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Migraine, Tension-Type Headache and Magnesium in Children

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Abstract

This study aimed to evaluate the relationship between migraine, tension-type headache (TTH), and magnesium (Mg) in order to shed light on possible treatment and prophylaxis options. The file registration information of patients under the age of 18 who presented with headache complaints and were diagnosed with migraine and TTH according to the International Classification of Headache Disorders Criteria was retrospectively scanned. A total of 156 patients, 93 (60%) female and 63 (40%) male, were included in the study. No difference was detected between the Mg, vitamin D, and calcium levels of the migraine group, TTH group, and control group. We think that our study is important for investigating the relationship between migraine, tension headache, Mg, calcium, and vitamin D. It needs to be supported by more clinical and laboratory studies, to enable new treatment perspectives.

Keywords: Migraine, tension-type headache, magnesium

Introduction

Magnesium (Mg) has been used in medical treatments since the 17th century and is recognized as an essential mineral crucial for maintaining numerous physiological processes in the human body[1]. Historically, Epsom salt—primarily consisting of Mg sulfate—was commonly used to address conditions such as abdominal pain, constipation, and muscle cramps. In contemporary medicine, Mg has gained attention for its therapeutic benefits in pain management, largely due to its ability to regulate calcium influx into cells and block N-methyl-D-aspartate (NMDA) receptors[2].

Globally, migraine is one of the most prevalent causes of acute and recurrent headaches. In the United States, it affects approximately 18% of women and 6% of men, with more than half of sufferers reporting impaired productivity in their daily lives[3]. Among children, migraines not only disrupt academic performance, but also significantly diminish family quality of life due to symptoms such as nausea, vomiting, sensitivity to light (photophobia), sensitivity to sound (phonophobia), and occasional visual or sensory disturbances. Mg's role in stabilizing neuronal electrical activity is particularly relevant here[4]. Research has identified a link between migraines and reduced Mg levels in both

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serum and cerebrospinal fluid, suggesting that Mg deficiency could contribute to migraine development. As a result, Mg is often recommended for both prevention and treatment of migraines[5].

Tension-type headache (TTH) represents another frequent primary headache disorder in children. Despite its high occurrence, TTH is often challenging to diagnose in clinical settings due to symptom overlap with migraines. Pediatric patients may exhibit migraine-like symptoms during TTH episodes, and vice versa. While the Mg-migraine connection has been extensively studied, there is limited research on Mg levels in children diagnosed with TTH.

This study aims to explore the relationship between serum Mg levels and two major headache types—migraine and TTH—in pediatric patients, with the goal of supporting the development of improved therapeutic and preventive strategies.

Highlights

- Magnesium (Mg) levels were evaluated in pediatric patients with migraine and tension-type headache (TTH).
- No significant difference in serum Mg levels was observed between migraine, TTH, and control groups.
- The study also assessed calcium and vitamin D levels, with no notable variations among the groups.
- Intracellular Mg and ionized calcium measurements may provide more definitive insights in future studies.
- Findings suggest that serum Mg alone may not be a reliable marker for pediatric primary headaches.
- Larger, prospective studies are recommended to explore the role of Mg, calcium, and vitamin D in headache pathogenesis.

Materials and Methods

This retrospective study was conducted by reviewing the medical records of patients under the age of 18 who presented to the Pediatric Neurology Department of Denizli State Hospital with complaints of headache between March and November 2023 and who were diagnosed with migraine or TTH based on the International Classification of Headache Disorders criteria[6].

The control group (CG) consisted of healthy children with no headache complaints who presented to our hospital for routine pediatric follow-up visits. Data on the patients' demographic characteristics, clinical findings, complete blood count, and biochemical parameters at the time of initial admission were recorded using a standardized data collection form. To minimize potential confounding factors, the CG was selected from the same sociodemographic region as the patient groups. Thus, both patients and controls were comparable in terms of general living conditions, dietary habits, and environmental factors such as sunlight exposure, which may influence vitamin D status. Furthermore, since both patients and controls were recruited during the same time period (March-November 2023), seasonal variations that might affect laboratory parameters such as vitamin D levels were avoided.

Patients with known chronic illnesses, those using dietary supplements, or those receiving any regular medication were excluded from the study.

Ethics Committee approval of the study was obtained with the Pamukkale University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee meeting dated 19.03.2024 and numbered 06. All participants and their legal guardians provided written informed consent prior to inclusion in the study.

It should be noted that only serum Mg levels were assessed, as ionized or intracellular Mg measurements could not be performed due to the unavailability of these assays in our laboratory.

Statistical Analysis

Statistical analyses were performed using the SPSS software package version 22.0 (IBM Corp., Armonk, NY, USA). The distribution of all variables was assessed using the Shapiro-Wilk test to determine whether they followed a normal or non-normal distribution. Variables with normal distribution were expressed as mean ± standard deviation, while categorical variables were presented as frequency and percentage (%).

For comparisons between two groups, the Independent Samples t-test was used for normally distributed variables, and the chi-square test was used for categorical variables. A p-value of <0.05 was considered statistically significant for all analyses.

Additionally, according to the post hoc power analysis, Cohen's d value was found to be 0.566, which indicates a medium effect size. Therefore, it is suggested that the sample size should be increased in future studies to obtain more meaningful and robust results.

Results

A total of 156 patients were included in the study, with a mean age of 13.9±1.9 years. Of these, 93 (59.5%) were female and 63 (40.5%) were male. The study population was divided into three groups: migraine group (MG), TTH group, and CG. No statistically significant differences were found between the groups in terms of age and sex. The mean number of headache days per month was 8.4±4.4 in the MG and 20.6±10.2 in the TTH group. The demographic and clinical characteristics of the study groups are presented in **Table 1**.

Patients in the MG and TTH groups were evaluated according to their clinical characteristics (**Table 2**). Among MG patients, 12 (21%) reported aura prior to headache onset; 7 (12%) described visual aura and 5 (9%) described sensory aura. Regarding headache frequency, 17 (30.4%) reported attacks every 2-3 days, 8 (14.3%) every 4-7 days, 19 (33.9%) once a week, and 12 (21.4%) once every two weeks. In terms of headache laterality, 40 (72%) of MG patients had unilateral headaches, and 11 (20%) had bilateral headaches. The most common location of pain was the temporal region (49 patients, 87%), followed by the frontal region (4 patients, 8%) and diffuse headache involving the entire head (3 patients, 5%).

Table 1.
Demographic and clinical characteristics of the study groups

Variable	MG (n=56)	TTHG (n=50)	CG (n=47)	p-value
Age (± SD)	13.6 (±2.1)	14.4 (±2.04)	13.5 (±1.71)	0.66
Gender, n (%)				0.359
Male	20	19	23	
Female	36	31	24	
Number of headache days per month	8.4 (±4.4)	20.6 (±10.2)	–	<0.001

MG: Migraine group, TTHG: Tension-type headache group, CG: Control group, SD: Standard deviation

Table 2.
Headache characteristics and associated symptoms of the study groups

Variable	Migraine (n=56)	TTHG (n=50)
Pain character (%)		
Unilateral	40 (72)	4 (8)
Bilateral	11 (20)	18 (36)
Occipital region	-	28 (56)
Temporal region	49 (87)	12 (24)
Frontal region	4 (8)	11 (22)
Holocranial	3 (5)	27 (54)
Aura (%)		
Visual	7 (12)	-
Sensory	5 (9)	-
Symptoms (%)		
Nausea	38 (67)	7 (14)
Vomiting	7 (12)	1 (2)
Photophobia-phonophobia (%)		
Both	41 (73)	4 (8)
Photophobia	1 (1.7)	1 (2)
Phonophobia	1 (1.7)	6 (12)
Headache frequency (%)		
Daily	-	26 (52)
Every 2-3 days	17 (30.4)	8 (16)
4-7 days/week	8 (14.3)	6 (12)
Once a week	19 (33.9)	9 (18)
Every 2 weeks	12 (21.4)	1 (2)
Family history (%)		
	43 (76)	11 (22)

TTHG: Tension-type headache group

During headache attacks in the MG group, 38 patients (67%) experienced nausea, 7 (12%) experienced vomiting, and 11 (20%) reported no accompanying symptoms. Both photophobia and phonophobia were reported by 41 (73%) patients; 13 (23%) reported neither, while 1 (1.7%) reported only photophobia and 1 (1.7%) only phonophobia. A family history of migraine (in at least one first-degree relative such as mother, father, or sibling) was reported in 43 patients (76%).

In the TTH group, 26 patients (52%) experienced daily headaches, 8 (16%) every 2-3 days, 6 (12%) every 4-7 days, 9 (18%) once a week, and 1 (2%) once every two weeks. Regarding headache location, 4 patients (8%) had a headache unilateral, 18 (36%) had a headache bilateral, and 28 (56%) had a headache localized in the neck region. Pain was described by 12 patients (24%) in the temporal area, by 11 patients (22%) in the frontal area, and by 30 patients (60%) in the occipital area.

During headache episodes in the TTH group, 7 patients (12%) reported nausea, 1 (2%) reported vomiting, and 42 (84%) reported no accompanying symptoms. Both photophobia and phonophobia were present in 4 (8%) patients. One (2%) had only photophobia. Six (12%) had only phonophobia, and 39 (78%) had neither symptom.

Regarding serum Mg levels, the overall mean Mg level for the entire study group was 2.03±0.14 mg/dL. When the participants were grouped into patient (MG+TTH) and CGs, the mean Mg level was 2.03±0.14 mg/dL in each group (p=0.8). When compared separately, the mean serum Mg levels were 2.02±0.11 mg/dL in the Mg group, 2.04±0.16 mg/dL in the TTH group, and 2.03±0.14 mg/dL in the CG. No statistically significant differences were found among the groups (p=0.75). Laboratory findings of the patients are summarized in **Table 3**.

Table 3.
Comparison of laboratory parameters between the groups

Variable	Migraine (n=56) Mean ± SD	TTHG (n=50) Mean ± SD	Control (n=50) Mean ± SD	p-value
Magnesium	2.02±0.114	2.04±0.168	2.035±0.141	0.750
Calcium	9.34±0.34	9.3±0.46	9.46±0.36	0.252
Vitamin D	11.5±5.2	12.61±5.38	10.7±4.49	0.248
Phosphorus	4.4±0.59	4.05±0.74	4.18±0.684	0.012

SD: Standard deviation, TTHG: Tension-type headache group

Discussion

This research provides valuable insights into the relationship between Mg and the two most prevalent types of pediatric headaches: migraine and TTH. In addition, this study highlights the clinical characteristics of pediatric patients diagnosed with these conditions.

Globally, severe headaches affect nearly 60% of children and adolescents, with migraines accounting for approximately 7.7% to 9.1% of these cases[7]. Similar to chronic illnesses such as rheumatoid arthritis or cancer, migraines in children can lead to reduced academic performance, diminished quality of life, and decreased overall productivity. As such, addressing migraines and other headache disorders through effective treatment strategies is crucial. Despite extensive research, the underlying mechanisms of migraine pathogenesis remain incompletely understood. Among various proposed triggers, hypomagnesemia has been identified as a potential contributor[8,9].

Fila et al.[10] suggested that dietary Mg supplementation and related compounds may help prevent or alleviate migraine attacks by reducing oxidative stress, which is believed to play a role in migraine development. However, the literature on serum Mg levels in migraine sufferers has yielded inconsistent findings. While some researchers have reported that patients with severe migraine attacks tend to exhibit lower Mg levels compared to those with milder symptoms, Talebi et al.[11] also noted significantly reduced serum Mg concentrations in migraine patients relative to healthy controls, and found an association between lower Mg levels and higher attack frequency. Conversely, other studies have observed no significant differences in serum Mg levels between migraine patients and healthy individuals. In this research, similarly, no statistically significant difference was found in serum Mg levels between the MG and controls. This may be partly explained by the fact that only about 1% of total body Mg is present in serum, and our analysis focused exclusively on serum measurements. Although there are studies in the literature that did not find a difference in serum Mg levels between migraine patients and healthy controls, Mg is currently used as one of the leading options in the treatment of migraine. The data from this study may contribute to the existing literature by providing insight into the reconsideration of the use of Mg in migraine therapy.

It is important to note that Mg does not provide direct pain relief but exerts its effects by inhibiting NMDA receptors and regulating calcium ion entry into neurons. This study also assessed serum Mg levels in pediatric patients with TTH. The results revealed no significant differences in Mg concentrations among the TTH, migraine, and CGs. This suggests no apparent variation in serum Mg levels across these cohorts. Nonetheless, future studies utilizing more advanced techniques, such as measuring intracellular Mg concentrations in erythrocytes, may yield more definitive findings.

Mg's role in blocking neuronal calcium influx, has also encouraged researchers to explore calcium metabolism in the context of migraine pathogenesis[12]. A large-scale retrospective study by Yin et al.[13], which analyzed over one million patient records, found an association between hypercalcemia and a 1.8-fold increased risk of migraine. In contrast, this study did not identify any significant differences in serum calcium levels among the migraine, TTH, and CGs. This outcome could be influenced by several factors, including the relatively small sample size, the timing of blood sample collection (outside of headache episodes), and the reliance on serum rather than ionized calcium measurements.

Another notable aspect of this study was the evaluation of vitamin D levels, which are known for their anti-inflammatory, antioxidant, and neuroprotective effects, as well as their role in calcium homeostasis. Existing randomized controlled trials on this topic have produced conflicting results. For example, a study of 73 migraine patients found no significant difference in vitamin D levels between patients and controls. However, Cayir et al.[15] in a study conducted in Türkiye, reported that vitamin D supplementation in combination with standard migraine therapy reduced migraine attack frequency[14]. Another local study observed higher vitamin D levels in healthy controls compared to migraine patients[16]. In our study, no significant differences were detected in vitamin D levels across the patient and CGs.

Study Limitations

This study has several limitations. First, blood samples were collected at the time of diagnosis rather than during active headache episodes. Additionally, serum calcium rather than ionized calcium was measured, and resource constraints prevented the assessment of intracellular Mg levels. Nevertheless, although intracellular Mg concentrations could not be determined, therapeutic decisions regarding Mg supplementation are typically based on serum Mg levels. Furthermore, data on lifestyle factors such as sunlight exposure and physical activity, which may affect vitamin D status, were not adequately documented.

Conclusion

In conclusion, we believe that our study is valuable in investigating the relationship between migraine TTH, and the levels of calcium, Mg, and vitamin D. Although our sample size is limited, we hope our findings will contribute to future research in this field. Further clinical and laboratory studies are needed to clarify these relationships and develop new treatment perspectives.

Ethics

Ethics Committee Approval: Ethics Comittee approval of the study was obtained with Pamukkale University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee meeting dated 19.03.2024 and numbered 06.

Informed Consent: All participants and their legal guardians provided written informed consent prior to inclusion in the study.

Footnotes

Author Contributions: Barin GG: Concept, Design, Data Collection or Processing, Analysis or Interpretation, Literature Search, Writing; Acer H: Concept, Design, Data Collection or Processing, Analysis or Interpretation, Literature Search, Writing.

Conflict of Interest: The authors declare no conflicts of interest.

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