

Comparison of clinical and laboratory parameters in patients with migraine or tension-type headaches: A case-control study

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Ethics Committee Approval

The study was approved by the Clinical Research Ethics Committee of Bolu Abant Izzet Baysal University (Decision No: 2020/224, Date: 13.10.2020).

All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest

No conflict of interest was declared by the authors.

Financial Disclosure

The authors declared that this study has received no financial support.

Published

2021 August 28

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Published by JOSAM

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Abstract

Background/Aim: Migraine and tension-type headaches (TTH) are common headache disorders that are not caused by or attributed to another disorder, and it is important to elucidate the clinical and laboratory features in patients with these diseases. This study aimed to compare the clinical and laboratory features of migraine patients with TTH.

Methods: Nineteen patients with TTH, 73 patients with migraine, and 30 volunteers without headache who visited Bolu Abant Izzet Baysal Training and Research Hospital between January 2018 and December 2018 were included in this case-control study. Patients' Fazekas score, age, gender, muscle score, hemogram parameters, parathyroid hormone, protein C, Protein S, Antithrombin III, low-density lipoprotein cholesterol, vitamin D, folate, vitamin B12 levels, antiphospholipid, anticardiolipin, thyroid autoantibodies, and ANA positivity were noted.

Results: The mean age in the migraine, TTH, and control groups were 43.54 (11.60), 47.05 (12.09), and 47.23 (12.33) years, respectively ($P=0.261$). There was no difference between the groups in terms of gender distribution ($P=0.115$). The Fazekas scores of the migraine (1[0-3]) and TTH groups (1[0-3]) were higher than controls (0[0-2]) ($P<0.001$).

Conclusion: Considering the Fazekas scores and antithrombin III levels in clinical and laboratory evaluation will be useful in the diagnosis and differentiation of migraine and TTH.

Keywords: Hormones, Migraine, Tension-type headache

Introduction

Migraine, which is quite common all over the world, presents with recurrent headaches due to neurovascular pathophysiology and often negatively affects life [1]. Tension-type headache (TTH) is estimated to be more common than migraine; however, it is usually a less severe condition [2]. According to the global burden of disease study, TTH ranked third and migraine ranked sixth among the most common diseases [3]. Migraine is one of the main causes of disability worldwide, especially because of its relatively higher frequency among young adults and middle-aged women. Globally, migraine and TTH are suggested to account for 6.5% of disabled years [3].

Migraine and TTH are headache disorders that are not caused by or attributed to another disorder. Migraine and TTH are primarily clinical diagnoses, and currently, there are no laboratory tests of serum and cerebrospinal fluid samples or imaging studies that can be utilized for the confirmation of the diagnosis of migraine or TTH. Generally, tests are used to exclude possible underlying causes of secondary headaches [4, 5]. However, reports show that some laboratory tests, especially those measuring neuropeptides, may be used as biomarkers in patients with chronic headaches [6]. Therefore, it is important to elucidate the clinical and laboratory features (and the possible relationships between the two) in patients with migraine and TTH, which are the most common types of chronic headaches.

This study aimed to compare the clinical and laboratory features of migraine and TTH.

Materials and methods

In this case-control study, patients with tension headache, migraine, and volunteers without headache (healthy controls) who visited Bolu Abant Izzet Baysal Training and Research Hospital between January 2018 and December 2018 were evaluated.

Patients

Nineteen patients with TTH, 73 patients with migraine, and 30 controls without headache were included. All migraine patients had auras. All patients with TTH were selected consecutively from patients diagnosed in the neurology department. Patients with any chronic disease, psychiatric or neurological disease, and individuals without patient files, and those with missing relevant data were excluded. Healthy volunteers comprised the control group.

Ethics

The Clinical Research Ethics Committee of Bolu Abant Izzet Baysal University (Decision No: 2020/224, Date: 13.10.2020) approved the study. All principals in the Helsinki Declaration and Good Clinical Practice Guideline were followed during the study.

Measurements

The diagnoses of the patients were made in the Neurology Clinic according to international guidelines. In addition to the demographic characteristics of the patients, we determined and recorded Fazekas scores, hemogram parameters, parathyroid hormone (PTH), protein C, Protein S, Antithrombin III, low-density lipoprotein cholesterol (LDL), vitamin D, folate,

vitamin B12 levels, ANA positivity, ENA profile, and antiphospholipid, anticardiolipin, thyroid autoantibody levels.

Evaluation of the Fazekas score

Two experienced neuroradiologists evaluated the White matter hyperintensity (WMH) independently from patients' imaging files via the semi-quantitative Fazekas scale. The Fazekas scale grades WMH on a four-point scale as follows: 0 points: None, 1 point: Dotted foci in the periventricular area, 2 points: Spread to periventricular halo or deep white matter, 3 points: Extension of periventricular WMH into the deep white matter [7].

Statistical analysis

PASS 11 program was used to calculate the sample size. Using the biochemical data gathered from the study conducted by Sarıcam [8], with 0.80 power and 0.05 alpha error, a minimum of 47 patients were required in each group.

SPSS v20 program was used for the data analysis. A normality check was performed using the Shapiro-Wilk test. In the expression of continuous data, we used median, lowest, and highest (min-max), or mean (standard deviation) values according to distribution. The Kruskal Wallis test or ANOVA was used to compare continuous data according to distribution. A pairwise comparison was performed using the Bonferroni test. Categorical data were compared using the Pearson Chi-Square test. *P*-value <0.05 value was considered significant.

Results

Ninety-four (77.0%) patients in the study groups were female, 28 (23.0%) were male and the mean age was 45.0 (11.8) years. Migraine, TTH, and control groups were similar in terms of age and gender distribution. The median Fazekas scores of the migraine and TTH groups were higher compared to the control group (*P*<0.001).

The antithrombin III values of the TTH group were significantly higher when compared to the other groups (*P*=0.011). Other parameters, including ENA profile, antiphospholipid, anticardiolipin, thyroid autoantibodies, and ANA positivity were similar between the groups (Table 1).

Table 1: Comparison of some features of migraine, TTH and the control group

	Control group	Migraine group	TTH group	<i>P</i> -value
Age (year) mean (SD)	47.2 (12.3)	43.5 (11.6)	47.0 (12.0)	0.261*
Gender, n (%)				
Female	19 (20.2%)	59 (62.8%)	16 (17.0%)	0.115*
Male	11 (39.3%)	14 (50.0%)	3 (10.7%)	
Fazekas score, median (min-max)	0 (0-2)	1 (0-3)	1 (0-3)	<0.001
CRP	1.5(0-6.1)	1.1 (0-36.6)	1.3 (0-6.13)	0.638 ^β
WBC (×10 ³ μl)	5.7 (3.4-12.0)	6.2 (3.3-10.3)	6.2 (3.3-12.6)	0.517 ^β
Neutrophil (×10 ³ μl)	3.5 (1.6-8.0)	3.5 (1.3-7.7)	3.7 (1.5-8.7)	0.919 ^β
Lymphocyte (×10 ³ μl)	1.9 (0.6-3.1)	2.0 (0.1-55.2)	1.9 (0.8-3.0)	0.684 ^β
Hemoglobin (g/dl)	14.0 (10.2-17.4)	13.6 (10.1-17.8)	14.3 (11.8-185)	0.132 ^β
Hematocrit (%)	41.7 (31.9-52.2)	40.3 (32.5-49.9)	41.6 (36.5-48.1)	0.116 ^β
MCV (fL)	87 (67-93)	86 (62-96)	86 (75-108)	0.764 ^β
RDW (%)	15.8 (14.7-19.2)	15.4 (12.8-82.7)	15.2 (12.9-17.0)	0.061 ^β
Platelet (×10 ³ μl)	243 (116-362)	252 (16-433)	252 (144-404)	0.674 ^β
MPV (fL)	8.0 (5.8-10.9)	8.1 (4.9-18.9)	7.7 (6.0-11.2)	0.523 ^β
PDW (%)	17.6 (15.6-21.2)	17.3 (9.2-21.3)	17.5 (16.2-20.0)	0.242 ^β
Homocysteine (mmol /L)	12.9 (4.9-25.1)	11.6 (0-33.8)	12.5 (6.5-15.3)	0.837 ^β
Protein C (μg/mL)	114 (26-151)	98 (55-182)	102 (43-145)	0.150 ^β
Protein S (μg/mL)	88 (28-173)	85 (9-134)	75 (48-121)	0.436 ^β
Antithrombin III (μg/mL)	100 (79-133)	100 (74-138)	109 (100-137)	0.011 ^β
LDL (mg/dl)	121 (48-199)	121 (11-223)	134 (52-178)	0.433 ^β
PTH (pg/mL)	62 (10-192)	61 (0-125)	68 (33-142)	0.565 ^β
Vitamin D (ng/mL)	15.0 (5.6-52.3)	10.2 (1.5-112.6)	13.3 (5.8-42.8)	0.062 ^β
Folate (ng/mL)	7.9 (2.3-17.4)	6.8 (0-16.3)	7.8 (4.0-10.5)	0.787 ^β
Vitamin B12 (pg/mL)	288 (151-2000)	317 (135-1383)	335 (208-1588)	0.244 ^β

x: Chi-square test, * ANOVA test, ^β Kruskal Wallis test, CRP: C-reactive protein, WBC: White blood cell, MCV: Mean corpuscular volume, RDW: Red Cell Distribution Width, MPV: Mean Platelet Volume, PDW: Platelet Distribution Width, LDL: Low density lipoprotein, PTH: Parathormone

Discussion

In our study, patients with migraine and TTH and those without headaches were compared in terms of laboratory results. The median Fazekas scores of the migraine and TTH groups were higher compared to the control group, but the distribution of Fazekas scores between migraine patients and those with TTH did not differ significantly.

The Fazekas score is a scoring system that is generally used to evaluate changes in white matter in the examination of cerebrovascular events, and it can be measured via both magnetic resonance imaging and computed tomography [7, 9]. Studies with Fazekas scoring mostly focused on patients with migraines, and it has been shown that white matter changes are greater in these patients when compared to healthy controls without headaches [10-13]. Furthermore, in the few studies in which patients with TTH were evaluated, it has been reported that TTH also causes WMH [14]. For instance, in a study comparing the Fazekas scores of 4 groups (controls, migraine, TTH, and unclassified headaches), patients with TTH had more intense WMH relative to the control group. Interestingly, the study did not report any significant difference in terms of WMH when controls were compared with patients with migraines or unclassified headaches [14]. Conversely, in our study, it was found that the Fazekas scores of both the TTH and migraine groups were significantly higher compared to controls. In this context, we believe that it will be important to include both TTH and migraine groups in future WMH studies. This is especially important since most laboratory tests compared in this study were similar among the groups.

In a study evaluating hematological parameters in patients with migraines, no significant difference was found in WBC, MPV, and platelet counts [8]. Ulusoy et al. [15] reported that MPV values were higher in migraine patients compared to those with TTH and those without headaches. Similarly, some previous studies suggested impairment in platelet functions in the presence of various types of headaches [16, 17]. However, in our study, platelet counts and MPV values were similar in all three groups. Although previous studies suggested that migraine patients and individuals without headaches were similar in terms of platelet count and MPV, some other inflammation markers, such as CRP, were relatively increased when compared to controls [8]. Since the CRP value was not studied in our study, a comparison could not be made in this respect, but the groups were similar in terms of white blood cell count. There is a need for comprehensive studies assessing whether systemic inflammation is triggered during attacks or attack-free periods and whether there are differences in platelet count or MPV levels in migraine patients.

In our study, there was a significant difference between the groups in terms of antithrombin III level, which was higher in the TTH group compared to the other groups. Since some studies reported that headaches may occur due to thrombosis secondary to antithrombin III deficiency [18, 19], future studies may benefit from assessing this particular parameter in migraine patients with migraine or TTH.

Limitations

The main limitations include the retrospective nature of the study, the inability to control all confounding factors and

exclusionary criteria, and the relatively small sample size. Additionally, migraine and TTH patients in this study were treated in a tertiary medical center; therefore, the patient group may have been biased towards a population with relatively severe disease.

Conclusions

Considering the Fazekas scores and antithrombin III levels in clinical and laboratory evaluation will be useful in the diagnosis and differentiation of migraine and TTH. Conducting comprehensive studies evaluating the laboratory parameters of migraine and TTH patients will be useful in elucidating conflicting results.

References

- Burch RC, Buse DC, Lipton RB. Migraine: Epidemiology, Burden, and Comorbidity. *Neurologic Clinics*. 2019;37(4):631-49. doi: 10.1016/j.ncl.2019.06.001.
- Schwartz BS, Stewart WF, Simon D, Lipton RB. Epidemiology of tension-type headache. *JAMA*. 1998;279(5):381-3. doi: 10.1001/jama.279.5.381.
- Global, regional, and national burden of migraine and tension-type headache, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurology*. 2018;17(11):954-76. doi: 10.1016/s1474-4422(18)30322-3.
- Evans RW. Diagnostic Testing for Migraine and Other Primary Headaches. *Neurologic Clinics*. 2019;37(4):707-25. doi: 10.1016/j.ncl.2019.08.001.
- Burch R. Migraine and Tension-Type Headache: Diagnosis and Treatment. *Medical Clinics of North America*. 2019;103(2):215-33. doi: 10.1016/j.mena.2018.10.003.
- Riesco N, Cernuda-Morollón E, Pascual J. Neuropeptides as a Marker for Chronic Headache. *Curr Pain Headache Rep*. 2017;21(4):18. doi: 10.1007/s11916-017-0618-8.
- Fazekas F, Chawluk JB, Alavi A, Hurlig HI, Zimmerman RA. MR signal abnormalities at 1.5 T in Alzheimer's dementia and normal aging. *AJR: American Journal of Roentgenology*. 1987;149(2):351-6. doi: 10.2214/ajr.149.2.351.
- Saricam G. Relationship between migraine headache and hematological parameters. *Acta Neurologica Belgica*. 2020. doi: 10.1007/s13760-020-01362-x.
- Rudilosso S, San Román L, Blasco J, Hernández-Pérez M, Urrea X, Chamorro Á. Evaluation of white matter hypodensities on computed tomography in stroke patients using the Fazekas score. *Clinical Imaging*. 2017;46:24-7. doi: 10.1016/j.clinimag.2017.06.011.
- Kruit MC, Van Buchem MA, Hofman PA, Bakkers JT, Terwindt GM, Ferrari MD, et al. Migraine as a risk factor for subclinical brain lesions. *JAMA*. 2004;291(4):427-34. doi: 10.1001/jama.291.4.427.
- Palm-Meinders IH, Koppen H, Terwindt GM, Launer LJ, Konishi J, Moonen JM, et al. Structural brain changes in migraine. *JAMA*. 2012;308(18):1889-97. doi: 10.1001/jama.2012.14276.
- Hamedani AG, Rose KM, Peterlin BL, Mosley TH, Coker LH, Jack CR, et al. Migraine and white matter hyperintensities: the ARIC MRI study. *Neurology*. 2013;81(15):1308-13. doi: 10.1212/WNL.0b013e3182a8235b.
- Kurth T, Mohamed S, Maillard P, Zhu YC, Chabriat H, Mazoyer B, et al. Headache, migraine, and structural brain lesions and function: population based Epidemiology of Vascular Ageing-MRI study. *BMJ*. 2011;342:c7357. doi: 10.1136/bmj.c7357.
- Honningsvåg LM, Häberg AK, Hagen K, Kvistad KA, Stovner LJ, Linde M. White matter hyperintensities and headache: A population-based imaging study (HUNT MRI). *Cephalalgia*. 2018;38(13):1927-39. doi: 10.1177/0333102418764891.
- Ulusoy EK. Use of MPV and MPV/Plt Ratio in the Differentiation of Migraine and Tension-Type Headache. *Acta Haematologica Polonica*. 2018;49(1):15-9.
- Sarchielli P, Alberti A, Coppola F, Baldi A, Gallai B, Floridi A, et al. Platelet-activating factor (PAF) in internal jugular venous blood of migraine without aura patients assessed during migraine attacks. *Cephalalgia*. 2004;24(8):623-30. doi: 10.1111/j.1468-2982.2003.00717.x.
- Jernej B, Vladić A, Cicin-Sain L, Hranilović D, Banović M, Balija M, et al. Platelet serotonin measures in migraine. *Headache*. 2002;42(7):588-95. doi: 10.1046/j.1526-4610.2002.02145.x.
- Findakly D, Komro J. Not Just Another Headache: Cerebral Venous Sinus Thrombosis in a Patient With Isolated Antithrombin III Deficiency. *Cureus*. 2020;12(5):e8383. doi: 10.7759/cureus.8383.
- Mehta A, Danesh J, Kuruvilla D. Cerebral Venous Thrombosis Headache. *Curr Pain Headache Rep*. 2019;23(7):47. doi: 10.1007/s11916-019-0786-9.

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