

Evaluation of The Relationship Between the Frequency of Attacks and Vitamin Levels in Patients Admitted to The Emergency Department With Migraine Headache

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Abstract

Introduction: Migraine is a common multifactorial, neurovascular primary headache disorder that develops due to the increased excitability of the central nervous system (CNS) and causes limitations in the quality of life of individuals. In this study, it was aimed to evaluate the relationship between the frequency of attacks and vitamin levels of patients who had migraine attacks and presented to the emergency department with a migraine attack. Method: The study is a retrospective cross-sectional study. 54 patients who were diagnosed with migraine headache according to the International Headache Classification between January 1, 2019, and January 1, 2020, in the Emergency Medicine clinic of Yozgat Bozok University (Group 1). There was no history of systemic diseases such as diabetes mellitus, hypertension, heart disease, or goiter. The control group consisted of individuals who were examined for a general medical examination during the same period, whose migraine history was not in their anamnesis and history, and who did not receive vitamin supplements (Group 2). Mann-Whitney U test was used in statistical evaluations according to the status of the statistically nonparametric variables and the correlated variables were categorical (nominal or ordinal) and numerical independent group. Spearman rank correlation method was used in nonparametric data for correlations between data. The results were evaluated for a significance level of $p < 0.05$. Results: A total of 51.4% ($n = 54$) migraine patients (Group 1) and 48.6% ($n = 51$) healthy control group (Group 2) were included in the study. Of group 1 patients, 85.7% ($n = 46$) were female and 14.3% ($n = 8$) were male. Vitamin B12, Folate and Vitamin D levels were significantly lower in Group 2 (< 0.05). While there was a moderate negative correlation with vitamin D level, there was a weak negative correlation with vitamin B12 and Folate parameters (< 0.05). Vitamin D level was found to be significantly lower in migraine patients with aura in the migraine patient group (< 0.05). Conclusion: Especially vitamin D, vitamin B12, and folate levels have an important place among the causes of migraine headaches. Besides, we think that low Vitamin D level is important in migraine-type with aura. Therefore, prospective studies are needed, especially on vitamin D and migraine subgroups.

Key words: vitamin D, vitamin B12, Migraine, emergency department

Introduction

Migraine is a common multifactorial, neurovascular primary headache disorder that develops due to the increased excitability of the central nervous system (CNS) and causes limitations in the quality of life of individuals¹. Although the pathogenesis of migraine remains uncertain, basically; It is a result of a complex neurovascular imbalance with stimulation of central pain pathways². Nausea, vomiting, and headache accompanied by light sensitivity are more common in females³. In approximately 25% of migraine patients, temporary visual, sensory or speech-related neurological dysfunction findings, called the aura, appear before the onset of pain^{4,5}.

Although drugs such as anticonvulsants and beta-blockers have been used in the treatment of migraine so far, magnesium and vitamin groups have also been used as prophylactic treatments⁶. It is emphasized that vitamin D deficiency is associated with many painful disorders including headaches⁷. In the literature, vitamin B12 used in migraine dis-

ease is effective in pain transmission, hyperalgesia, chronic pain, inflammation, central sensitizing pathways caused by nitric oxide (NO). It is emphasized that it is a NO scavenger⁸. Although vitamin levels are considered separately in the treatment of migraine disease, studies investigating the frequency of migraine and vitamin levels are limited in the literature.

In this study, it was aimed to evaluate the relationship between the frequency of attacks and vitamin levels of patients who had migraine attacks and presented to the emergency department with a migraine attack.

Method

GPower 3.1 software (Universität Kiel, Kiel, Germany) was used to clarify the adequacy of the sample size in all calculations for this study before data collection. Type 1 was determined as 51 people for both groups (healthy control and patient group) with $\alpha 0.05$ error and 85% power analysis. The

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Table 1. Vitamin level analysis between groups

| Group | Calcium | Magnesium | Phosphorus | Folate | B12 vitamin | vitamin D |
|------------------|----------|-----------|------------|----------|-------------|------------|
| Group 1(mean±sd) | 9,51±,43 | 1,92±,14 | 3,37±,60 | 5,44±1,7 | 322,1±123,2 | 11,99±7,74 |
| Group 2(mean±sd) | 9,49±,37 | 1,95±,19 | 3,39±,57 | 8,18±4,4 | 439,1±152,7 | 16,47±5,6 |
| P value | 0,814 | 0,447 | 0,883 | 0,012* | 0,003* | 0,010* |

As statistical analysis, Mann-Whitney U test was used. * sign = $p < 0.05$ was considered significant.

study is a retrospective cross-sectional study. 54 patients who were diagnosed with migraine headache according to the International Headache classification between January 1, 2019, and January 1, 2020, in the Emergency Medicine clinic of Yozgat Bozok University (Group 1). There was no history of systemic diseases such as diabetes mellitus, hypertension, heart disease, or goiter. The control group consisted of individuals who were examined for a general medical examination during the same period, whose migraine history was not in their anamnesis and history, and who did not receive vitamin supplements (Group 2). The study was approved by the local ethics committee.

Statistical analysis

In statistical analysis; We analyzed our data using the SPSS® 17.0 package program. Kolmogorov-Smirnov test was used for the compatibility of the data to normal distribution. When evaluating the data in the study, if it was qualitative, the Chi-Square test was used. While evaluating the study data, numerical values were expressed as mean \pm standard deviation. Mann-Whitney U test was used in statistical evaluations according to the status of the statistically nonparametric variables and the correlated variables were categorical (nominal or ordinal) and numerical independent group. Spearman rank correlation method was used in non-parametric data for correlations between data. The results were evaluated for a significance level of $p < 0.05$.

Results

A total of 51.4% ($n = 54$) migraine patients (Group 1) and 48.6% ($n = 51$) healthy control group (Group 2) were included in the study. Of group 1 patients, 85.7% ($n = 46$) were female and 14.3% ($n = 8$) were male. The healthy control

group was 72.5% ($n = 37$) women and 27.5% ($n = 14$) men. The mean age of the patients in group 1 was 32.5 ± 11 , and the mean age of the healthy group was 39.2 ± 12 . There was no statistically significant difference between the groups in terms of age factor ($p = 0.507$). While 61.4% ($n = 33$) of the patients described migraine without aura, 38.6% ($n = 21$) had migraine with aura. The mean frequency of the patients applying to the emergency department was 2.3 ± 4.5 days.

Vitamin levels between groups are shown in Table 1. According to this; Vitamin B12, Folate and Vitamin D levels were significantly lower in Group 2 (< 0.05). No statistically significant difference was found between the groups in the laboratory parameters of calcium, magnesium, phosphorus (> 0.05). When the relationship between migraine headache and vitamin levels was evaluated; While there was a moderate negative correlation with vitamin D level, there was a weak negative correlation with vitamin B12 and Folate parameters (< 0.05) (Table 2).

Vitamin D level was found to be significantly lower in migraine patients with aura in the migraine patient group (< 0.05). However, there was no significant difference in other laboratory parameters between migraine with and without aura groups (> 0.05) (Table 3). When the relationship between vitamin levels according to the type of migraine is evaluated; A moderate negative correlation with vitamin D was found ($rs: 0.418$; $p = 0.045$).

When the frequency of presentation according to the gender of the patients who applied to the emergency service with migraine headache symptoms; There was no significant difference in the frequency of admission between the groups (> 0.05). When the frequency of admission was evaluated according to the type of migraine, no statistically significant difference was found between the groups (> 0.05).

Discussion

According to the results we evaluated in our study; It was seen that migraine headache and vitamin levels were affect-

Table 2. Correlation analysis between migraine headache and vitamin levels

| Laboratory Parameters | Corr. Coef. (r) | P value |
|-----------------------|-----------------|---------|
| Vitamin D | -0.415 | 0.012 |
| B12 vitamin | 0.374 | 0.004 |
| Folate | -0.275 | 0.040 |

Spearman Correlation Method was used. The level of significance was considered $p < 0.05$ in all comparisons.

Table 3. Vitamin levels according to aura and non-aura type Migraine groups

| Group | Calcium | Magnesium | Phosphorus | Folate | B12 vitamin | vitamin D |
|--|----------|-----------|------------|---------|-------------|-----------|
| Migraine with aura (mean±sd) | 9,5±0,45 | 1,92±0,15 | 3,2±,58 | 5.3±1.7 | 303.5±107 | 10±7.4 |
| Migraine without aura (mean±sd) | 9,4±0,4 | 1,93±0,12 | 3,48±,65 | 5,5±3,6 | 349.4±142.8 | 14.8±6.8 |
| P value | 0,945 | 0,795 | 0,508 | 0,682 | 0,293 | 0,06* |

As statistical analysis, Mann-Whitney U test was used. * sign =p<0.05 was considered significant

ed by vitamin B12, folate, and vitamin D. It was also associated with the level of vitamin D in the aura type in migraine disease.

Migraine is a heterogeneous disease caused by the interaction of many genetic and environmental risk factors¹⁴. Studies on abnormal vitamin D levels, inflammatory agent production around neurons and cerebrospinal fluid, low serotonin levels, homocysteine, and nitric oxide (NO) have been studied to elucidate the pathogenesis of migraine¹⁵.

Gazerani et al. Emphasized that the use of vitamin D is effective in migraine patients. Besides, they state that it can be used in the treatment where it is effective in periods with aura⁹. Significantly low levels of vitamin D in our study, especially in the type of migraine with aura, support the literature. In our study, vitamin levels were lower than normal limits in both the control group and the patient group, and this lowness was significant in migraine patients. In a study in the literature, it was reported that 40% of migraine patients had vitamin D deficiency¹⁰. However, in another study, it was emphasized that migraine attacks were triggered especially in the winter and spring months. Although our country is exposed to sunlight in latitude and longitude, we think that vitamin D is low due to the low utilization of sunlight as a society. Some studies emphasize that low vitamin D increases migraine attacks¹¹. This literature information supports our study.

Vitamin D is effective against anti-inflammatory cytokines or relieving muscle pain¹². Reducing the pain symptom due to vitamin D use has also been directed to the study of vitamin D in many studies in migraine cases¹³. In our study, magnesium and calcium levels were not found to be significant except for vitamin D. In the literature, it is reported that Magnesium and Calcium are effective in migraine cases like vitamin D in the treatment of migraine. Unlike these studies, we believe that the low vitamin D level associated with our study is one of the main factors, and the Ca and Mg used during the treatment is supportive of vitamin D.

Although the pathophysiological causes that trigger migraine attacks are not fully understood, among the mechanisms that are thought to trigger migraine attacks include increased nitric oxide (NO), neurogenic inflammation, trigeminovascular system activation, vascular dysfunction, nitric oxide (NO) release, and hyperhomocysteinemia¹⁵. Vitamin B12 and folate levels were lower than the healthy con-

trol group. Considering that vitamin B12 somewhat lowers the homocysteine level, low B12 causes high homocysteine, and high NO and migraine attack. However, in our study, the frequency of attacks and in migraine with aura was not associated with B12 and Folate. In our study, although the vitamin levels of the control group and migraine patients were different, there was no correlation with the admission to the emergency service due to the frequency of attacks.

One of the major limitations of our study is that it is retrospective and has a small sample. Consequently, the attacks of the patients could not be evaluated except for emergency service applications.

Conclusions

Especially vitamin D, vitamin B12, and folate levels have an important place among the causes of migraine headaches. Besides, we think that low Vitamin D level is important in migraine-type with aura. Therefore, prospective studies are needed, especially on vitamin D and migraine subgroups.

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