



Mean Platelet Volume in Children with Chronic Spontaneous Urticaria

Kronik Spontan Ürtikerli Çocuklarda Ortalama Trombosit Hacmi

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ABSTRACT

Objective: It has been suggested that mean platelet volume can be used as a marker of inflammation in some inflammatory diseases. This marker has not been investigated adequately in children with allergic disease. The aim of this study was to evaluate mean platelet volume in children with chronic spontaneous urticaria.

Materials and Methods: Fifty-four children with chronic spontaneous urticaria (26 boys and 28 girls, mean age 13.70±3.66 years) were included in this retrospective study. The demographic characteristics, complete blood count, serum total IgE, erythrocyte sedimentation rate, and skin prick tests results of the patients were recorded. Sixty healthy children were included as the control group. Only complete blood count results of the control group were recorded. Platelet count, mean platelet volume, platelet distribution width, leukocyte count, and hemoglobin values were compared between the two groups. Correlations between mean platelet volume with age, disease duration, atopy, serum total IgE, and erythrocyte sedimentation rate were analyzed in the patient group.

Results: There was no statistically significant difference in terms of age and sex between the two groups (p=0.09, p=0.60, respectively). Mean platelet volume and platelet count in the patient group were significantly higher than those in the control group (p=0.005, p=0.01, respectively). Platelet distribution widths in the patient group were significantly lower than those in the control group (p<0.001). There was no significant difference in leukocyte count and hemoglobin values between the two groups (p>0.05). Mean platelet volumes in the patient group were not correlated with age, disease duration, atopy, serum total IgE, and erythrocyte sedimentation rate.

ÖZ

Giriş: Ortalama trombosit hacminin, bazı inflamatuvar hastalıklarda inflamasyonun bir belirteci olarak kullanılabileceği ileri sürülmektedir. Bu belirteç allerjik hastalığa sahip çocuklarda yeterli kadar çalışılmamıştır. Çalışmanın amacı, kronik spontan ürtikerli çocuklarda ortalama trombosit hacminin değerlendirilmesidir.

Gereç ve Yöntem: Bu retrospektif çalışmaya kronik spontan ürtikerli 54 çocuk dahil edildi (26 erkek, 8 kız, ortalama yaş 13.70±3.66 yıl). Demografik özellikler, tam kan sayımı, total serum IgE, eritrosit sedimentasyon hızı ve deri prik testi sonuçları kaydedildi. Kontrol grubu olarak 60 sağlıklı çocuk dahil edildi. Kontrol grubun sadece tam kan sayımı sonuçları kaydedildi. Her iki grubun trombosit sayısı, ortalama trombosit sayısı, trombosit dağılım genişliği, lökosit sayısı ve hemoglobin değerleri karşılaştırıldı. Hasta grubunda ortalama trombosit hacmi ile yaş, hastalık süresi, deri testi pozitifliği, total serum IgE ve eritrosit sedimentasyon hızı karşılaştırıldı.

Bulgular: İki grup arasında yaş ve cinsiyet açısından istatistiksel olarak anlamlı farklılık yoktu (sırasıyla, p=0.09, p=0.60). Hasta grubun ortalama trombosit hacmi ve trombosit sayısı kontrol grubunkine göre anlamlı olarak daha yüksekti (sırasıyla, p=0.005, p=0.01). Hasta grubun trombosit dağılım genişliği kontrol grubunkine göre anlamlı olarak daha düşüktü (p<0.001). Her iki grubun lökosit sayısı ve hemoglobin sayısı arasında anlamlı farklılık yoktu (p>0.05). Hasta grubun ortalama trombosit hacmi ile yaş, hastalık süresi, deri testi pozitifliği, total serum IgE ve eritrosit sedimentasyon arasında ilişki bulunmadı.

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Conclusion: Mean platelet volumes and platelet counts are increased in children with chronic spontaneous urticaria. However, the mean platelet volume does not appear to be associated with the erythrocyte sedimentation rate and atopy.

Key words: Children, chronic spontaneous urticaria, mean platelet volume, platelet distribution width

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Sonuç: Kronik spontan ürtikerli çocuklarda ortalama trombosit hacmi ve trombosit sayısı artmaktadır. Bununla beraber ortalama trombosit hacmi eritrosit sedimentasyon ve atopiyi gösteren testlerle ilişkili görülmemektedir.

Anahtar kelimeler: Çocuklar, kronik spontan ürtiker, ortalama trombosit hacmi, trombosit dağılım genişliği

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INTRODUCTION

Chronic spontaneous urticaria (CSU) is a chronic inflammatory disease without physical stimulus characterized by itchy and erythematous swellings which last longer than 6 weeks in every day or in every few days (1). It may be accompanied by angioedema. The prevalence of urticaria in general population is estimated to be 1% (2). Although different results have been reported, its incidence in children generally varies between 0.1 and 3% (3). The most-known pathophysiologic factors are infections, auto-reactive mechanisms, foods and drugs (4). However, most causes remain unknown. As in acute urticaria, chronic urticaria significantly adversely affects the quality of life not only in admission to emergency clinics but also in the social life (5).

Platelets are known to aggregate in the site of inflammation and inflammatory cells also accumulate in the target tissue via the mediators secreted by thrombocytes (6,7). Thrombocytes lead to histamine release from both mast cells and basophils and consequently cause allergic inflammation via serotonin secretion (7,8). However, histamine also leads to platelet activation (9). The active role of platelets in both allergic and non-allergic reactions leads to researchers to investigate the thrombocytes activation markers as an alternative inflammatory marker in all inflammatory diseases.

Platelet activation markers such as platelet factor-4, beta-thromboglobulin, P-selectin and platelet aggregation are not routinely measured in patient assessment. In contrast, mean platelet volume (MPV), platelet distribution width (PDW) and platelet count can be used as markers associated with platelet function and activation (7,10-12). These are measured in routine blood counts. Elevated MPV is observed in cases where platelet activation is increased (11,13). Platelet counts, MPV, PDW are much more cost

effective and more available compared to other methods (platelet factor-4, beta-thromboglobulin, P-selectin and platelet aggregation) (11,14).

In recent studies, alterations in MPV as a marker of inflammation have been investigated in allergic and non-allergic disease. However, studies investigating MPV in children with CSU are limited (15). Therefore, we compared MPV, PDW and platelet counts in children with CSU with those in healthy children in this study.

MATERIALS and METHODS

Study Group

This retrospective study included children with chronic urticaria admitted to Ondokuz Mayıs University, Children's Hospital, division of Allergy and Immunology department between December 2012 and December 2015. The diagnosis of CSU was established by pediatric allergist. Diagnosis criterion is the urticaria attacks lasting longer than six weeks without any physical causes (16). Those with inflammatory disease or acute infection were excluded. A total of 54 patients (aged 6-18 years) who met the above-mentioned criteria were enrolled. Symptom durations of the patients were recorded. Control group consisted of sixty healthy children without any chronic inflammatory disease, acute infection or allergic disease. For this type of retrospective study formal consent is not required. The study was approved by the Clinical Research Ethical Committee of Ondokuz Mayıs University.

Laboratory Tests

After establishing CSU diagnosis following a detailed evaluation, complete blood count, serum total IgE and erythrocyte sedimentation rate (ESR) measurements were performed in the patient group. Erythrocyte sedimentation rate (ESR) was used as an inflammatory marker (16). In

control group, only complete blood count was performed. Venous blood was taken into BD vacutainer K2 3.6 mg (Plus blood collection tubes, UK) tube. Complete blood count measurements were performed via Advia 2120 hematology system (Siemens, Germany). Serum total IgE levels were measured using nephelometry method (nephelometry BN2 Siemens, Germany). For erythrocyte sedimentation rate (ESR) measurements, venous blood samples (in fasting state in the morning) were collected into 3.8% Sodium Citrate 4NC tubes and samples were studied in vacuplus ES 120 device (Ankara, Turkey - infrared barrier).

Skin prick test was performed for atopy measurement. Histamine was used as positive control in the skin test. Normal saline was used as negative control. The test was considered positive if the mean diameter of the wheal was at least 3 mm greater than the negative control test after 15-20 minutes (17). The following allergens were used in the skin prick test: tree mix (*Castanea vulgaris*, *Quercus robur*, *Fagus sylvatica* ACE), grass mix (*Anthoxanth odoratum*, *Dactylis glomerata*, *Lolium perenne*, *Phleum pratense* France, *Poa pratensis*), weeds (*Chenopodium album*, *Amaranthus retroflexus*), *Dermatophagoides farinae*, *Dermatophagoides pteronyssinus*, *Alternaria Alternata*, *Aspergillus mix*, *Blattella Germanica*, and cat feathers (Stallergenes SA, 92160 Antony, France).

Two groups were compared in terms of platelet count (PLT), mean platelet volume (MPV), platelet distribution width (PDW), leukocyte (WBC) and hemoglobin (Hb) levels. In patient group, the correlations between MPV and patients' age, the duration of the disease, skin prick test positivity, ESR and IgE levels were analyzed.

Statistical Analysis

Data were analyzed using an IBM SPSS software package (V.21, Chicago, USA). Normality was tested via Kolmogorov-Smirnov testing. T-test was used for the comparison of normally-distributed quantitative data. Non-normally distributed data were analyzed using the Mann-Whitney U test. Since the data were not normally distributed, the relationship between the variables was examined using Spearman correlation analysis. Continued variables were expressed as mean ± standard deviation and median (min-max), categorical variables were expressed as frequency and percent. P value of <0.05 was considered significant.

RESULTS

The mean age of the patients (26 males, 28 females) was 13.7±3.6 years. The mean age in the control group (26 males, 34 females) was 12.4±3.6 years. These two groups did not differ significantly in terms of age and gender (p values were 0.098 and 0.606, respectively) (Table I).

MPV values in the patient group were significantly higher than those in the control group (p=0.005). PLT values in the patient group were significantly higher than those in the control group (p=0.011). PDW values in the patient group were significantly lower than those in the control group (p=0.001). No difference was observed between two groups with respect to WBC and Hb values (p>0.05) (Table II). Spearman correlation test revealed no correlation between MPV and age, symptom duration, ESR, and serum total IgE (Table III). The patients were divided into two groups based on skin test results. Mean MPV value in positive skin prick test group was 7.8±0.9 fL, mean MPV value in negative skin prick test group was 7.4±0.8 fL. No difference was observed between these two groups with respect to MPV values (p=0.243).

DISCUSSION

In our study, we found higher MPV levels and PLT counts but lower PDW in children with CSU than those in healthy controls. In addition, no correlation was observed between MPV and erythrocyte sedimentation rate (ESR),

Table I. Demographic and baseline characteristics of children with CSU

	CSU (n=54)
Age (years) (mean±SD)	13.70±3.66
Male gender, [number (%)]	26 (48.1)
Symptom duration (%)	
6 week-3 month	17 (31.5)
3-6 month	13 (24)
6-12 month	6 (11)
≥12 month	18 (33.5)
Eosinophils (/mm ³) [median (min-max)]	200 (20-700)
Total IgE (IU/mL) [median (min-max)]	125 (2-1320)
Sedimentation (mm/h) [median (min-max)]	12 (3-30)
Atopy in skin prick test [number (%)]	18 (33)

IgE: Immunoglobulin E, CSU: Chronic spontaneous urticaria, SD: Standard deviation.

Table II. The laboratory characteristics of children with CSU and control groups

	CSU group (n=54)	Control group (n=60)	<i>p</i>
MPV (fL) [median (min-max)]	7.40 (6.20-10.20)	7.0 (5.90-9.10)	0.005
Platelets (x10 ³ /μL) [median (min-max)]	324 (173-532)	307.5 (143-497)	0.011
PDW (%) [median (min-max)]	43 (15-64.5)	49.6 (16.6-69.0)	<0.001
WBC (count/μL)	7595 (4460-15300)	7175 (4130-10570)	0.124
Hb (g/dL) (mean±SD)	12.9±1.1	13.0±1.0	0.490

MPV: Mean platelet volume, WBC: White blood cells, PDW: Platelet distribution width, Hb: Hemoglobin, CSU: Chronic spontaneous urticaria, SD: Standard deviation.

Table III. Correlation of mean platelet volume with age, symptom duration, sedimentation, and IgE

	Mean platelet volume	
	<i>r</i> Value *	<i>p</i> Value
Age	0.136	0.149
Symptom duration	0.223	0.105
Sedimentation	0.013	0.938
Total IgE	0.028	0.849

*Spearman correlation was used.

IgE: Immunoglobulin E; *r*: Spearman correlation factor.

serum total IgE and skin test positivity. Different results were obtained in studies investigating platelet counts in patients with CSU. Although there are studies showing increased MPV in adults and children with CSU (11,15), studies showing no changes in the number of platelets in adult patients with CSU are also available (18,19). Kasperska-Zajac et al. observed increases in platelet counts only in adults with severe CSU (12). Similarly, we observed increased platelet counts in children with CSU. This finding is consistent with the results of another study investigating the MPV values in children with CSU (15).

Increased MPV has been reported in adults with CSU (11,18,20). Consistent with the literature, we also found high MPV value in our study. While increase in MPV has been observed in some studies related to chronic inflammatory disease (18,21,22), other studies involving similar disease group revealed reduction in MPV values (23,24). In our patient group, mostly leukocyte count and erythrocyte sedimentation rate (ESR) were studied as a marker of inflammation. Unlike literature, we found that only five out of 54 patients had active inflammation that can be shown with high ESR. Magen et al., found higher C-reactive protein (CRP) and MPV values in autologous serum skin test-positive (ASST-positive) patients with

chronic urticaria than those in autologous serum skin test-negative (ASST-negative) patients and healthy controls (18). Since autologous serum skin test is not routinely recommended (25), it was not studied in our patient group. We did not measure the ESR in controls, but the correlations between ESR and MPV values were analyzed in patient group. We observed no correlation between ESR and MPV in patient group. We compared the leukocyte counts as an inflammatory marker between two groups and no difference was revealed. These findings were not consistent with the literature.

There is one study in the literature investigating the inflammatory role of MPV in children with CSU (15). In this study, although CRP levels were higher in patient group than those in healthy controls, MPV values were found to be significantly lower in the patient group than those in healthy controls. However, this finding was consistent with that related to nonallergic inflammatory disease (23, 24). In another study involving adult patients with CSU, MPV values in the patient group were reported to be higher than those in healthy controls (11). Our results regarding MPV were not consistent with the study involving children with CSU (15). This difference may be due to high one of the conventional inflammatory marker (CRP) was found in patient group than controls in their study.

Studies evaluating the platelet distribution width (PDW), one of the platelet markers in complete blood count, are very scarce in the literature. Vagdatli et al. showed that PDW can also be used as platelet activation marker (13). In a study involving adults with chronic urticaria, increased PDW, MPV, PLT were found in patient group compared to healthy controls, but conventional inflammatory markers were not studied in this study (11). Although Kasperska-Zajac et al. (12), found that increased CRP in patients with chronic urticaria compared to healthy controls, there were

no difference between these groups with respect to PDW, MPV and PLT values. Unlike literature, we found decrease in PDW in children with CSU compared to healthy controls. It has been reported that delays in blood sample examination may lead to reduction in PDW and increase in MPV (13). In this study, blood samples were studied within the first 1 hour. However, in our study, blood samples of patients and controls were studied within the same time. We think that our finding may be significant. Our findings related with PDW have not been previously investigated in children with CSU. Previously, no reduction in PDW has been detected in children with CSU.

The correlation between MPV and atopy has not been investigated yet. In present study, skin prick test was used for atopy measurement. No correlation was found between the presence of atopy and MPV in skin test. We did not find any correlation between serum IgE and MPV either. In a recent study, no correlation was found between atopy and platelet markers other than MPV (26). Comprehensive studies are needed on this issue.

Consistent with the literature, we did not find correlation between MPV and chronic urticaria period (12). The correlation between conventional inflammatory markers and MPV has not been examined sufficiently in patients with chronic urticaria. Kasperska-Zajac et al. did not find any correlation between MPV and CRP (12). Magen et al. detected higher CRP values in ASST-positive patients with chronic urticaria and a positive correlation between "urticaria activity score" (UAS) and MPV (18). Instead of CRP, ESR was studied in our study and for the first time in the literature, we showed that there was no correlation between MPV and ESR in children with CSU. Contradictory results were obtained in studies investigating the correlation between MPV and conventional inflammatory markers in nonallergic inflammatory diseases (27). Therefore, clinical use of MPV is recommended for cardiovascular and hematological diseases rather than inflammatory diseases (28). Further studies are needed to make interpretations on the use of platelet markers in specific allergic diseases.

Recently we have been suggested that MPV can not be used as an indicator of inflammation in children with allergic rhinitis (AR) (29). Allergic rhinitis has less complex pathogenicity and more specifically allergic inflammation compared to CSU. Therefore, we may conclude that MPV can not be used as an inflammatory marker in children with

allergic inflammation. Also, we had not found significant differences between children with AR and healthy controls in terms of MPV (29), whereas we found the increased MPV in children with CSU. This difference may be caused by the complex nature of the pathogenesis of urticaria (16).

Our study has some limitations. Firstly, UAS was not studied. Secondly, CRP values were not available. The relationship between UAS, CRP, ESR and platelets indexes have not been studied yet, in children with CSU. Further studies will shed light to clinicians.

CONCLUSION

As in adults with chronic urticaria, increased MPV can be observed in children with CSU. However, MPV does not appear associated with erythrocyte sedimentation rate and atopy. Further studies are needed to make an inference on platelets markers can be used as inflammatory markers in children with CSU.

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