients

Basal parameters	Chronic migraine Mean±SD	Chronic TTH Mean±SD	P value
Age (years)	30.79±3.525	32.72±5.35	0.106
BMI	25.10±1.86	25.19±2.27	0.882
Mean heart rate	84.08±3.47	79.48±4.11	1.033
Systolic BP	121.96±6.19	118.84±7.73	0.122
Diastolic BP	81.08±3.35	79.92±4.09	0.278

*P<0.05 Significant, TTH: Tension-type headaches, BMI: Body mass index, BP: Blood pressure, SD: Standard deviation

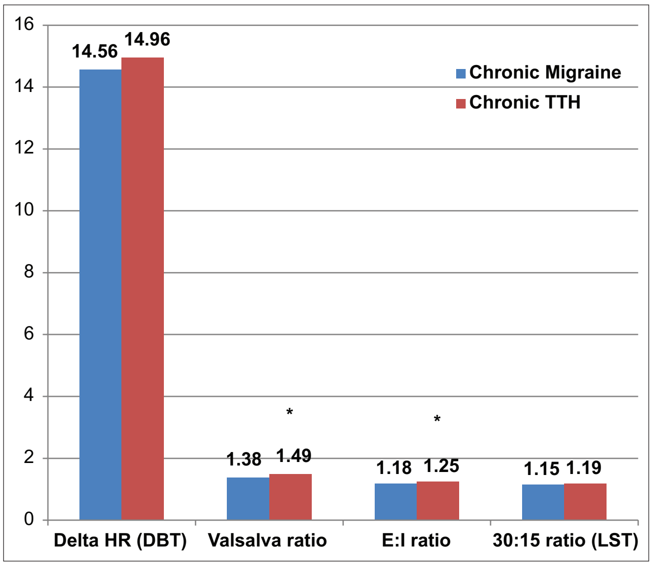

Figure 1: Comparison of parasympathetic reactivity tests between patients of chronic migraine and chronic tension-type headaches (TTH) group. *P<0.05 Significant. Valsalva ratio and expiratory–inspiratory ratio were significantly decreased in chronic migraine as compared to chronic TTH

Comparison of parasympathetic reactivity tests between patients of chronic migraine and chronic TTH group

DBT

(i) Comparison of mean delta HR DBT
The ΔHR in DBT of chronic migraine (mean=14.56±1.39 bpm) as opposed to chronic TTH (mean=14.96±1.43 bpm) patients. The variance was noted to be insignificant (P=0.320) as shown in Table 2 and Figure 1.

(ii) Comparison of mean E: I ratio in DBT
The E: I ratio in chronic migraine was lower as compared to the chronic TTH (1.18±0.03 vs.

Table 2: Comparison of parasympathetic reactivity tests between patients of chronic migraine and chronic TTH group

Parasympathetic reactivity tests	Chronic Migraine Mean±SD	Chronic TTH Mean±SD	P value
ΔHR (DBT)	14.56±1.39	14.96±1.43	0.320
E: I ratio (DBT)	1.18±0.03	1.25±0.77	0.000*
VR	1.38±0.10	1.49±0.19	0.022*
30:15 ratio (LST)	1.15±0.08	1.19±0.10	0.090

*P<0.05 Significant. DBT: Deep breathing test, LST: Lying to standing test, TTH: Tension-type headaches, SD: Standard deviation, E: I: Expiratory inspiratory, ΔHR: Delta heart rate, VR: Valsalva ratio

1.25±0.77) as depicted in Table 2 and Figure 1 which was statistically significant (P=0.000*).

The E: I ratio and ΔHR values were decreased in the chronic migraine group as compared to chronic TTH group.

VR

Table 2 and Figure 1 show comparison in the chronic migraine and chronic TTH (1.38±0.10 vs. 1.48±0.19) and difference was statistically significant (P=0.022*).

Comparison of mean 30:15 ratio (lying to standing test [LST])

The 30:15 ratio in chronic migraine as compared to the chronic TTH (1.15±0.08 vs. 1.19±0.10) was statistically insignificant P=0.090 as depicted in Table 2 and Figure 1.

DISCUSSION

Parasympathetic reactivity tests

DBT

It has two components: (1) E: I ratio and (2) ΔHR

In our study, the E: I ratio was reduced in chronic migraine group (mean=1.15±0.08) as compared to chronic TTH group (mean=1.25±0.77) and was statistically significant (P=0.000). E: I ratio should normally be ≥1.21. Values between 1.11 and 1.20 are considered to be borderline and ≤1.10 are considered to be abnormal.[13]

ΔHR was decreased in chronic migraine (mean=14.56±1.39 bpm) as compared to chronic TTH group (mean=14.96±1.43 bpm). The difference was found to be insignificant (P=0.320). It should normally be ≥15 bpm. Values between 11 and 15 bpm are considered to be borderline and ≤10 bpm are considered to be abnormal.[13]

The E: I ratio and ΔHR values were decreased in the chronic migraine group as compared to chronic TTH group.

Valsalva maneuver - VR

VR was significantly reduced (P=0.022*) in chronic migraine group (mean=1.38±0.10) as compared to chronic TTH group (mean=1.49±0.19). Although both groups displayed values in the normal range, the difference between the two groups VR should normally be ≥1.21. Values between 1.11 and 1.20 are considered to be borderline and ≤1.10 are considered to be abnormal.[13]

LST - 30:15 ratio

The LST 30:15 ratio was reduced in chronic migraine group (mean=1.15±0.08) as compared to chronic TTH group (mean=1.19±0.10). The difference was statistically insignificant (P=0.090). Its normal value should be ≥1.04. Any value between 1.02 and 1.03 is considered borderline and ≤1.01 is considered to be abnormal.[13] Both chronic migraine and chronic TTH groups show mean values in the normal range but chronic migraine group shows a decrease in value as compared to the chronic TTH group.

The chronic migraine group showed decrease in all the above tests for parasympathetic reactivity; this signifies decreased parasympathetic tone depicting autonomic dysfunction when compared to chronic TTH group, but these differences were not statistically significant.

Bearing similarity with our observations, a study by Gass and Glaros[14] examined the cardiovascular reflex test and found a reduced variability of the consecutive RR intervals in migraineurs, which reflects sympathetic overdrive and a reduced parasympathetic tone in migraineurs. In our study, the E: I ratio and ΔHR values which are the parsympathetic reactivity tests were decreased in the chronic migraine patients, and these tests signify reduced parasympathetic tone.

Yerdelen et al.[15] examined a recovery in heart rate after exercise as an index of vagal parasympathetic activity in migraine and tension headache patients (TTH) and controls and showed that sympathetic tone was increased in migraineurs, although parasympathetic function was impaired in migraine as compared to TTH patients. Our study also revealed similar results, VR was significantly reduced in chronic migraine group as compared to chronic TTH group, signifying reduced parasympathetic tone. 30:15 ratio was reduced, although it was not statistically significant.

Peroutka postulated that ANS has a significant role in migraine. He said that there is overwhelming amount of data on the fact that migraineurs have a chronic sympathetic hypofunction. He also said that ANS has a role in many migraine symptoms such as nausea, vomiting, diarrhea, and polyuria.[16,17] Our findings confirmed previous findings of decreased parasympathetic tone causing autonomic dysfunction in migraine patients.

The migraine attacks can be associated with cranial autonomic symptoms (CAS) which are characteristic of trigeminal autonomic cephalalgias (TAC). CAS includes redness of eye, tearing, nasal congestion, facial sweating, and rhinorrhea. The prevalence of CAS in migraine is around 27–73%.[1] The cause of this autonomic dysfunction is postulated to be activation of the trigeminovascular system, and our study also yielded the same results showing decreased parasympathetic tone in patients with Migraine patients.

Migraineurs with CAS have prolonged peripheral sensitization which may trigger the trigeminal autonomic reflex that contributes in the development of autonomic symptoms. These patients have higher rates of photophobia, phonophobia, and osmophobia as compared to migraineurs without autonomic symptoms.[18]

The activation of the trigeminovascular system is thought to be the cause of this autonomic dysfunction; thus, alleviating this permanent state of autonomic dysregulation is the primary goal of current treatment strategies for migraine patients. This state of autonomic dysregulation is caused by migraine, and restoring parasympathetic reactivity improves autonomic functions. Behavioral therapies such as relaxation, biofeedback, and stress management have been proven to be beneficial in the treatment of migraine.[19] Aerobic exercise is also beneficial because aerobic exercise improves the strength of parasympathetic nervous system. Hence, parasympathetic autonomic dysfunction is reversed by aerobic exercise.

Thus, in these patients, parasympathetic reactivity tests will be useful in improving parasympathetic tone, which may have beneficial effects on the recovery of autonomic balance in the trigeminovascular system.

As a result, routine monitoring of parasympathetic reactivity in patients with chronic migraine patients may significantly improve the early identification of risk for stroke and cardiovascular events in the future. Both chronic migraine and chronic TTH patients may utilize it as a screening tool to identify autonomic (parasympathetic) dysfunction and get preventative care or counselling. To have a better understanding, more research with a larger sample size is needed.

Cardiac autonomic reflex tests can be used for screening. Despite being an indirect measure of autonomic functions, these tests are considered the gold standard in autonomic testing. Heart rate variations during deep breathing, the Valsalva maneuver, and lying to standing are indicators of primarily parasympathetic function. Because these tests are non-invasive, safe, clinically relevant, simple to perform, sensitive, specific, reproducible, and standardized, they are regarded as consolidated, gold-standard measures of autonomic function.

Limitations of the study

Limitation of the study was that we have performed this study on a small sample size of 25 patients. For more in depth results, larger sample size can is required.

CONCLUSION

The cardiovascular reflex tests such as parasympathetic reflex activity revealed a statistically significant decrease in the group of individuals with chronic migraines. This showed that the group with chronic migraine had lower overall sympathovagal modulation than the group with chronic TTH. We therefore draw the conclusion from the findings that regular monitoring of the parasympathetic reflex activity can be very helpful in predicting cardiovascular risk for these patients in addition to the standard treatment practices for chronic migraine and chronic TTH, which include regular exercise and medication.

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UBZ- Definition of intellectual content, Literature survey, Prepared first draft of manuscript, implementation of study protocol, data collection, data analysis, manuscript preparation and submission of article; **MNY-** Concept, design, clinical protocol, manuscript preparation, editing, and manuscript revision;
SDH- Design of study, statistical Analysis and Interpretation; **HR-** Review Manuscript; **RB-** Review Manuscript; **NN-** Literature survey and preparation of Figures; **AS-** Coordination and Manuscript revision.

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