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Original Article / Çalışma - Araştırma

Evaluation of mean platelet volume and its ratio over platelet count in children with obstructive sleep apnea syndrome

Tıkayıcı uyku apne sendromu olan çocuklarda ortalama trombosit hacmi ve ortalama trombosit hacminin trombosit sayısına oranının değerlendirilmesi

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ABSTRACT

Objectives: This study aims to determine the association between obstructive sleep apnea syndrome (OSAS) caused by adenotonsillar hypertrophy and mean platelet volume (MPV) and MPV/platelet count ratio in children, and to evaluate the impact of adenotonsillectomy on these two parameters.

Patients and Methods: This prospective study consisted of 73 child patients (38 boys, 35 girls; mean age 8.6±3.3 years, range 2 to 17 years) with chronic adenotonsillar hypertrophy who applied to Gaziosmanpaşa University Faculty of Medicine, Ear, Nose and Throat policlinics due to witnessed apnea and snoring in January 2011 and January 2013. Also, 56 age and sex matched pediatric patients (28 boys, 26 girls; mean age 8.0±3.2 years; range 3 to 13 years) who admitted to our clinic due to reasons besides OSAS were included in the study as control group. Preoperative and postoperative third month hemoglobin, white blood cell, thrombocyte count, and MPV values of the patients were recorded.

Results: Although ratio of MPV/platelet count was higher in patient group than in control group, the difference was not statistically significant. Mean platelet volume level was 7.68±1.07 fL in patient group and 7.21±0.84 fL in control group. Preoperative MPV level in patient group was significantly higher than that in control group ($p<0.05$). A statistically significant decrease was detected in postoperative third month MPV level and platelet count compared with preoperative MPV and platelet count (7.68±1.07 fL and 7.17±0.97 fL, respectively; $p<0.05$).

Conclusion: High MPV and MPV/platelet count in children with adenotonsillar hypertrophy may be an important risk factor for cardiopulmonary and cerebrovascular morbidities which may develop both in childhood and in adulthood. Adenotonsillectomy may reduce this risk significantly.

Keywords: Adenotonsillectomy; mean platelet volume; pediatric obstructive sleep apnea.

ÖZ

Amaç: Bu çalışmada çocuklarda adenotonsiller hipertrofinin neden olduğu tıkayıcı uyku apne sendromu (TUAS) ile ortalama trombosit hacmi (OTH) ve OTH/trombosit sayısı oranı arasındaki ilişki belirlendi ve adenotonsillektominin bu iki parametre üzerindeki etkisi değerlendirildi.

Hastalar ve Yöntemler: Bu prospektif çalışmaya Ocak 2011 - Ocak 2013 tarihleri arasında Gaziosmanpaşa Üniversitesi Tıp Fakültesi Hastanesi Kulak Burun Boğaz Polikliniği'ne tanıklı apne ve horlama nedeni ile başvuran, kronik adenotonsiller hipertrofisi olan 73 çocuk hasta (38 erkek, 35 kız; ort. yaş 8.6±3.3 yıl; dağılım 2-17 yıl) dahil edildi. Ayrıca kliniğimize TUAS dışı nedenlerle başvuran, yaş ve cinsiyet uyumlu 56 çocuk hasta (28 erkek, 26 kız; ort. yaş 8.0±3.2 yıl; dağılım 3-13 yıl) kontrol grubu olarak çalışmaya alındı. Hastaların ameliyat öncesinde ve ameliyat sonrası üçüncü ayda hemoglobin, beyaz kan hücresi, trombosit sayısı ve OTH değerleri kaydedildi.

Bulgular: Hasta grubunda OTH/trombosit sayısı oranı kontrol grubuna göre yüksek olsa da fark istatistiksel olarak anlamlı değildi. Ortalama trombosit hacmi düzeyi hasta grubunda 7.68±1.07 fL, kontrol grubunda 7.21±0.84 fL idi. Ameliyat öncesi OTH düzeyi hasta grubunda kontrol grubundan anlamlı olarak yüksekti ($p<0.05$). Ameliyat sonrası üçüncü aydaki OTH düzeyi ve trombosit sayısında ameliyat öncesi OTH düzeyi ve trombosit sayısına göre istatistiksel olarak anlamlı bir azalma saptandı (sırasıyla, 7.68±1.07 fL; 7.17±0.97 fL; $p<0.05$).

Sonuç: Adenotonsiller hipertrofili çocuklarda yüksek OTH ve OTH/trombosit sayısı, hem çocukluk hem de yetişkin dönemde gelişebilen kardiopulmoner ve serebrovasküler morbiditeler için önemli bir risk faktörü olabilir. Adenotonsillektomi bu riski anlamlı olarak azaltabilir.

Anahtar Sözcükler: Adenotonsillektomi; ortalama trombosit hacmi; pediatrik tıkayıcı uyku apnesi.

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Sleep-disordered breathing (SDB) ranges from simple snoring to upper airway resistance syndrome and the most serious form of obstructive sleep apnea syndrome (OSAS).[1,2] Sleep-disordered breathing in children often develops as a result of hypertrophic adenotonsillitis and therefore, adenotonsillectomy is the primary treatment of USB.[2] Obstructive sleep apnea syndrome-dependent cardiovascular morbidities in adults are observed in moderate to severe OSAS and may lead to mortality. Among the OSAS-dependent cardiovascular morbidities in adults are heart failure, hypertension, pulmonary hypertension, cardiac arrhythmias, acute myocardial infarction and stroke.[3]

Intermittent obstruction of airways and desaturation cause changes in autonomic nervous system in children with OSAS, leading to cardiovascular morbidities.[4] There are limited studies dealing with cardiovascular morbidities caused by OSAS in children. OSAS associated morbidities such as changes in heart rate, decreases in echocardiography morphology-functions and hypertension have been reported in children.[2,4] Even the serious morbidities associated with OSAS such as heart failure and cor pulmonale are often remedied by adenotonsillectomy. When left untreated, pediatric OSAS could lead to negative cardiovascular consequences in adult life.

Platelet activation and aggregation is closely associated with cardiovascular complications. In many studies, platelet activation and aggregation have been reported to increase in patients with OSAS.[5,6] Mean platelet volume (MPV) is a parameter used as an indicator of platelet activation. Larger platelets are more reactive than normal-sized ones and have higher prothrombotic potentials. Mean platelet volume is considered as a marker of atherosclerosis.[5-10] In previous studies, MPV has been reported to increase in adult cerebrovascular and cardiovascular conditions such as hypertension, unstable angina pectoris, myocardial infarction and stroke.[9] It has been shown that elevated MPV levels could be associated with the prognoses of these diseases.[7,9] It has been reported in recent studies that MPV increases in obstructive septal deviation and nasal polyps in severe adult OSAS.[6,11,12] The ratio of MPV to platelet count (MPV/PC) is a current reliable marker just like MPV. Higher MPV/PC ratio is associated with myocardial infarction, anemia, deep vein thrombosis, infective endocarditis and hepatocellular carcinoma.[13-16] There are limited studies pointing to the association between adenoid hypertrophy and MPV in pediatric OSAS.[10,17] However, to our knowledge, there is no study in the literature dealing with the association between pediatric OSAS and MPV/PC. In the present study, the association between OSAS caused by adenotonsillar hypertrophy and MPV and MPV/PC ratio in children with OSAS diagnosis was studied and the impact of adenotonsillectomy on these two parameters was evaluated.

PATIENTS AND METHODS

A total of 73 children (38 boys, 35 girls; mean age 8.6±3.3 years; range 2 to 17 years) with adenotonsillar hypertrophy who consulted at the Gaziosmanpaşa University Faculty of Medicine, Ear, Nose and Throat Polyclinics due to witnessed apnea and snoring between January 2011 and January 2013 were included in this prospective study. A control group consisting of 56 age- and sex-matched children (28 boys, 26 girls; mean age 8.0±3.2; range 3 to 13 years) was formed from the pediatric patients who consulted at the pediatric clinic due to complaints other than upper airway obstruction, acute or chronic infection and systemic diseases. Human experiment principles in the Helsinki Declaration were observed in the present study, and written approval was granted by the Ethics Committee of Clinical Research of Gaziosmanpaşa University Faculty of Medicine. Adenoids and tonsils of the patients were evaluated using transnasal and transoral flexible endoscopy. Adenoid classification was made as follows: Grade 1, adenoid tissue fills less than 25% of choana; grade 2, adenoid tissue fills 25-50% of choana; grade 3, adenoid tissue fills 50-75% of choana, and grade 4; adenoid tissue fills 75-100% of choana. Tonsil hypertrophy was classified using the Brodsky grading scale. In this classification, tonsil which caused less than 25% obstruction of airways were classified 1+, ones causing 25-50% obstruction were classified 2+, ones causing 50-75% obstruction were classified 3+ and ones more than 75% obstruction were classified 4+. Patients with grade 3 or 4 adenoids and patients with 3+ or 4+ tonsil hypertrophy were included in the study. Transoral adenoid curettage was applied on the patients who had adenoid hypertrophy, while cold-steel dissection

Table 1. Characteristics of study and control groups

	Study group (n=73)		Control group (n=56)		
	n	Mean±SD	n	Mean±SD	*p*
Age		8.6±3.3		8.0±3.2	0.449
Gender					
Male	38		28		0.982
Female	35		26		
White blood cell count x10^3/μL		8.35±2.63		7.90±1.76	0.544
Hemoglobin (g/dL)		12.39±0.92		12.58±1.02	0.371
Platelet count x10^3/μL		313.342±83.052		305.518±82.786	0.344
Mean platelet volume (fL)		7.68±1.07		7.21±0.84	0.012*
Mean platelet volume/platelet count ratio		0.026±0.009		0.03±0.007	0.705

* p<0.05; SD: Standard deviation; Average values of all parameters were given unless specified otherwise.

tonsillectomy was applied on patients who had accompanying chronic tonsillar hypertrophy. The patients who had accompanying nasal septum deviation, rhinosinusitis, hematological and chronic diseases and who had previous adenoidectomy were excluded from the study. Routine preoperative blood samples were taken from the antecubital vein into tubes containing EDTA. Whole blood counts were carried out in the central lab of our hospital. Results were taken from the data bank of the hospital computer system. White blood cell (WBC), platelet (Plt), hemoglobin (Hb) and MPV parameters were measured. Normal limits for MPV were considered to be 6-10 fL. Blood samples were taken again three months after the operation for postoperative follow-up examinations and parameters were measured again. Results were compared with the preoperative whole blood parameters.

Statistical analyses

Data were analyzed using IBM SPSS version 20.0 software program (IBM Corp., Armonk, NY, USA). The distribution of the data was assessed using the one-sample Kolmogorov Smirnov test. Qualitative data was presented as percentages, while quantitative data was presented as means and standard deviations. The Mann-Whitney U test was used for variables that did not have normal distribution, and chi-square test was used for categorical variables. For intragroup comparisons, Wilcoxon's signed rank test was performed. Statistical significance level was set at p<0.05.

RESULTS

Some characteristics of the study and control groups are given in Table 1. The average number of WBC, Hb levels, PC and MPV/PC ratio were not significantly different between study and control groups. Mean platelet volume levels were 7.68±1.07 and 7.21±0.84 fL in study and control groups, respectively. Preoperative MPV level in children with obstructive adenotonsillar hypertrophy was significantly higher compared to the control group (p<0.05) (Figure 1).

Statistically significant drops were observed in MPV level and platelet count of patients who had adenotonsillectomy in the third month after the operation compared to preoperative measurements (pre- and postoperative MPV levels were 7.68±1.07 and 7.17±0.97 fL; p<0.05) (Figure 2, 3). The difference between pre- and postoperative MPV/PC ratio was not significant (p>0.05).

DISCUSSION

Chronic adenotonsillar hypertrophy is the leading cause of OSAS in children. To our knowledge, the present study is the first to evaluate MPV/PC ratio along with MPV in children with adenotonsillar hypertrophy. It was found in the present study that MPV level was significantly higher in children with OSAS caused by adenotonsillar hypertrophy, and that adenotonsillectomy lowered MPV level.

Obstructive sleep apnea syndrome is not a simple breathing failure developing during sleeping. It is a systemic condition that might

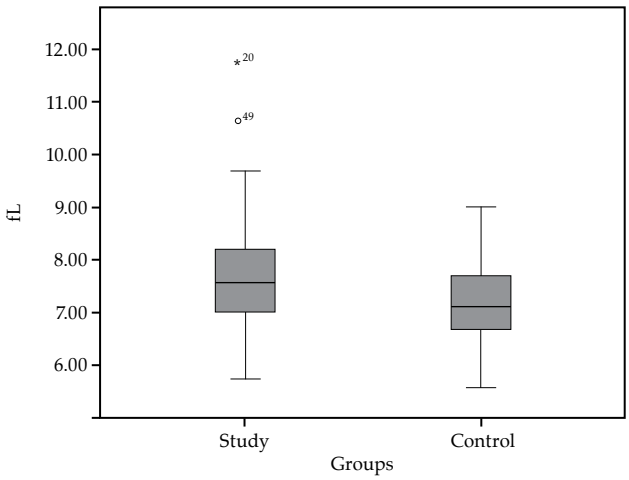

Figure 1. *The mean platelet volume values of the groups.*

lead to conditions such as coronary artery disease, cerebrovascular diseases and heart failure. It has not been shown clearly how OSAS leads to coronary artery and cerebrovascular diseases. Elevated cardiovascular disease incidence in OSAS might be due to impaired hypercoagulation and elevated plated activation observed in these patients.[5] In OSAS, platelets possibly become active through three mechanisms.[6] First, night hypoxemias and recurring wake ups result in sympathetic system activation characterized by epinephrine and norepinephrine increase. Epinephrine and norepinephrine cause dose-dependent activation of platelets. Second, acute or chronic intermittent hypoxia activates platelets directly or indirectly. Third, interleukin 6 (IL-6) and IL-3 released in inflammation caused by OSAS stimulate megakaryocytes, causing the production of platelets of larger granules that are more reactive and have higher thrombotic potentials. Interleukin 6 particularly stimulates megakaryocytes and results in increases in MPV levels. Higher MPV levels are considered indications of atherosclerosis and platelet activation.

Association of higher MPV levels with atherosclerosis and thromboembolic events in OSAS has been shown in adults. Although the association of OSAS with cardiovascular morbidities has been revealed, to our knowledge there is no report showing the association of MPV and atherosclerotic-thromboembolic events. In children with extreme OSAS, it has been shown that pulmonary hypertension and right hearth failure may develop.[4,18] Higher MPV levels were also reported in pulmonary hypertension.[19] It has been reported that OSAS results in decreases in movements of heart walls, irregularities in heart rate, diastolic hypertension and right heart failure. Obstructive sleep apnea syndrome dependent cardiovascular morbidities were reported in children despite the lack of cardiovascular symtoms.[4] These morbidities have been shown to turn back to normal through adenotonsillectomy. Although child and adult OSAS lead to cardiovascular morbidities through similar mechanisms, it is not known whether hypoxia that children are exposed to during sleep results in platelet aggregation and atherosclerosis. Previous studies have shown that environmental and genetic factors, diet and obesity play roles in childhood atherosclerosis. But to the best of our knowledge, there is no report in the literature

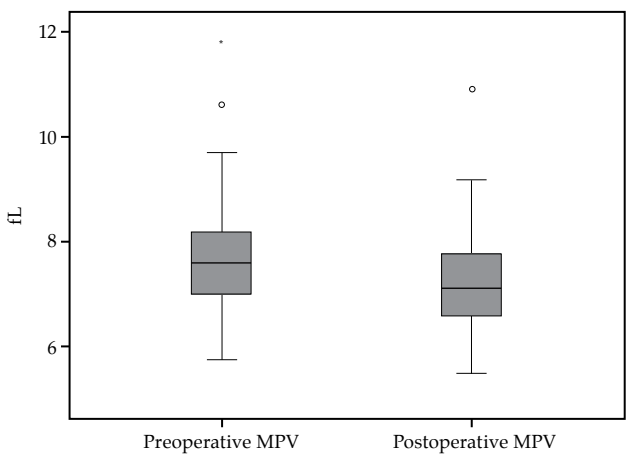

Figure 2. *Mean platelet volume (MPV) values of the study.*

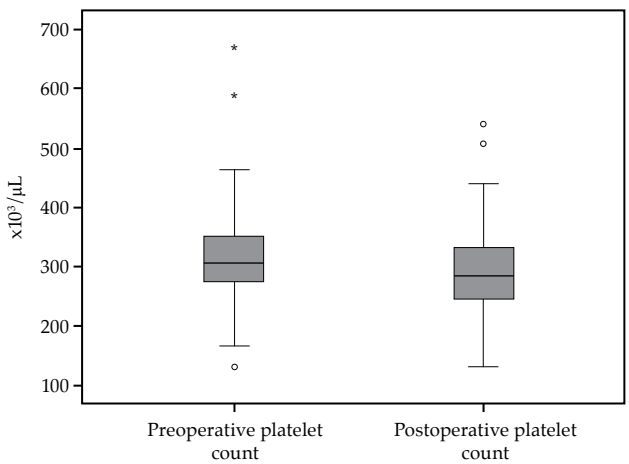

Figure 3. *Platelet count values of the study group.*

pointing higher MPV levels in pediatric OSAS as a risk factor for atherosclerosis and thrombosis. There are a limited number of studies dealing with the association between OSAS and MPV. Kucur et al.[17] observed statistically higher MPV levels in children with adenoid hypertrophy. In contrast, Cengiz et al.[10] found statistically lower MPV levels in children with chronic tonsillitis and adenoid hypertrophy. We included children having OSAS with hypertrophic tonsils which has not been studied so far, in addition to obstructive adenoids. We showed that MPV levels are significantly higher in children with advanced level of chronic adenotonsillar hypertrophy compared to the control group. In addition, we showed that adenotonsillectomy significantly lowered the MPV and platelet count. The association between MPV and platelet count has not been elucidated. While elevated MPV level indicates platelet activation and aggregation, higher platelet count is associated with reactive thrombocytosis and inflammation.[13] Many studies reported that elevated MPV levels result in a decrease in platelet number. This could be due to the excessive use of small platelets in order to maintain a fixed level of functional platelet mass.[7] Nevertheless, there are also studies reporting increases in platelet number along with MPV increases. In the present study, we examined the MPV/PC ratio which to our knowledge has not been studied so far in children with OSAS. Azab et al.[13] reported that higher MPV/PC ratio was a better parameter to determine long term mortality due to ischemic cardiovascular disease. Mean platelet volume/PC ratio has been shown to be higher in thromboembolic diseases such as deep vein thrombosis and infective endocarditis.[14,15] Azab et al.[13] has shown that long-term infarction-caused mortality rate is significantly higher in patient groups with very high (40 and more) and very low (30 and less) MPV/PC ratios compared to moderately higher patient group (MPV/PC ratios of 30-40). The authors mentioned that very high MPV/PC rates resulted from extremely high MPV levels (along with elevated platelet aggregation and activation) as well as from significant decreases in platelet number. Low MPV/PC ratios, on the other hand, were attributed to increased platelet number along with relatively small platelets (reactive thrombosis and elevated inflammation). Although preoperative MPV/PC ratio was relatively high compared to the control group, the difference was not significant, which could be due to higher platelet numbers in the study group. A limiting factor in the present study could be the fact that we did not perform polysomnography, which is an expensive, labor intensive and difficult technique to be employed in children. It was thus not possible to reveal the OSAS severity and association between MPV and parameters in polysomnography.

Conclusion

We report in the present study that MPV is higher in children with adenotonsillar hypertrophy and OSAS symptoms and that adenotonsillectomy lowers MPV levels. Higher MPV levels in children with untreated adenotonsillar hypertrophy could be an important risk factor for cardiopulmonary and cerebrovascular morbidities that could develop in childhood as well as in adulthood. Since cardiovascular morbidities in patients with pediatric OSAS could progress without symptoms, a simple and reliable laboratory parameter such as MPV will be beneficial for early determination and follow-up of these morbidities. More detailed studies are required dealing with MPV levels and MPV/PC ratios in pediatric OSAS patients.

Declaration of conflicting interests

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