Mean platelet volume and other hematological parameters in pediatric migraine

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Abstract

Introduction: According to our hypothesis, the mean platelet volume (MPV) value in migraine patients should be lower than in healthy individuals due to recurrent neuroinflammation during headache attacks. Therefore, this study aimed to identify differences between MPV and other hemogram parameters between pediatric patients with migraine and a healthy control group.

Material and methods: This study included a total of 80 people, 40 patients and 40 control subjects. Those with hematological diseases, using alcohol or smoking, with malignancy, pregnancy, or with any chronic disease were excluded from the study.

Results: Individuals in the control group were chosen to have the same age and same sex as the patient group ($p = 0.98$). The patient group had statistically significantly higher platelet counts than the control group ($p = 0.043$). MPV was lower in the patient group compared to the control group ($p = 0.001$), but platelet distribution width was higher in the patient group compared to the control group ($p = 0.034$)

Conclusions: Migraine patients in the pediatric period were shown in our study to have low MPV values and elevated platelet counts due to recurrent neuroinflammation. This result shows that inflammation especially plays a vital role in migraine pathophysiology.

Key words: pediatric migraine, platelets, hematological parameters, mean platelet volume

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Introduction

Headache is a health problem known from ancient times, and nearly everyone experiences it at least once in their life-time. It is the commonest cause of presenting to emergency services. The International Headache Society (IHS) has divided headaches into three groups: primary, secondary, and other headaches [1]. Migraine, recurrent headache attacks with stress-type pain, comprises most primary headache classes [2]. The most commonly suggested hypothesis for migraine pathophysiology is the trigeminovascular pathway hypothesis [3]. According to this hypothesis, vasodilation in the meningeal arteries causes the activation of inflammatory neuropeptides and inflammation in the brain tissue, activating the trigeminal system and initiating a vicious cycle. As a result, there is ongoing inflammation in the brain tissue. Neurogenic inflammation causes the release of vasoactive peptides such as neurokinin A, substance P from trigeminal and parasympathetic fibers. These vasoactive peptides release pro-inflammatory mediators such as prostanoids and bradykinin, causing vasodilation and extravasation. Thus, the event cycle of migraine occurs.

It is well known that lymphocytes and other leukocytic serial cells play roles in inflammation. Studies have been

performed recently showing variations related to inflammation of another hematological parameter, mean platelet volume (MPV). MPV is a standard hematological parameter demonstrating platelet functions. It can be easily measured with hemogram tests. Platelets that are more active in metabolic and enzymatic terms and with thrombogenic potential have a larger volume, while they have smaller volumes in situations related to chronic inflammation [4]. Due to the association with neurogenic inflammation, studies have been performed investigating whether there is a correlation between migraine and hemogram parameters. Some studies have identified significant correlations between migraine and MPV, while others have not [5, 6]. The common denominator of these studies is that they have generally been performed in adult patients. There have been few studies with pediatric patients [7].

According to our hypothesis, the MPV value should be lower in migraine patients than in healthy individuals due to recurrent neuroinflammation during headache attacks. Therefore, this study aimed to identify differences between MPV and other hemogram parameters between pediatric patients with migraine and a healthy control group.

Material and methods

This study included a total of 80 children, with 40 patients and 40 control subjects. The patient group was chosen from patients (6–18 years) who attended the Pediatric Neurology Clinic at Mustafa Kemal University School of Medicine, Hatay, Turkey with headache and who received a migraine diagnosis according to the IHS diagnostic criteria [1] (Table I). The control group was chosen from healthy children attending the hospital in the same distributions of gender and age. Those with iron, vitamin B_{12} or folic acid deficiency, with anemia or other hematological diseases, who were using alcohol or smoking, with any malignancy, pregnancy, with any chronic disease (e.g. hypertension, diabetes, pulmonary, renal, liver diseases), with acute or chronic inflammatory disease, or using antibiotics were excluded from the study.

In our study, children's age, gender, ferritin, serum iron levels, iron-binding capacity, vitamin B_{12}, folic acid and hemogram data were obtained from hospital files. In addition, the two groups were compared in terms of hemoglobin (Hb), white blood cell (WBC) count, platelets (PLT), neutrophil (Neu), lymphocyte (Lym), monocyte (Mon), MPV, platelet haematocrit (PCT), platelet distribution width (PDW) values, and neutrophil/lymphocyte (N/L), neutrophil/monocyte (N/M) and lymphocyte/monocyte (L/M) ratios.

For the study, blood samples were taken from arm veins in tubes containing ethylenediaminetetraacetic acid (EDTA) and stored at room temperature. Samples were studied within two hours. Complete blood count, thyroid hormones, routine blood biochemistry, and C-reactive protein results were recorded.

Analysis of data used the IBM SPSS Statistics Version 21 program. Categoric measures were given as number and percentages, while fixed measures used mean ± standard deviation (if necessary, median, min-max). The Kolmogorov-Smirnov test was used to determine whether data had parametric distribution or not. Investigating data with parametric distribution used the t-test, while non-parametric data was compared with the Mann-Whitney U test. Statistically, values of $p = 0.005$ and lower were accepted as significant.

Results

Eighty children were included in the study. Both the patient and the control group included 40 people, with 14 boys and 26 girls in each. The age range in the patient group was 6–18 years, while the age range in the control group was

Table I. Migraine diagnostic criteria

Migraine without aura	Migraine with aura
A. At least five attacks [1] fulfilling criteria B–D	A. At least two attacks fulfilling criteria B and C
B. Headache attacks lasting 4–72 h (untreated or unsuccessfully treated) [2, 3]	B. One or more of following fully reversible aura symptoms: 1. visual 2. sensory 3. speech and/or language 4. motor 5. brainstem 6. retinal
C. Headache has at least two of following four characteristics: a) unilateral location b) pulsating quality c) moderate or severe pain intensity d) aggravation by, or causing avoidance of, routine physical activity (e.g. walking or climbing stairs)	C. At least three of following six characteristics: 1. at least one aura symptom spreading gradually over ≥5 minutes 2. two or more aura symptoms occurring in succession 3. each individual aura symptom lasting 5–60 minutes [1] 4. at least one aura symptom being unilateral [2] 5. at least one aura symptom positive [3] 6. aura accompanied by, or followed within 60 minutes by, a headache
D. During headache, at least one of following: a) nausea and/or vomiting b) photophobia and phonophobia	D. Not better accounted for by another ICHD-3 diagnosis
E. Not better accounted for by another ICHD-3 diagnosis	

ICHD-3 — 3rd edition of the International Classification of Headache Disorders

Table II. Ages and genders of patient and control groups

Parameter	Patients	Controls	p
Age	12.92 ± 3.04	12.8 ± 3.07	0.98
Gender	N (%)	N (%)	
Male	14 (35)	14 (35)	
Female	26 (65)	26 (65)	

6–17 years. There was no significant difference between the patient and control groups regarding age (p = 0.98). The age intervals and gender distributions of both groups are set out in Table II.

The hemogram parameters and N/L, N/M and L/M ratios were compared in the patient and control groups (Table III). While the white blood cell value was slightly higher in the patient group, the hemoglobin value was higher in the control group. Still, there was no significant difference between the patient and control groups regarding hemoglobin and white blood cells (p = 0.181, p = 0.761). The patient group had statistically significantly higher platelet counts than the control group. While the mean platelet count in the patient group was 311.75 ± 82.79 [mean ± standard deviation (SD)], it was 275.52 ± 74.21 (mean ± SD) in the control group (p = 0.043). When the specific parameters of platelets i.e. MPV, PDW and PCT, were compared, MPV was lower in the patient group than the control group (p = 0.001), PDW was higher in the patient group than the control group (p = 0.034), and there was no difference between the two groups in terms of PCT value (p = 0.525). We did not identify any significant difference between the other hemogram parameters. Similarly, the N/L, N/M, L/M and (P/L) ratios were compared between the two groups. The most remarkable difference for these ratio comparisons was for the P/L ratio, but no comparison provided statistically significant results (Table III).

Discussion

Platelets are known to play roles in thrombosis, angiogenesis and inflammation. MPV is a good marker of platelet activation. There is an increase in MPV values in thrombotic and cardiovascular diseases, while a fall occurs in inflammatory situations [4]. Many studies performed in recent years have shown a correlation between platelets and inflammation [8–14]. A common feature of these studies is that they were performed for chronic inflammatory diseases emerging outside the central nervous system (CNS). Among CNS diseases, the correlation between migraine and MPV has mainly been investigated [6, 7, 15]. In these studies, MPV values in migraine cases were higher [15], or not different from [6] those in the control group. Our study identified a statistically significant difference between the MPV values in the patient and control groups (p = 0.001).

Table III. Comparison of hemogram parameters

Parameter	WBC	Hb	PLT	Neu	Lym	Mon	N/L	N/M	P/L	L/M	MPV	PCT	PDW
Patients	7.9 ± 2.3	13.1 ± 1,2	311.7 ± 82.7	4.3 ± 1.6	2.8 ± 1.2	0.5 ± 0.17	1.75 ± 0.89	9.31 ± 4.49	123.5 ± 49.1	5.95 ± 2.4	9.5 ± 0.88	0.291 ± 0.07	16.12 ± 1.87
Controls	7.3 ± 16	13.2 ± 0,8	275.5 ± 74.2	4.1 ± 1.6	2.5 ± 0.4	0.48 ± 0.15	1.75 ± 0.9	8.97 ± 3.35	111.9 ± 33.7	5.62 ± 1.79	10.2 ± 0.9	0.282 ± 0.054	15.99 ± 0.31
p	0.181	0.761	**0.043**	0.698	0.132	0.545	0.977	0.706	0.224	0.499	**0.001**	0.525	**0.034**

WBC — white blood cell; Hb — hemoglobin; PLT — platelets; Neu — neutrophil; Lym — lymphocyte; Mon — monocyte; N/L — neutrophil/lymphocyte; N/M — neutrophil/monocyte; P/L — platelets/lymphocyte; L/M — lymphocyte/monocyte; MPV — mean platelet volume; PCT — platelet haematocrit; PDW — platelet distribution width

This difference was due to the patient group's MPV value being lower than the control group. The previous studies were performed with adult migraine patients. A study of pediatric migraine patients by Poyrazoğlu et al. in 2020 [7] compared a 56-person patient group to a 45-person control group, but found no significant difference between the groups.

In our study, unlike previous studies, the low MPV values in migraine patients were linked to recurrent neuroinflammation during migraine attacks in the brain. Studies investigating MPV association with inflammation have identified that the MPV values were lower than control groups. Two different studies of patients with inflammatory bowel disease showed low MPV and elevated platelet counts [8, 9].

Similarly, our study identified the platelet count as significantly higher compared to the control group. This suggests that the results obtained in our study could be related to continuing inflammation in the brain. Studies obtaining different results about migraine and MPV may be explained by performing studies in adult groups and by results being affected by age and gender differences between the patient and control groups. In addition to many hormonal and immunological agents playing a role in the maturation of thrombopoietic cells [16], thrombopoietin release levels differ between the genders. There are higher levels of thrombopoietin secretion in males, especially [17]. Our study set up our patient and control groups to have exactly the same numbers of male and female individuals in order to prevent MPV ratios from being affected by external factors. Additionally, we were very careful to ensure that the individuals in the control group were the same age as those in the patient group ($p = 0.98$). In both groups, individuals were chosen from among children without anemia and with serum iron, ferritin, folate, vitamin B_{12} and TSH levels within normal limits.

It is known that leukocyte series cells in blood play a leading role in pro-inflammatory and anti-inflammatory mechanisms [18]. Many studies have shown the correlation between L/M, N/M, N/L and P/L ratios and systemic inflammation [19–22]. These studies showed that different ratios were more valuable, but a ratio with a typical value could not be shown. In our study, significant differences were not identified for any of these ratios in the patient and control groups. This result shows that these ratios should be investigated on a disease basis, and that different diseases may provide different results.

Conclusions

Migraine patients in the pediatric period in our study revealed low MPV values and elevated platelet counts due to recurrent neuroinflammation. This shows that inflammation especially plays a vital role in migraine pathophysiology.

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