How to Cite:
Aaghaz, S., Gupta, S., Alauddin, W., Bashir, M., & Bharti, I. (2022). A study of cardiac autonomic functions in patients with chronic migraine versus chronic Tension-type Headache (TTH) in adults cardiac autonomic functions in headache. *International Journal of Health Sciences*, *6*(S1), 7003–7013. https://doi.org/10.53730/ijhs.v6nS1.6506

A study of cardiac autonomic functions in patients with chronic migraine versus chronic Tension-type Headache (TTH) in adults cardiac autonomic functions in headache

Shams Aaghaz
Post graduate student, Department of Physiology, VMMC & Safdarjung Hospital, New Delhi, India.
Email: drshamsaaghaz@icloud.com

Supriya Gupta
Professor, Department of Physiology, VMMC & Safdarjung Hospital, New Delhi, India.

Waqas Alauddin
Assistant Professor, Department of Physiology, HBTMC & Dr. RN Cooper Hospital, Juhu, Mumbai, India.
Email: dr.waqas7@gmail.com

Musharaf Bashir
Lecturer, Department of Physiology, GMC & SMHS hospital, Srinagar, J&K, India.
Email: dr.musharaf.mb@gmail.com

Imtiyaz Bharti
Post Graduate student, Department of Physiology, VMMC & Safdarjung Hospital, New Delhi, India.
Email: imtiyaz197981@gmail.com

***Abstract*---**Objective: To assess cardiac autonomic functions in patients with chronic migraine and chronic tension-type headache (TTH) in adults using heart rate variability (HRV). Methods: Two groups of patients having chronic migraine (n = 25) and chronic TTH (n = 25) were enrolled for this study. HRV was analyzed with the help of BIOPAC MP150. Statistical analysis was performed with SPSS version 21. Unpaired t-test and Mann-Whitney test were used for parameters with normal and nonnormal distribution, respectively. Results: In chronic migraine group, SDNN (38.90 ± 22.14 vs 41.71 ± 20.81 ms, p=1.000), RMSSD (39.20 ± 25.14 vs 64.11 ± 156.74 ms, p=0.437) and pNN50 (13.37 ± 17.94 vs 18.56 ± 20.42, p=0.496) were

International Journal of Health Sciences ISSN 2550-6978 E-ISSN 2550-696X © 2022.
Manuscript submitted: 18 Feb 2022, Manuscript revised: 09 March 2022, Accepted for publication: 27 April 2022

lower than in chronic THH group. Frequency domain parameters like LF (614.20 ± 604.89 ms^2 vs 595.81 ± 597.08 ms^2, p=0.823) and HF (1190.68 ± 1330.87 ms vs 832.52 ± 1356.70 ms^2, p=0.148 were higher for chronic THH group compared to chronic migraine group. The total power for chronic THH group was higher compared to chronic migraine group (2447.93 ± 2215.03 ms^2 vs 1845.27 ± 1550.38 ms^2, p=0.308). The LF/HF ratio in chronic migraine group was higher than in chronic THH group (1.11 ± 0.69 vs 0.91 ± 0.77, p=0.162). Conclusion: In this preliminary study, it may be concluded that overall sympatho-vagal modulation has decreased in the chronic migraine group compared to the chronic THH group. Thus, regular monitoring of the HRV can be very useful in predicting cardiovascular risk for these patients.

***Keywords*---**TTH, Tension headache, HRV, Migrane, Ischaemic stroke.

Introduction

Migraine is a common neurological disorder affecting millions of people worldwide, and Chronic tension-type headaches (TTH) are also very common, with lifetime prevalence in the general population ranging from 30% to 78% in various studies, both of which have been associated with autonomic symptoms.[1] While migraines are inherently one-sided and pulsatile, and tension-type headache is typically bilateral with an oppressive or tense quality and usually of mild/moderate intensity that lasts hours/days without remission.[1] The etiology of migraines and tension headaches is unknown, but factors such as genetic predisposition, stress, excessive fatigue along with unhealthy lifestyle and environmental factors can contribute to both types of headache.[2] Stress is one of the most important trigger factors in both types of headache. A migraine complication has been observed in association with ischemic stroke[2] and some studies have also shown that the risk of stroke and coronary artery disease is higher in migraineurs than in other healthy people, but its association with tension headaches is largely unknown[3].

The involvement of the autonomic nervous system in both migraines and chronic tension-type headache is still debated as there are still no clear explanations for the modulation of the sympathetic and parasympathetic nervous systems. Only a few case-control studies of cardiovascular function in migraineurs report both underactive sympathetic and overactive parasympathetic reactivity and tension headaches are involved in the development of chronic migraine and chronic tension headache (TTH)[4-9]. A better understanding of sympathetic dysfunction associated with migraines and tension headaches can help effectively diagnose, prevent, and/or treat these headache sufferers. The activation of the trigeminovascular system consisting of somatic and autonomic nerves and meningeal vessels plays a central role in the pathogenesis of migraines.[10]

Although several studies examined the autonomic functions in migraineurs and TTH patients, the results were controversial and inconclusive. The main aim of this study is to assess the status of autonomic regulation through HRV to find out the type of dysautonomia. Several studies have shown a significant correlation between the impairment of the autonomic nervous system and adverse cardiac events.[11] It is well documented fact that the normal heart rate variation depends on the balance between the sympathetic and parasympathetic activity. A high HRV is a sign of good adaptability, which implies proper functioning of the autonomic control mechanisms, and a lower variability indicates abnormal and insufficient adaptability of the ANS.[11] Reduced HRV has been shown to be a powerful indicator of the risk of adverse events in patients with a variety of medical conditions. Compared to conventional tests, HRV analysis is a practical, reproducible and non-invasive method for detecting early autonomic impairments, which enables a better quantitative and qualitative assessment. Literature suggests that sympathovagal modulation of cardiovascular function depends on the interaction between the sympathetic and parasympathetic branches of the autonomic nervous system and at rest, time and frequency domain indices primarily reflect vagal modulation[12]

Material and Methods

This cross-sectional study was carried out after ethical approval by the Institutional Ethical Committee. The study was carried out from November 2019 to April 2021. Written consent was obtained from each patient prior to the examination. This study included 25 patients with chronic migraine and 25 patients of chronic TTH of both sexes and adults aged 30-45 years. Patients with a history of autoimmune diseases, uncontrolled high blood pressure, diabetes mellitus, heart failure, congenital heart defects, arrhythmias, valvular heart disease, neuropsychiatric diseases and other medical comorbidities were excluded from this study.

Study Design

(a) Heart rate variability (HRV) analysis

The protocol of the HRV analysis was explained to them beforehand. The subjects were instructed to lie down on their backs. The electrodes for recording the EKG were placed in lead II and the subjects were allowed to rest for 10-15 minutes, after which the EKG was recorded for 5 minutes. During admission, subjects were instructed to close their eyes and avoid speaking, moving, coughing, and sleeping. Both time and frequency domain parameters were determined.

Time domain analysis: Parameters recorded by time-domain analysis were mean heart rate (MHR), standard deviation of all R-R intervals (SDNN), Square root of mean squared differences of successive NN intervals (RMSSD), number of intervals differing by >50 ms from adjacent interval (NN50), and percentage of NN50 (pNN50).

Frequency domain analysis: Was performed using a nonparametric method of fast Fourier transform (FFT). The power spectrum was subsequently quantified into standard frequency-domain measurements as defined previously,[13] including total variance, LF (0.04–0.15 Hz), HF (0.15–0.40 Hz) and LF/HF. The 0.15-0.4 Hz band of R-R power considered as high frequency (HF) reflects parasympathetic nerve activity to the heart, whereas 0.04-0.15 Hz considered as low frequency (LF) represents sympathetic activity. The ratio of LF: HF represents sympatho-vagal balance.[14]

Statistical Analysis

Data was compiled and entered in MS Excel and analyzed using licensed statistical software SPSS version 21.0. The values were expressed in mean ± SD. Statistical significance of the differences between pre and post intervention were carried out by Paired student t test or non- parametric test. Multivariate analysis was done using regression analysis and Pearson's coefficient of correlation. The level of significance was considered as $P<0.05$.

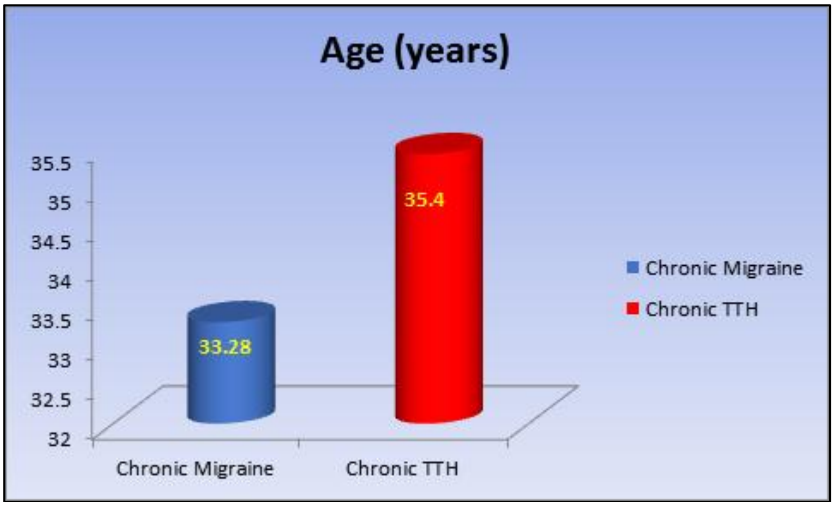
Results

This study included 25 patients with chronic migraine and 25 patients of chronic TTH of both the sexes aged 30-45 years. The mean age of chronic migraine group was 33.28 ± 9.01 years, whereas the mean age of chronic TTH group was 35.40 ± 7.89 years as shown in Table 1 and Figure 1. The mean BMI of chronic migraine group was 22.24 ± 3.30 kg/m^2, whereas mean BMI of chronic TTH group was 22.20 ± 1.88 kg/m^2 as shown in Table 2 and Figure 2.

Table 1
Comparison of mean age between patients of chronic migraine and chronic TTH group

Age (years)	Chronic Migraine	Chronic TTH	p value
Mean ± SD	33.28 ± 9.01	35.40 ± 7.89	0.38

**p value < 0.05 Significant*



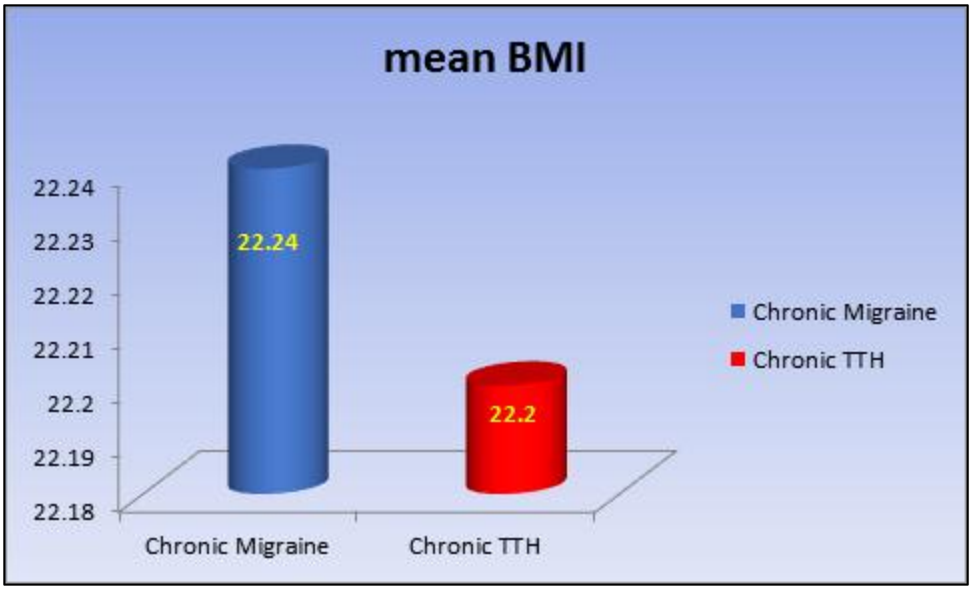
Mean Age (in years) in patients with chronic migraine group was 33.28 and chronic TTH group was 35.4

Figure 1. Comparison of mean Age between patients of chronic migraine and chronic TTH group

Table 2
Comparison of mean BMI between patients of chronic migraine and chronic TTH group

BMI	Chronic Migraine	Chronic TTH	p value
Mean ± SD	22.24 ± 3.30	22.20 ± 1.88	0.962

**p value < 0.05 Significant*



Mean BMI in patients with chronic migraine group was 22.24 and with chronic TTH group was 22.20

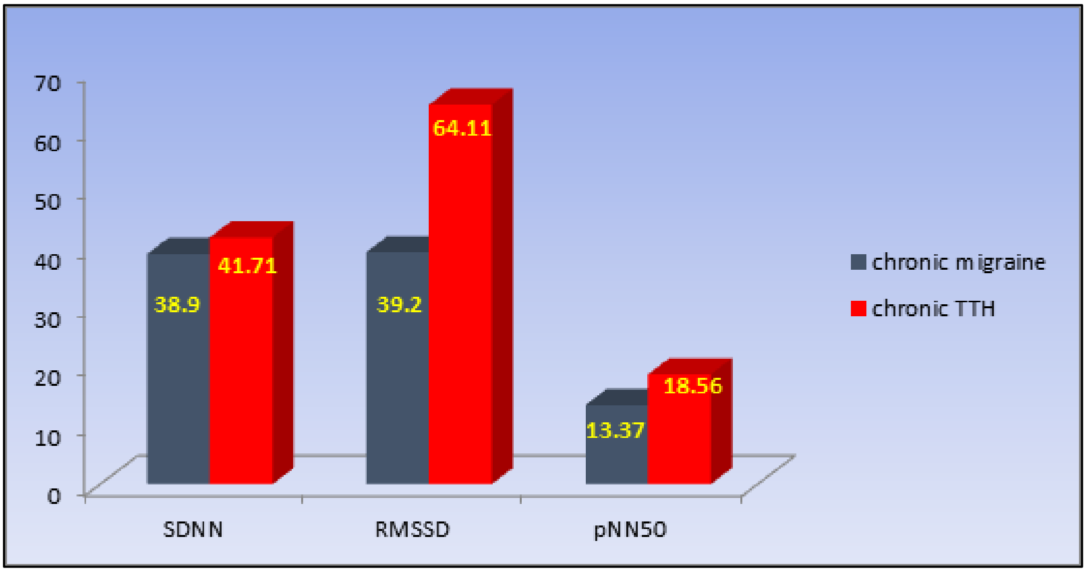
Figure 2. Comparison of mean BMI between patients of chronic migraine and chronic TTH group

Time domain parameters in chronic migraine group, SDNN (38.90 ± 22.14 vs 41.71 ± 20.81 ms, p=1.000), RMSSD (39.20 ± 25.14 vs 64.11 ± 156.74 ms, p=0.437) and pNN50 (13.37 ± 17.94 vs 18.56 ± 20.42, p=0.496) were lower than in chronic THH group as depicted in Table 3 and Figure 3. Frequency domain parameters like LF (614.20 ± 604.89 ms^2 vs 595.81 ± 597.08 ms^2, p=0.823) and HF (1190.68 ± 1330.87 ms^2 vs 832.52 ± 1356.70 ms^2, p=0.148) were higher for chronic THH group compared to chronic migraine group also the total power (TP) for chronic THH group was higher compared to chronic migraine group (2447.93 ± 2215.03 ms^2 vs 1845.27 ± 1550.38 ms^2, p=0.308) as depicted in Table 4 and Figure 4. The LF/HF ratio in chronic migraine group was higher than in chronic THH group (1.11 ± 0.69 vs 0.91 ± 0.77, p=0.162) as depicted in table 4 and figure 5, although these differences were not statistically significant.

Table 3
Time Domain Parameters

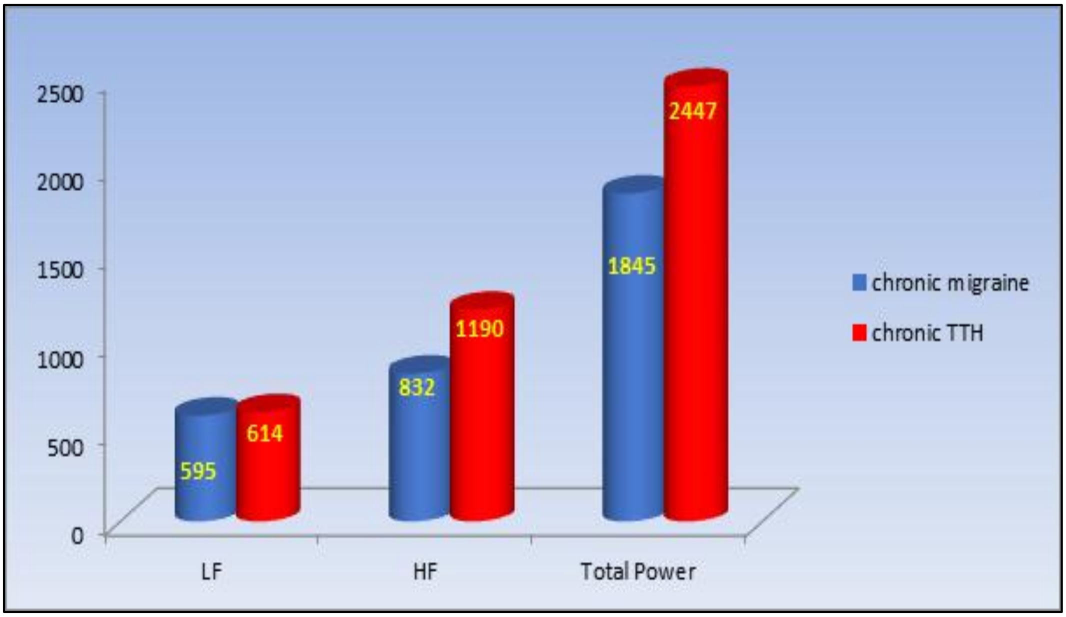
Parameters	Chronic Migraine	Chronic TTH	p Value
SDNN (ms) (Mean ± SD)	38.90 ± 22.14	41.71 ± 20.81	0.645
RMSSD (ms) (Mean ± SD)	39.20 ± 25.14	64.11 ± 156.74	0.437
pNN50 (%)	13.37 ± 17.94	18.56 ± 20.42	0.496

*HRV - heart rate variability; SDNN - standard deviation of the normal to normal R-to-R interval; RMSSD - square root of mean squared differences of successive NN intervals; pNN50; ms - millisecond; *p value<0.05, statistically significant*



SDNN- standard deviation of the normal-to-normal R-to-R interval; RMSSD- square root of mean squared differences ofsuccessive NN intervals; Chronic TTH group showed higher mean SDNN, RMSSD and pNN50 as compared to Chronic migraine group

Figure 3. Comparison of mean SDNN, RMSSD and pNN50 in between patients of chronic migraine and chronic TTH group



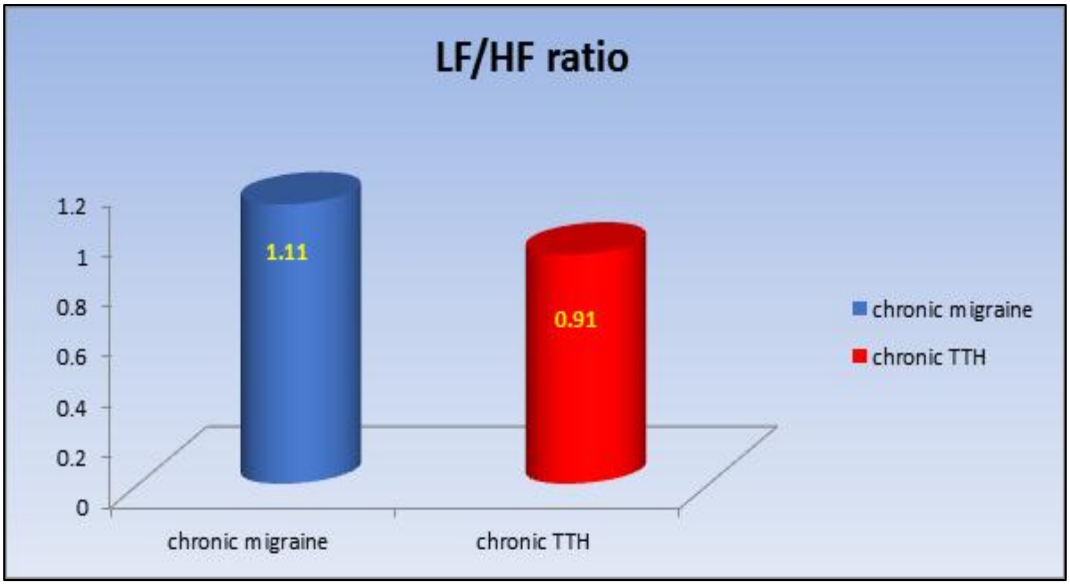
LF – low frequency; HF – high frequency;
Chronic TTH group showed higher mean LF, HF and Total power (TP) as compared to Chronic migraine group

Figure 4. Comparison of mean LF, HF and Total power in between patients of chronic migraine and chronic TTH group

Table 4
Frequency Domain Parameters

Parameters	Chronic Migraine	Chronic TTH	p Value
LF (ms^2) (Mean ± SD)	595.81 ± 597.08	614.20 ± 604.89	0.823
HF (ms^2) (Mean ± SD)	832.52 ± 1356.70	1190.68 ± 1330.87	0.148
LF/HF (ms^2) (Mean ± SD)	1.11 ± 0.69	0.91 ± 0.77	0.162
Total Power (ms^2) (Mean ± SD)	1845.27 ± 1550.38	2447.93 ± 2215.03	0.308

HRV- heart rate variability; LF – low frequency; HF- high frequency; LF/HF – ratio; ms^2 - millisecond squared;
**p value<0.05, statistically significant*



Chronic migraine group showed higher LF:HF ratio as compared to chronic TTH group

Figure 5. Comparison of mean LF/HF between patients of chronic migraine and chronic TTH group

Discussion

The time and frequency domain parameters of HRV, namely SDNN and LF/HF ratio, are widely accepted as accurate predictors of cardiac autonomic status.[15] The standard deviation of the mean of R-R intervals (SDNN) represents a general measurement of autonomic nervous system balance.[15] In our study, chronic migraine group showed a decreased value of SDNN (38.90 ± 22.14 ms) as compared to chronic TTH group (41.71 ± 20.81 ms), the trend being statistically not significant (p=0.645).

RMSSD (root mean square of successive differences), which represents parasympathetic activity, was increased in chronic TTH (64.11 ± 156.74 ms) and 39.20 ± 25.14 ms for chronic migraine) but the difference was not statistically significant (p=0.437).

The percentage of R-R intervals differing from each other by more than 50 ms, or pNN50, predominantly reflects parasympathetic activity. In our study, the chronic migraine group had a decreased value of pNN50 (mean=13.37 ± 17.94) as compared to the chronic TTH group (mean=18.56 ± 20.42), but this was not statistically significant (p=0.496).
The findings in the time domain parameters implies a reduction in vagal activity in chronic migraine. In this study we observed a significant negative correlation between time domain parameters of RMSSD and pNN50 with BMI. This implies that subjects with a low BMI with chronic TTH, there was an increased HRV.

In the frequency domain, spectral analysis of R-R intervals can detect two major components: high-frequency component (HF) of physiologic HRV (spectral components in the band from 0.16 Hz to 0.5 Hz), and the low frequency (LF) component (spectral band from 0.04 Hz to 0.15 Hz). The former is modulated predominantly by the parasympathetic nervous system, whereas the latter is under the influence of both the parasympathetic and sympathetic systems.[16]

In our study, the values in LF band did not show statistically significant difference (p=0.823) between the chronic migraine and chronic TTH group (mean=595.81 ± 597.08 ms^2 and 614.20 ± 604.89 ms^2 respectively). Similarly, HF band also did not show a statistically significant difference (p=0.148) between chronic migraine group (mean=832.52 ± 1356.70 ms^2) and chronic TTH group (mean=1190.68 ± 1330.87 ms^2), though the values in chronic migraine showed a fall from the chronic TTH group. The LH/HF ratio in the present study showed a higher value in the chronic migraine group (mean=1.11 ± 0.69) as compared to the chronic TTH group (mean=0.91 ± 0.77) but it was not statistically significant (p=0.162). This shows that overall, there was a parasympathetic deficit and predominance of the sympathetic modulation of the heart in the chronic migraine group as compared to the chronic TTH group. The total power showed a marked decrease in chronic migraine group (1845.27 ± 1550.38 ms^2) as compared to chronic TTH group (2447.93 ± 2215.03 ms^2) with a statistical insignificant (p=0.308).

Bearing similarity with our observations, a study by Gass et al.[17] examined the HRV and found a reduced variability of the consecutive RR intervals in migraineurs, which reflects sympathetic overdrive and a reduced parasympathetic tone in migraineurs. Yerdelen et al.[18] 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 not impaired in migraine and TTH patients was of the tension-type compared to patients with episodic headache. Our findings correlate with the above studies, that is, fall in SDNN, RMSSD and pNN50 in chronic migraine, but these were statistically not significant.

Thus, regular HRV monitoring of chronic Migraine and Chronic Tension type headache patients may significantly improve the early detection of risk for occurrence of stroke and cardiovascular events in future. HRV can be used as a screening tool to detect autonomic (Sympathetic) dysfunction in both chronic migraine and chronic TTH patients and prophylactically treat or counsel them. Further studies with increased sample size are required to get a deeper insight.

Conclusion

All time domain parameters of the HRV (RMSSD, SDNN, pNN50) showed a decrease in the group of chronic migraines that was not statistically significant. In frequency domain, Total power showed a decrease in patients with chronic migraine. This showed that the overall sympathovagal modulation decreased in the group with chronic migraine compared to the group with chronic TTH. Although HF was reduced, the LF/HF ratio was increased in the chronic migraine group than in the chronic TTH group, suggesting that the sympathetic tone was increased compared to the parasympathetic in chronic migraine. However, this was not significant. Therefore, we conclude from the results that, in addition to the usual treatment practices for chronic migraine and chronic TTH, which include regular exercise and medication, regular monitoring of the HRV can be very useful in predicting cardiovascular risk for these patients.

References

1. Headache Classification Committee of the International Headache Society (IHS) The International Classification of Headache Disorders, 3rd edition. Cephalagia. 2018;38:1-211.
2. Welch KMA. Migraine: a behavioral disorder. Arch Neurol 1987; 44:323-327.
3. Bousser MG, Welch KM. Relation between migraine and stroke. Lancet Neurol 2005; 4: 533-542.
4. Martin R, Ribera C, Molto JM, Ruiz C, Galiano L, MatiasGuiu J. Cardiovascular reflexes in patients with vascular headache. Cephalalgia 1992; 12:360–364.
5. Pogacnik T, Sega S, Peknik B, Kiauta T. Autonomic function testing in patients with migraine. Headache 1993; 33:545–550.
6. Anthony M. Biochemical indices of sympathetic activity in migraine. Cephalalgia 1981; 1:83–89.
7. Schoeman J, De Noordhout AM, Delwaide PJ. Plasma catecholamines in headache: patients, clinical correlations. In: Headache 1985: Proceedings of the Second International Headache Congress; Copenhagen, Denmark, Skargaard Jensen 1985:23–24.
8. Vijayalakshmi I, Shankar N, Bhatia MS, Saxena A, Gupta R. Evaluation of neurophysiological parameters: autonomic status and acute pain perception in migraneurs. Delhi psychiatry journal. 2010;13.79-85.
9. Havanka-Kanniainen H, Tolonen U, Myllylä VV: Autonomic Dysfunction in Migraine: A Survey of 188 Patients. Headache 1988; 28:465-470.
10. Edvinsson L, Uddman R (2005) Neurobiology in primary headaches. Brain Res Rev 48:438–456
11. Maayan C, Axelrod FB, Akselrod S, Carley DW, Shannon CD. Evaluation of autonomic dysfunction in familial dysautonomia by power spectral analysis. J AutonNervSyst1987;21:51-8.
12. Aharon-Peretz J, Harel T, Revach M, Ben-Haim A. Increased sympathetic and decreased parasympathetic cardiac innervation in patients with Alzheimer's disease. Arch Neurol 1992;49:919-22.
13. Lloyd-Jones D, Adams RJ, Brown TM, Carnethon M, Dai S, De Simone G et al. American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Executive summary: heart disease and stroke statistics–2010 update: a report from the American Heart Association. Circulation. 2010;121:948-54.

14. Evrengul H, Tanriverdi H, Kose S, et al. The relationship between heart rate recovery and heart rate variability in coronary artery disease. Ann Noninvasive Electrocardiol. 2006;11(2):154-162.
15. Hirsh JA, Bishop B. Respiratory sinus arrhythmia in humans; how breathing pattern modulates heart rate. Am J Physiol. 1981;241:620–9.
16. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology : "Heart rate variability: standards of measurement, physiological interpretation, and clinical use". Circulation 1996**;** 93**:** 1043.
17. Gass JJ, Glaros AG. Autonomic dysregulation in headache patients. Appl Psychophysiol Biofeedback. 2013; 38:257–263.
18. Yerdelen D, Acil T, Goksel B, Karatas M. Heart rate recovery in migraine and tensiontype headache. Headache. 2008; 48:221–225.