Original Article / Özgün Araştırma

Turkish Journal of Pediatric Disease
Türkiye Çocuk Hastalıkları Dergisi

Evaluation of Platelet Activation During an Asthmatic Attack in Children

Çocuklarda Astım Atağında Trombosit Aktivasyonun Değerlendirilmesi

Tuğçe TURAL KARA[1], Özlem YILMAZ ÖZBEK[2], Burcu TAHİRE KÖKSAL[2]

[1]Baskent University Faculty of Medicine, Department of Pediatrics, Ankara, Turkey
[2]Baskent University Faculty of Medicine, Department of Pediatric Allergy, Ankara, Turkey

ABSTRACT

Objective: Asthma is a chronic inflammatory disease of the airways. Allergic inflammation is characterized by accumulation of various cells, particularly mast cells, eosinophils, T lymphocytes and platelets. We investigated whether changes in mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT) and p-selectin levels of children with asthma during and at least 1 month after the attack can be used as a marker.

Material and Methods: The study was performed in 40 children who suffered asthma attacks. Blood samples were taken for MPV, PDW, PCT, p-selectin, eosinophil and platelet values during and at least 1 month after the attack.

Results: Mean platelet volume, PCT, and p-selectin levels were significantly lower at the time of the attack when compared to those at least 1 month after the attack.

Conclusion: Our findings suggest that MPV and PCT, common parameters in routine practice, can be used to determine an asthma attack.

Key Words: Asthma, Mean platelet volume (MPV), Platelet distribution width (PDW), Plateletcrit (PCT), P-selectin

ÖZET

Amaç: Astım havayollarının kronik inflamatuvar bir hastalığıdır. Allerjik inflamasyon özellikle mast hücreler, eozinofiller, T lenfositler ve trombositlerin toplanmasıyla karakterizedir. Astımlı çocuklarda atak anında ve ataktan en az 1 ay sonraki dönemde ortalama trombosit hacmi (MPV), trombosit dağılım aralığı (PDW), plateletcrit ve p-selektin düzeylerindeki değişimlerin belirlenerek atak sırasında bir belirteç olarak kullanılabilirliğinin olup olmadığını araştırdık.

Gereç ve Yöntemler: Çalışmaya astım atağındaki 40 çocuk alındı. Hastalardan atak anında ve ataktan en az 1 ay sonra MPV, PDW, PCT, p-selektin, eozinofil ve trombosit sayılarını değerlendirmek için kan örnekleri alındı.

Bulgular: Atak anındaki MPV, PCT ve p-selektin düzeyleri ataktan bir ay sonrası ile karşılaştırıldığında daha düşük bulundu.

Sonuç: Bulgularımız rutin pratikte sık kullanılan parametreler olan MPV ve PCT değerlerinin astım atağını belirlemede kullanılabileceğini göstermiştir.

Anahtar Sözcükler: Astım, Ortalama trombosit hacmi (MPV), Trombosit dağılım aralığı (PDW), Plateletcrit, P-selektin

INTRODUCTION

Asthma is the most common chronic disease of the childhood (1). It affects about 300 million people in the world. According to the latest data on prevalence, cumulative asthma frequency varies between 13.7 and 15.3% in our country (2). Chest tightness, shortness of breath, repeated wheezing and cough are the important clinical features of asthma. These episodes are associated with variable airway narrowing and are usually reversed either spontaneously or with treatment (3). As an inflammatory disease, mast cells, eosinophils, T lymphocytes, dendritic cells, macrophages and neutrophils may play a role in the pathogenesis of asthma (4,5). In vitro studies have shown that platelets also have an important role in inflammatory processes (6). When platelets are activated, increased surface receptor expression together with secretion of a variety of inflammatory molecules that contribute to the immune response and inflammation occur (7,8). Structural and volumetric changes in platelets may guide the differential

Correspondence Address / Yazışma Adresi:
Özlem YILMAZ ÖZBEK
Başkent Üniversitesi, Tıp Fakültesi, Pediatrik Alerji Bölümü, Ankara, Türkiye
E-mail: ozlemyozbek@gmail.com

Received / Geliş tarihi : 26.05.2015
Accepted / Kabul tarihi : 26.06.2015
Online published : 03.11.2015
Elektronik yayın tarihi
DOI: 10.12956/tjpd.2015.187

diagnosis of various diseases. Mean platelet volume (MPV) has been suggested as an indirect indicator of platelet function and activation (9,10). The volume of a platelet is determined when it is separated from the megakaryocyte. Some cytokines such as interleukin (IL)-3, IL-6, IL-11, granulocyte-macrophage colony-stimulating factor (GM-CSF), erythropoietin and thrombopoietin may have an effect on megakaryocytes that leads to the production of more reactive and larger platelets (11).

Platelet distribution width (PDW), another platelet activation marker, is the result of deformation in active platelets due to pseudopod formation (10). Therefore it is accepted as a more specific platelet activation marker compared to MPV in some studies (12). Plateletcrit (PCT) represents the percentage of the platelets in total blood volume. It may be useful in diseases with low platelet count, but large platelet diameters. In these patients, platelet functions are sufficient even if the platelet count is low due to large, active platelets (10). When platelets are activated, the release of p-selectin from the alpha granules occurs. This then passes through the surface and accumulates in the plasma, resulting in increased levels of platelets and soluble p-selectin. Therefore, p-selectin is suggested as a marker of platelet activation, together with platelet factor 4 (PF4) and beta thromboglobulin (BTG) (13). A recent study has revealed that patients with asthma have higher serum p-selectin levels after exercise-induced bronchoconstriction compared to healthy subjects, suggesting platelet activation in asthma patients (14).

Studies that evaluate the relationship between MPV, PDW and some inflammatory diseases such as familial Mediterranean fever, rheumatoid arthritis and diabetes have been published. The result of these studies have revealed that MPV and PDW values change during the periods of exacerbation (15,16). In our study, we aimed to determine changes in MPV, PDW, PCT values and p-selectin levels of asthmatic patients during and at least 1 month after the attack and to evaluate whether these values can be used as a marker for predicting an exacerbation.

METHODS

Forty patients who admitted to our hospital with astma attack during the period of April-July 2011 were included in the study. Patients were divided into two groups as mild/moderate and severe according to the severity of asthma attacks. The enrolled patients were evaluated for age, sex, body weight, height, atopy, history of domestic animals, cigarette exposure, and concomitant symptoms of allergic rhinitis and family history of allergic disease. In order to avoid possible effect of drugs and diseases on platelet function, patients who had taken oral steroid therapy before admission and those with chronic diseases were excluded from the study.

The patients who were included in the study were evaluated according to GINA criteria (17). In the acute stage, the presence of cough, recurrent wheezing and/or shortness of breath history, rhoncus and/or prolonged expirium on physical examination, and pulmonary function tests (PEF, FEV1) showing a decrease compared to the previous values were considered to be indicative for acute asthma attacks. Patients who were admitted with wheezing and prolonged expirium during the study period were excluded. All asthmatic patients were using either fluticasone 200 µcg or budesonide 400 µg. Two ml of blood was drawn into a tube anticoagulated with ethylenediaminetetraacetic acid and then evaluated with a hemocytometer (Abbott Cell-Dyn 3700 system, Abbott Diagnostics, Santa Clara, CA, USA) that was calibrated daily. Mean platelet volume, PDW, PCT, eosinophil and platelet counts were recorded. In order to determine the level of p-selectin, 3 ml of venous blood samples drawn into standard biochemical tubes were centrifuged for 20 minutes. The serum was separated and stored in a -80°C freezer. Inhaled steroids, inhaled short-acting β2-agonist and oral steroids were administered to patients to treat acute attacks. At least 1 month after the attack, patients were reevaluated when they were symptom free. Samples for MPV, PDW, PCT, p-selectin, eosinophil and platelet count were drawn and pulmonary function tests were performed. After the completion of the study, all sera were thawed and p-selectin levels were measured by ELISA (RayBiotech, Inc. Canada). Pulmonary function tests were performed with spirometry (Flowhandy Spirometer ZAN 100, ZAN Messgeräte GmbH, Germany). Forced expiratory volume in one second (FEV1), forced vital capacity (FVC), FEV1/FVC and forced expiratory flow (FEF25-75) were measured.

This study was supported by the Baskent University Research Fund (KA11/33). The study was approved by the Baskent University Ethics Committee and written informed consent was obtained from all subjects and their family prior to the study.

STATISTICAL ANALYSES

Statistical analysis of the data set in SPSS 17.0 statistical software (Statistical Package for Social Sciences Ver. 17.0, SSPS Inc, Chicago, IL USA) were used. The results of statistical analysis were expressed as number of observations (n), mean ± standard deviation (Mean±SD), median and minimum–maximum values M (min–max). A p value <0.05 was considered statistically significant. Shapiro-Wilk's test was used to assess the normality of distributions of the variables and Levene's test was used to assess the homogeneity of variances among groups. In the comparison of mild/moderate and severe asthma attack groups, if parametric test assumptions are available two independent groups were compared by Student's t-test and correlations between variables were analysed by Pearson correlation coefficient. If assumptions are not available Mann-Whitney U test were used and correlations between variables were analysed by Spearman's rho correlation coefficient. T-Test Paired Samples Statistics Test and Wilcoxon Signed Rank Test were used to compare asthmatic patients during and at least 1 month after attack. Correlations between variables are evaluated by Spearman's rho correlation coefficient.

RESULTS

Eighteen girls (45%) and 22 boys (55%) were included in the study. According to the severity of the attack, 22 of them were categorized as the mild/moderate asthma attack group (7 girls, 15 boys) and 18 as the severe asthma attack group (11 girls, 7 boys). The mean age of all children was 8.7 ± 2.6 years (range 6-16, median 8.2) and did not differ significantly between the two groups (p>0.05). When compared according to the body weight and height, there was also no statistically significant difference between the two study groups (p>0.05). The demographic features are presented in Table I.

When we analyzed all asthmatic children, the white blood cell (WBC) and polymorphonuclear leukocyte (PMNL) counts were significantly high during the attack compared to those after attack while MPV, PCT and p-selectin values were significantly low (Table II). When the mild/moderate and severe asthma attack groups were separately evaluated, MPV and PCT levels were still significantly lower during attack (Table III). Although statistically insignificant, p-selectin levels were lower during the attack compared to those after the attack in both groups.

During the attack, only the severe asthma attack group had a negative correlation between platelet count and FEV1 (Spearman rho= -0.475, p<0.05). When all patients were examined after the attack, PDW was positively correlated with FEV1 act (Spearman rho= 0.480, p<0.05), FVC (Spearman rho= 0.481, p<0.05), FVC act (Spearman rho= 0.472, p<0.05) and FEF25-75 (Spearman rho= 0.536, p<0.05). Considering all the patients, no correlation between MPV, PDW, PCT, p-selectin values and age at diagnosis, smoking exposure, concomitant allergic rhinitis, or family history of asthma was evident.

DISCUSSION

Recent studies have suggested that platelets play a role in the allergic inflammatory response and airway remodeling (18-20). Identification of the presence of megakaryocytes in the lungs has been the premise of platelet studies in airway disorders (21). It was then detected that the platelet count was higher in the lungs than in the blood and this was associated with platelet production in lungs (22). Some studies suggest that intravascular platelet activation can be determined by measuring some chemokines such as BTG and PF-4, which are secreted by platelets (19). Similar to studies showing platelet activation in response to allergen stimulus, increased bronchial hyperreactivity has been related to increased platelet activation in patients with asthma (20). In our study, we questioned whether complete blood count parameters, commonly used in routine practice such as platelet count, MPV, PDW, PCT and p-selectin levels are markers of asthmatic attack. We found that MPV, PCT and p-selectin levels were significantly lower at the time of an attack compared to those at symptom-free period. On the other hand, the numbers and percentage of WBCs and PMNLs were significantly higher during an attack than those obtained during the attack-free period in our patients.

Our study revealed that MPV values were significantly lower during asthma attack compared to those obtained at least 1 month after attack in both patient groups. However, there was no correlation between MPV values and severity of attacks. We found only one study in the literature concerning MPV values in asthmatic children. In this retrospective study, comparison of platelet count and platelet volume of asthmatic children during and after attack with healthy subjects revealed no significant difference (23). However, recent studies have proposed MPV to be a marker for the diagnosis of acute exacerbations in some chronic inflammatory diseases. Similar to our study, MPV levels were found to be lower compared to those in healthy subjects during the acute attacks of familial Mediterranean fever and rheumatoid arthritis (15,16). The release of small volume platelets by cytokines that induce stimulation of megakaryocytes in bone marrow and/or consumption of large volume/active platelets during inflammation have been suggested as the possible

Table I: Demographic characteristics of asthmatic patients.

	All asthmatic patients n=40	Mild/ Moderate asthma attack group n=22	Severe asthma attack group n=18	p
Gender (female/male)	18/22	7/15	11/7	
Age (year±SD)	8.7±2.6	9.4±3.1	7.9±1.78	0.37
Length (cm±SD)	134.1±16.8	137.8±18.3	129.6±14.1	0.31
Weight (kg±SD)	33±12.9	35.7±14.4	29.7±10.3	0.20
History of atopy [n (%)]	21 (%52.5)	11 (%50)	10 (%55.6)	0.68
Allergic rhinitis [n (%)]	37 (%92.5)	21 (%95.5)	16 (%88.9)	0.43
Asthma in the family [n (%)]	15 (%37.5)	10 (%45.5)	5 (%27.8)	0.33
Allergic rhinitis in the family [n (%)]	24 (%60.0)	14 (%63.6)	10 (%55.6)	0.60
Smoking in the house [n (%)]	11(%27.5)	6 (%27.3)	5 (%27.8)	0.97
Domestic animals [n (%)]	6 (%15)	5 (%22.7)	1 (%5.6)	0.11

reasons for this finding (24). Our study further supports this theory that MPV can also be a marker for acute attacks in children with asthma. We found no difference in PDW values between patients during and at least 1 month after the attack in our study.

Animal studies have revealed a positive correlation between PCT and platelet count; when the platelet counts decrease, PCT values decrease or vice versa (25). It has been emphasized that these parameters could be markers of platelet consumption. In our study, PCT values were significantly lower during the attack compared to those obtained at least one month after the attack in both patient groups. However, despite the decreased PCT, platelet counts were higher during the attack compared to the values obtained during the attack-free period. These findings indicate that platelets with larger volume consumed due to acute inflammation result in decreased PCT even in the presence of an increased number of platelets.

Table II: Platelet activation markers and blood cell counts during and after the attack in all asthmatic patients.

	During attack	After the attack	p
PLT (x10³K/µL)±SD Min-max Median	322.92±71.76 204.00-524.00 317.00	313.5±69.46 313.50-520.00 314.00	0.320
MPV(fL) ±SD Min-max Median	6.38±0.92 5.01-8.22 6.35	7.27±0.81 6.06-9.51 7.05	0.000
PDW (GSD) ±SD Min-max Median	17.33±0.84 16.3-20 17.1	17.38±0.96 16.1-20.6 17.2	0.580
PCT (GSD)±SD Min-max Median	207.48±35.09 125-289 204.5	214.10±39.10 139-331 213.0	0.028
P-selectin(pg/ml) ±SD Min-max Median	24.11±11.16 11.32-48.6 23.09	27.99±12.22 0.07-42.9 32	0.038
Eosinophil (K/µL) ±SD Min-max Median	432.9±777.2 3-453 191.5	260.8±212.6 38-779 186.5	0.280
Eosinophil (%) ±SD Min-max Median	4.26±6.14 0.02-30.8 2.30	3.56±2.83 0.77-12.1 2.47	0.960
WBC (K/µL) ±SD Min-max Median	9272.2±3489.4 4560-19300 8800	7273±1894.9 4890-12100 7120	0.001
PMNL (K/µL) ±SD Min-max Median	5345.7±3039.9 1470-13800 5045	3368±1298.5 1310-6770 3110	0.000

PLT: *Platelet,* ***MPV:*** *Mean platelet volume,* ***PDW:*** *Platelet distribution width,* ***PCT:*** *Plateletcrit,* ***WBC:*** *White blood cell,* ***PMNL:*** *Polymorphonuclear leukocytes.*

Table III: Platelet activation markers in mild/moderate and severe asthma attack groups.

	Mild/moderate asthma attack group (n=22)			Severe asthma attack group (n=18)		
	During attack	After the attack	p	During attack	After the attack	p
PLT (x10³K/µL)±SD	320.0±66.4	301.5±67.5	0.380	326.4±79.6	328.1±70.8	0.380
MPV(fL) ±SD	6.5±0.8	7.1±0.7	0.001	6.2±1.1	7.4±0.9	0.001
PDW (GSD) ±SD	17.3±0.9	17.4±0.7	0.945	17.3±0.8	17.3±1.2	0.395
PCT (GSD) ±SD	201.9±33.7	205.1 ±34.4	0.043	214.2±36.3	225.1±42.5	0.044
P-selectin (pg/ml) ±SD	21.4±10.9	27.0±11.9	0.079	27.4±10.8	29.1±12.8	0.449

In the literature, it has been reported that platelets of asthmatic patients secrete beta-thromboglobulin and platelet factor-4 after bronchial provocation (19). A positive association between p-selectin and eosinophilic cationic protein in the nasal wash of pediatric patients with asthma suggests a common pathophysiological mechanism involving p-selectin and inflammation in asthmatic patients (26). Another study has disclosed findings suggesting that the p-selectin on activated platelets, or acquired from plasma or endothelial cells, activates eosinophil a4b1 integrin and stimulates eosinophils to adhere to activated endothelium and move to the airway. The authors concluded that targeting p-selectin–triggered eosinophil b1 integrin activation could represent a new therapeutic approach in asthma (27). Intrabronchial challenge of house dust mite-sensitive asthmatic patients revealed a significant increase in beta-thromboglobulin and PF-4 after 30 minutes of challenge but the levels decreased and returned to normal levels after 24 hours (28). These studies suggest that platelets are activated and the release of p-selectin increases during an asthmatic attack. However, due to timing of blood sampling, conflicting results have been observed concerning levels of beta-thromboglobulin and platelet factor-4. Since our patients are usually admitted to hospital in a relatively late period of an asthma attack, low levels of p-selectin in our study during attack compared to those after the attack may be due to this exhaustion. Drawing blood for p-selectin analysis at the very early phase of attack is necessary, if possible, in order to obtain more reliable results. Furthermore the p-selectin level of the severe attack group was higher than the mild/moderate attack group. This can be explained by parents of asthmatics in mild/moderate attack possibly neglecting the symptoms and delaying admission to the hospital, whereas parents of asthmatics with a severe attack coming to the hospital earlier. On the other hand, p-selectin was shown to increase after inhaled steroid treatment in a study, although results were not statistically significant (29). Systemic and/or inhaled steroids given during and after the asthmatic attacks may cause increased p-selectin levels. Steroids can be responsible for these results.

A recent study found that the number of platelets in asthmatic patients during and after the attack compared to healthy subjects had no significant difference (23). Similarly, we observed no significant change in platelet count in our study when we evaluated patients during an attack and in the symptom-free period. We did not find a correlation between platelet count and the severity of the asthma attack. However, we determined that FEV1 decreases when platelet count increases in the severe asthma attack group. We therefore believe platelets play a role in inflammation and the pulmonary function test is affected.

In conclusion, we found that MPV, PCT and p-selectin levels were lower in patients during an asthmatic attack in our study. We think that low levels of mean platelet volume could be caused by activation of platelets during inflammation, which results in consumption of large volume platelets with small volume platelets remaining in the bone marrow. Reduction of the PCT level during an attack supports the consumption of platelets. Platelet characteristics may help to predict an imminent exacerbation. Assessing platelet characteristics during a probable attack may influence treatment decisions. In addition, the increase of white blood cells and PMNL count during an attack also indicates activation of inflammation. The most important limitation of our study was the number of patients and we therefore suggest larger and timely studies to demonstrate the clinical significance of platelet activation markers during an asthmatic attack more clearly.

REFERENCES

1. Eder W, Ege MJ, von Mutius E. The asthma epidemic. N Engl J Med 2006; 355: 2226-35.
2. Akçakaya N, Kulak K, Hassanzadeh A, Camcioğlu Y, Cokuğraş H. Prevalence of bronchial asthma and allergic rhinitis in Istanbul school children. Eur J Epidemiol 2000;16: 693-9.
3. Panettieri RA Jr, Covar R, Grant E, Hillyer EV, Bacharier L. Natural history of asthma: Persistence versus progression-does the beginning predict the end? J Allergy Clin Immunol 2008;121:607-13.
4. Robinson DS. The role of the mast cell in asthma: Induction of airway hyperresponsiveness by interaction with smooth muscle? J Allergy Clin Immunol 2004;114:58-65.
5. Larche M, Robinson DS, Kay AB. The role of T lymphocytes in the pathogenesis of asthma. J Allergy Clin Immunol 2003;111:450-63.
6. Metzger WJ, Sjoerdsma K, Richerson HB, Moseley P, Zavala D, Monick M, et al. Platelets in bronchoalveolar lavage from asthmatic patients and allergic rabbits with allergen-induced late phase responses. Agents Actions Suppl 1987;21:151-9.
7. Pitchford SC, Page CP. Platelet activation in asthma: Integral to the inflammatory response. Clin Exp Allergy 2006;36:399-401.
8. Kasperska-Zajac A, Rogala B. Platelet activation during allergic inflammation. Inflammation 2007;30:161-6.
9. Park Y, Schoene N, Harris W. Mean platelet volume as an indicator of platelet activation: Methodological issues. Platelets 2002;13:301-6.
10. Wiwanitkit V. Plateletcrit, mean platelet volume, platelet distribution width: Its expected values and correlation with parallel red blood cell parameters. Clin Appl Thromb Hemost 2004;10:175-8.
11. Thompson CB, Jakubowski JA. The pathophysiology and clinical relevance of platelet heterogeneity. Blood 1988;72:1-8.
12. Vagdatli E, Gounari E, Lazaridou E, Katsibourlia E, Tsikopoulou F, Labrianou I. Platelet distribution width: A simple, practical and specific marker of activation of coagulation. Hippokratia 2010;14:28-32.
13. Tomer A, Harker LA, Kasey S, Eckman JR. Thrombogenesis in sickle cell disease. J Lab Clin Med 2001;137:398-407.
14. Zietkowski Z, Skiepko R, Tomasiak MM, Bodzenta-Lukaszyk A. Soluble CD40 ligand and soluble P-selectin in allergic asthma patients during exercise-induced bronchoconstriction. J Invest Allerg Clin 2008; 18: 272-8.
15. Makay B, Türkyilmaz Z, Unsal E. Mean platelet volume in children with familial Mediterranean fever. Clin Rheumatol 2009; 28: 975-8.

16. Gasparyan AY, Sandoo A, Stavropoulos-Kalinoglou A, Kitas GD. Mean platelet volume in patients with rheumatoid arthritis: The effect of anti-TNF-alpha therapy. Rheumatol Int 2010; 30:1125-9.
17. Bateman ED, Hurd SS, Barnes PJ, Bousquet J, Drazen JM, FitzGerald M, et al. Global strategy for asthma management and prevention: GINA executive summary. Eur Respir J 2008;31:143-78.
18. Kemona-Chetnik I, Bodzenta-Lukaszyk A, Butkiewicz A, Dymnicka-Piekarska V, Kemona H. Thrombocytopoesis in allergic asthma. Pol Arch Med Wewn 2007;117:9-13.
19. Yasuba H, Chihara J, Kino T, Satake N, Oshima S. Increased releasability of platelet products and reduced heparin-induced platelet factor 4 release from endothelial cells in bronchial asthma. J Lipid Mediat 1991;4:5-21.
20. Gresele P, Dottorini M, Selli ML, Iannacci L, Canino S, Todisco T, et al. Altered platelet function associated with the bronchial hyperresponsiveness accompanying nocturnal asthma. J Allergy Clin Immunol 1993;91:894-902.
21. Martin JF, Slater DN, Trowbridge EA. Platelet production in the lungs. Agents Actions Suppl 1987;21:37-57.
22. Aliberti G, Proietta M, Pulignano I, Tritapepe L, Di Giovanni C, Schiappoli A, et al. The lungs and platelet production. Clin Lab Haematol 2002; 24:161-4.
23. Tuncel T, Uysal P, Hocaoglu AB, Erge DO, Karaman O, Uzuner N. Change of mean platelet volume values in asthmatic children as an inflammatory marker. Allergol Immunopathol (Madr) 2012; 40:104-7.
24. Bath PM, Butterworth RJ. Platelet size: Measurement, physiology and vascular disease. Blood Coagul Fibrinolysis 1996;7:157-61.
25. Yilmaz Z, Eralp O, Ilcol YO. Evaluation of platelet count and its association with plateletcrit, mean platelet volume, and platelet size distribution width in a canine model of endotoxemia. Vet Clin Pathol 2008;37:159-63.
26. Benton AS, Kumar N, Lerner J, Wiles AA, Foerster M, Teach SJ, et al. Airway platelet activation is associated with airway eosinophilic inflammation in asthma. J Investig Med 2010;58:987.
27. Johansson MW, Mosher DF. Activation of beta1 integrins on blood eosinophils by P-selectin. Am J Respir Cell Mol Biol 2011;45:889-97.
28. Kowal K, Pampuch A, Kowal-Bielecka O, DuBuske LM, Bodzenta-Łukaszyk A. Platelet activation in allergic asthma patients during allergen challenge with Dermatophagoides pteronyssinus. Clin Exp Allergy 2006;36:426-32
29. Kose S, Karaman O, Islekel H, Uzuner N, Babayigit A, Olmez D, et al. Circulating adhesion molecules in sera of asthmatic children before and after steroid therapy. Allergy Asthma Proc 2007;28:199-203.