Original paper

Can mean platelet volume be used as a biomarker for asthma?

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Abstract

Introduction: Platelets play important roles in airway inflammation and are activated in inflammatory lung diseases, including asthma.

Aim: We evaluated the mean platelet volume (MPV), used as a marker of platelet activation, in asthmatic patients during asymptomatic periods and exacerbations compared to healthy controls to determine whether MPV can be used as an indicator of inflammation.

Material and methods: Our patient group consisted of 95 children with exacerbation of asthma who were admitted to our allergy clinic. The control group consisted of 100 healthy children matched for age, gender, and ethnicity. Mean platelet volume values of the patient group obtained during exacerbation of asthma were compared to those of the same group during the asymptomatic period and with the control group. We investigated factors that can affect the MPV values of asthma patients, including infection, atopy, immunotherapy treatment, and severity of asthma exacerbation.

Results: The patient group consisted of 50 (52.6%) boys and 45 (47.4%) girls with a mean age of 125 ±38 months old. Mean MPV values in the exacerbation period, the healthy period, and in the control group were 8.1 ±0.8 fl, 8.1 ±1.06 fl, and 8.2 ±0.9 fl, respectively; there were no significant differences between groups ($p > 0.05$). The severity of asthma, severity of asthma exacerbation, immunotherapy, coinfection, eosinophil count, and IgE level also had no effect on MPV ($p > 0.05$).

Conclusions: Although platelets play a role in the pathophysiology of asthma, MPV measurement is insufficient to detect inflammation through platelets.

Key words: mean platelet volume, asthma, childhood, atopy, immunotherapy.

Introduction

Asthma is the most common chronic inflammatory airway disease in the pediatric population [1, 2]. Chronic inflammation varies due to the severity of disease in the airways of children, which is caused by mediators released from eosinophils, mast cells, macrophages, and neutrophils [1, 3, 4]. Recent studies have shown that platelets also play a role in this inflammation and are activated during inflammatory diseases of the lungs, including asthma [5]. Mean platelet volume (MPV) is an indicator of platelet activation and is correlated with platelet function and activation [6].

Aim

In the present study, we investigated MPV count differences between children with asthma during exacerbation or the asymptomatic period compared to healthy children to determine whether MPV is a useful indicator of inflammation in asthma. In addition, we evaluated the effects of factors, such as immunotherapy, infection, atopy, severity of asthma, and severity of asthma exacerbation, on the MPV values of asthma patients both during periods of exacerbation and remission.

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Material and methods

Patient population, study design, and hospital setting

All of the patients referred to the İzmir Dr Behçet Uz Children's Hospital Allergy Department with exacerbation of asthma were included in our study. Complete blood counts (CBCs) were taken from all of the patients during both exacerbation and asymptomatic periods. Asthma was considered to be under control by the asthma control test at least 3 months after the last exacerbation. Asthma diagnosis, classification, and classification of exacerbation severity were all performed using the Global Strategy for Asthma Management and Prevention guidelines developed by the Global Initiative for Asthma (GINA) [1]. According to GINA guidelines, our cases have been classified as intermittent, mild persistent, moderate persistent and severe persistent asthma. If the patient had intermittent asthma, initial treatment was started from step 1, whereas if the patient had mild persistent asthma, initial treatment was started from step 2, and if the patient had moderate persistent asthma, initial treatment was started from step 3. Patients with severe persistent asthma commenced initial therapy from step 4. Skin prick tests were applied in all of the cases with the same allergens. The study was approved by our local ethics committee.

One hundred healthy children without any chronic diseases, who were referred to our hospital for general medical examination, were chosen as the control group. The mean age and gender ratios were similar between the control group and the study group. Complete blood counts were taken and MPV values were noted. Children who were diagnosed with sepsis, iron deficiency anemia, obesity, hyperlipidemia, diabetes mellitus, hypertension, chronic renal failure, nephrotic syndrome, inflammatory bowel disease or connective tissue disease were excluded from our study as it was previously reported that these diseases affected MPV values.

Skin prick test

Skin prick tests were applied to the anterior surface of the forearm when the subjects were appropriate for testing (e.g. when not taking antihistamines). Skin prick tests for common aeroallergens (*Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*), a mixture of grass pollens (*Lolium perenne*, *Dactylis glomerata*, *Phleum pratense*, *Anthoxanthum odoratum*, *Poa pratensis*, *Festuca elatior*, *Agrostis vulgaris*, *Holcus lanatus*, *Cynodon dactylon*, *Avena sativa*, *Avena fatua*, *Lotus Corniculatus*), a mixture of grain pollens (oats, wheat, barley, corn), a mixture of tree pollens (*Acer pseudoplatanus*, *Aesculus hippocastanum*, *Robinia pseudoacacia*, *Tilia platyphyllos*, *Platanus vulgaris*), weed-mix pollens (*Medicago sativa*, *Trifolium pratense*, *Brassica nigra*, *Urtica dioica*, *Rumex acetosa*), *Alternaria alternaria*, cockroaches (*Blattella germanica*), and cat and dog dander (Stallergenes SA, 92160 Antony, France) were performed using a Stallerpoint device. Histamine (10 mg/ml) and physiological saline were used as positive and negative references, respectively. Skin reactions were evaluated 20 min after the skin test. A positive reaction was characterized as wheal diameter ≥ 3 mm. Atopy was classified as at least one positive reaction to allergen sensitivity in the skin test.

Asthma Control Test

The control of asthma was assessed using the Asthma Control Test (ACT) questionnaire consisting of five questions regarding daytime and nighttime asthma symptoms, rescue medication use, and level of impairment in daily activities due to asthma. An ACT score of 25 points was considered full control, 20–24 points as partial control, and < 20 points as uncontrolled [1].

Counting blood samples

Whole blood count (WBC) was performed via Beckman Coulter LH 780 and blood samples which were anticoagulated with K3EDTA were used. The Coulter principle is volumetric analysis. The cells in suspension pass through a small aperture between two chambers between which there is an electrical current. As each cell passes, it creates an impulse which is considered to be proportional to the volume of the cell detected between the two electrodes. In the LH780 analyzers, particles between two and 20 fl are counted as platelets, with possible extrapolation up to 60.00 fl. A log-normal curve is fitted to these points. The curves have a range of 0–70 fl, and the platelet count and parameters are derived from this curve. The hemoglobin level, WBC, platelet count, and MPV values were recorded for each patient. The reference range for MPV was between 7.0 and 11 fl.

Statistical analysis

The data were primarily evaluated using descriptive statistical methods. For the numerical data, mean and median as measures of central tendency, and standard deviation (SD) and interquartile range (IQR) as measures of spread were used. The Kolmogorov-Smirnov test and the coefficient of variation were used to assess the distribution of the data and histograms, stem and leaf diagrams, and box plot graphs were also used. The numerical data were compared using the Mann-Whitney *U* test and *t*-test, and categorical data were compared using the χ^2 and Fisher's exact test between groups. SPSS 15.0 was used for statistical analyses, and $p < 0.05$ was taken to indicate statistical significance.

Results

In our retrospective cohort study, the study group consisted of 95 children with asthma and the control

group consisted of 100 healthy children with similar age and gender distribution. The study group was composed of 50 (52.6%) boys and 45 (47.4%) girls with a mean age of 125 ±38 months. The median age at hospital admission was 78.5 (IQR 60, min 10, max 168) months and the median of the starting age of the symptoms was 43 (IQR 62, min 1, max 144) months. Cases were classified according to the severity of asthma as mild intermittent (1.1%), mild persistent (37.9%), moderate persistent (58.9%), and severe persistent (2.1%). The median eosinophil count and IgE measurement values were 360 mm^3 (IQR 400, min 0, max 1800) and 340 (IQR 356, min 3, max 3949) IU/ml, respectively. According to skin test results, 64 (67.4%) and 31 (32.6%) patients were atopic and non-atopic, respectively. Sixteen (16.8%) patients were receiving immunotherapy. Asthma exacerbation was mild in 7 (7.4%) patients, moderate in 87 (91.6%), and severe in 1 (1.1%) patient. A diagnosis of coexisting infection was made in 34 (35.8%) cases (Table 1).

Mean MPV counts in the study group during asthma exacerbation and during the asymptomatic period were 8.1 ±0.8 fl and 8.1 ±1.06 fl, respectively, whereas that in the control group was 8.2 ±0.9 fl. There were no significant differences in mean MPV values between the exacerbation period and asymptomatic period (p = 0.62), the exacerbation period and the control group (p = 0.64), and the asymptomatic period and the control group (p = 0.37). However, the platelet counts in the patient group were significant higher during both the exacerbation and asymptomatic periods than that in the control group (p = 0.001) (Table 2).

Various factors, including immunotherapy, infection, atopy, severity of asthma, eosinophil count, and severity of asthma exacerbation had no effect on the MPV values of asthma patients both during periods of exacerbation and remission. Mean platelet volume values were only higher during the asymptomatic period in cases of severe persistent asthma compared to the other asthma groups (p = 0.025) (Table 3).

Discussion

Chronic airway inflammation is detected at the bronchial walls caused by eosinophils, mast cells, macrophages, lymphocytes, and mediators released from some other cells in asthma. Recent studies have shown that platelets play a role in the inflammation during asthma [5, 7–10]. Previous studies in adults have suggested roles of platelet activation in different inflammatory lung diseases, including asthma [11, 12].

Table 1. Demographic characteristics of the study group and control group

Parameter	Study group	Control group	*P*-value
Age [months]	124 (60)*	144 (69)*	0.11
Gender, female *n* (%)/male *n* (%)	45 (47.4%)/50 (52.6%)	52 (52%)/48 (48%)	0.51
Age at disease onset [months]	43 (62)*		
Application age [months]	78.5 (60)*		
Eosinophil count [/mm^3]	360 (400)*		
IgE level [IU/l]	340 (356)*		
Atopy, *n* (%)	64 (67.4)		
Immunotherapy, *n* (%)	16 (16.8)		
Infection, *n* (%)	34 (35.8)		

**Data are shown as means ± standard deviation for normally distributed variables.*

Table 2. Comparison of CBCs in the patient group obtained during exacerbation (group 1) and asymptomatic periods (group 2) with the control group (group 3)

Parameters	*n*	Group 1	*n*	Group 2	*n*	Group 3	Group 1–2 *P*-value	Group 2–3 *P*-value	Group 1–3 *P*-value
MPV [fl]	95	8.1 ±0.8	95	8.1 ±1.06	100	8.2 ±0.9	0.62	0.64	0.37
Plt [× 10^3/µl]	95	321 ±81	95	344 ±89	100	285 ±60	0.015	< 0.001	0.001
Hb [g/dl]	95	12.6 ±1.1	95	12.6 ±1.06	100	12.9 ±0.8	0.832	0.013	0.026
WBC [× 10^3/µl]	95	9.1 (5.6)*	95	8.7 (3.9)*	100	7.4 (2)*	0.02	< 0.001	< 0.001
CRP [mg/l]	95	1.3 (1.5)*	95	0.33 (0)*	100	–	< 0.001	–	–

*Plt – platelet, WBC – white blood cell, Hb – hemoglobin, CRP – C-reactive protein. *Data are shown as means ± standard deviation for normally distributed variables; variables without a normal distribution are shown as the median (interquartile range).*

Table 3. Comparison of the exacerbation and remission MPV values in the patient group in terms of immunotherapy, infection, atopy, eosinophil count, severity of asthma, severity of exacerbation, and number of exacerbations

Parameter		*N* (%)	Exacerbation MPV	Remission MPV	*P*-value
Immunotherapy	Yes	16 (16.8)	8.3 ±0.6	8.2 ±0.9	0.71
	No	79 (83.2)	8.09 ±0.89	8.1 ±1.08	0.49
	P		0.38	0.85	–
Asthma severity	Mild intermittent	1 (1.1)	7.7	7.2	–
	Mild persistent	36 (37.9)	8.1 ±0.8	8 ±0.9	0.38
	Moderate persistent	56 (58.9)	8.1 ±0.89	8.2 ±1.07	0.41
	Severe persistent	2 (2.1)	8.8 ±0.2	10.05 ±1.2	0.33
	P		0.49	0.025	–
Asthma exacerbation severity	Mild	7 (7.4)	8.4 ±0.3	8.01 ±0.5	0.15
	Moderate	87 (91.6)	8.1 ±0.8	8.1 ±1.1	0.44
	Severe	1 (1.1)	7.8	7.9	–
	P		0.26	0.92	–
Infection	Yes	34 (35.8)	8.1 ±0.6	8.1 ±0.89	0.6
	No	61 (64.2)	8 ±0.9	8.2 ±1.1	0.37
	P		0.51	0.76	–
Skin test	Atopic	64 (64.7)	8.2 ±0.9	8.1 ±1.1	0.62
	Non-atopic	31 (32.6)	7.9 ±0.6	8.2 ±0.9	0.08
	P		0.18	0.64	–
Number of asthma exacerbations	< 2	36 (36.7)	8.1 ±1.05	7.9 ±0.9	0.09
	≥ 2	59 (61.2)	8 ±0.7	8.3 ±1.1	0.102
	P		0.63	0.1	–
Eosinophil count	< 500	72 (75.8)	8 ±0.8	8.1 ±1.1	0.76
	500–1500	20 (21.1)	8.1 ±0.79	8.2 ±0.98	0.59
	1500–5000	3 (3.2)	8.7 ±0.1	8.7 ±0.32	0.89
	P		0.46	0.57	–

**Data are shown as means ± standard deviation for normally distributed variables.*

Atopic individuals have higher levels of chemokines, β-thromboglobulin, and platelet factor 4 (PF4) compared to healthy subjects after allergen exposure, which is evidence of an increase in thrombopoiesis and a role of platelets in airway inflammation [10]. Kowal *et al.* [13] investigated activation of platelets after exposure to house dust mites in asthmatic patients, and they reported that prolonged airway inflammation after allergen exposure of asthmatic patients was related to intravascular platelet activation. Similarly, recent studies indicated that β-thromboglobulin and PF4 levels were increased in the plasma and bronchoalveolar lavage fluid of symptomatic asthma patients [12, 14]. Studies in animal models showed that platelet activation plays an important role in transmigration of circulating lymphocytes and eosinophils to the airways of patients with allergic asthma [15, 16].

Mean platelet volume was shown to be correlated with platelet function and activation [6, 17]. Thus, platelet activation during inflammation can be measured indirectly from the MPV. Mean platelet volume alone reflects both platelet stimulation and the speed of platelet production [17]. CD62, CD63, GP IIb/IIIa, PF4, and thromboglobulin can be used as markers of platelet activation [18]. On the other hand, these tests are not routinely performed due to their high costs and requirements for specialized equipment. However, MPV measurement is cheap, effective, easy, and was suggested be a useful method to assess platelet function and activation [19]. Considering all of these advantages, we used MPV and platelet number to assess platelet activation in cases of lower respiratory tract infection and inflammation.

To assess whether MPV value reflects platelet activation in asthmatic children with lower respiratory tract inflammation, we compared MPV values of patients during periods of exacerbation and asymptomatic periods with the control group. The results indicated no significant dif-

ferences between the groups. Similar to our study, Tuncel *et al*. [20] also found no significant differences in MPV between asthmatic and control/symptomatic patients and in asymptomatic periods in asthma patients. In contrast, however, Sun *et al*. [21] reported that MPV values were lower during periods of asthma exacerbation compared to asymptomatic periods.

In the present study, platelet count was significantly higher in the patient group in both exacerbation and asymptomatic periods compared to the control group ($p = 0.001$). Kemona-Chetnik *et al*. [9] reported that platelet count and percentage of reticulated platelets were significantly higher in asthmatic children than in controls; they also reported that thrombopoietin concentration was higher in asthmatic patients, but the difference was not statistically significant. Compatible with the findings of Kemona-Chetnik *et al*. [9] platelet counts were significantly higher in the patient group in our study during both periods of exacerbation and remission. Taken together, these results suggest that an increased platelet count in asthmatic children may play a role in inflammation in asthma, but that MPV measurement is not sufficient to detect the inflammation via platelets.

Asthma, severity of asthma exacerbation, immunotherapy, infection, atopy, and eosinophil count were shown to have no effect on MPV. We only found that MPV values were significantly higher in severe persistent asthma during the asymptomatic period compared to the other asthma groups. The main reason for this difference may be the higher airway inflammation in severe persistent asthma. However, the number of patients with severe asthma in our cohort was small, which represented a limitation of our study. Studies in larger numbers of patients with severe asthma are required to confirm whether these patients tend to have higher MPV measurements. There have been no previous reports regarding the factors that affect the MPV of the asthmatic patients, so we could not perform comparisons with our results.

Conclusions

This study focused on the MPV values of asthmatic patients during periods of exacerbation and remission of asthma. We also examined whether the MPV values were affected by several factors, including immunotherapy, atopy, infection, asthma, and the severity of asthma. Our study was important due to the conflicting results reported previously in the literature. There were no differences in MPV values of asthmatic patients and controls both during periods of asthma exacerbation and asymptomatic periods. In addition, the severity of asthma, the severity of exacerbation, atopy, immunotherapy, and coexisting infection did not affect the MPV values. On the other hand, platelet counts were significantly higher in the patient group during both periods of exacerbation and remission. Taken together, these results suggest that an increased platelet count in asthmatic children may play a role in the inflammation in asthma, but MPV measurement is not sufficient to detect the inflammation via platelets.

Conflict of interest

The authors declare no conflict of interest.

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