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Original Article

Evaluation of mean platelet volume and platelet count in patients with schizophrenia

Şizofreni hastalarında ortalama trombosit hacminin değerlendirilmesi

Memduha Aydin[a], Bilge Cetin Ilhan[b], Tuba Serife Elmas[b], Yusuf Cokunlu[b], Ibrahim Eren[b]

[a]Selcuk University, Faculty of Medicine, Department of Psychiatry, Konya, Turkey

[b]Konya Training and Research Hospital, Department of Psychiatry, Konya, Turkey

ABSTRACT

Introduction: Compared to the general population, cardiovascular diseases are more common in schizophrenia patients and the mortality rate is higher than the general population. One of the explanations for increased cardiovascular events in patients with schizophrenia is the increase in platelet activity. Platelets are essential for progression of atherosclerotic lesions, plaque destabilization, and thrombus formation. Mean platelet volume (MPV) is a measure of platelet size and a good marker of platelet function and activation, which increases in cardiovascular diseases. MPV is routinely reported during complete blood count analysis. The aim of the present study was to evaluate MPV values of patients with schizophrenia.

Methods: In this retrospective study, hospital-records of the patients who were consecutively admitted to psychiatry inpatient clinic between January 2015 and January 2017 with the diagnosis of schizophrenia were reviewed. Healthy subjects with no personal history of psychiatric disorder were included as a control group.

Results: A total of 100 (59 female, 41 male) schizophrenic patients who had been consecutively admitted to the psychiatry inpatient clinic and 37 (20 female, 17 male) healthy controls were included in this retrospective study. There were no significant differences between the patient group and control group in the terms of age (mean age patient group vs control group: 37.72 vs 35.03, p=0.081) and sex (p=0.603). Body mass index (BMI) was found to be significantly different between groups, higher in the patient group (p=0.001). The MPV was found to be significantly higher in patient group compared with the control group (MPV, patient group vs control group: 10.34 fL vs 9.97 fL, p=0.041). Platelet count (PC) was significantly lower in the patient group (PC, patient group vs control group: 234.36 vs 267.38, p=0.008) There was no correlation between MPV and BMI (p=0.354, r=0.10), and duration of illness (p=0.530, r=0.06).

Conclusions: As a result, increased MPV and decreased PC were found in a group of schizophrenic patient in this study. Since increased MPV and decreased PC are evaluated as risk factors for cardiovascular diseases in the general population, they can also be considered as a predictor of risk factors for cardiovascular diseases that are more frequently encountered in schizophrenia.

Keywords: Cardiovascular diseases, mean platelet volume, schizophrenia

ÖZ

Giriş: Şizofreni hastalarında genel popülasyona kıyasla kardiyovasküler hastalıklara daha sık rastlanmaktadır, mortalite oranı genel popülasyona göre daha yüksektir. Şizofreni hastalarında artmış kardiyovasküler olayların açıklamalarından biri de trombosit aktivitesinin artmasıdır. Trombositler aterosklerotik lezyonların progresyonu, plak destabilizasyonu ve tromboz oluşumu için gereklidir. Ortalama trombosit hacmi (MPV), trombosit büyüklüğünün ve kardiyovasküler hastalıklarda artan platelet fonksiyonunun ve aktivasyonunun iyi bir göstergesidir. Tam kan sayımı analizi sırasında MPV rutin olarak bakılmaktadır. Bu çalışmanın amacı şizofreni hastalarının MPV değerlerini değerlendirmektir.

Yöntem: Bu retrospektif çalışmada psikiyatri kliniğine Ocak 2015 – Ocak 2017 tarihleri arasında ardışık olarak başvurmuş olan şizofreni hastalarının hastane dosya kayıtları incelendi. Kişisel psikiyatrik öyküsü olmayan sağlıklı bireyler kontrol grubu olarak alındı.

Bulgular: Psikiyatri polikliniğine ardışık olarak başvuran toplam 100 (59 kadın, 41erkek) şizofreni hastası ve 37 (20 kadın, 17 erkek) sağlıklı kontrol bu retrospektif çalışmaya alındı. Hasta grubu ve sağlıklı kontrol grubu arasında yaş (hasta grubu ve kontrol grubu ortalama yaş, sırasıyla 37,72 ve 35,03, p=0,081) ve cinsiyet bakımından anlamlı bir fark yoktu (p=0,603). Vücut kitle indexi (VKİ) hasta grubunda daha yüksek olmasıyla gruplar arasında anlamlı fark bulunmuştur (p=0,001). MPV kontrol grubuna kıyasla hasta grubunda anlamlı yüksek bulundu (hasta grubu ile kontrol grubu MPV sırayla; 10,34 fL ve 9,97 fL, p=0,041). Platelet sayısı (PC) hasta grubunda anlamlı düşük bulundu (hasta grubu ile kontrol grubu platelet sayısı sırayla: 234,36 ve 267,38, p=0,008). MPV ve VKİ arasında herhangi bir ilişki bulunmadı (p=0,354, r=0,10), MPV ile hastalık süresi arasında herhangi bir ilişki bulunmadı (p=0,530, r=0,06).

Sonuç: Sonuç olarak, bu çalışmada bir grup şizofreni hastasında artmış MPV ve azalmış PC bulundu. Artmış MPV ve azalmış PC, genel popülasyonda kardiyovasküler hastalıklar için risk faktörü olarak değerlendirildiğinden, şizofrenide daha sık karşılaşılan kardiyovasküler hastalıklar için risk faktörlerinin bir göstergesi olarak da düşünülebilir.

Anahtar kelimeler: Kardiyovasküler hastalıklar, ortalama trombosit hacmi, şizofreni

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Correspondence: Memduha Aydin, MD. Selcuk University, Faculty of Medicine, Department of Psychiatry, 42100 Konya, TURKEY

Introduction

Schizophrenia is a progressive, chronic and devastating mental disorder characterized by psychotic symptoms such as hallucinations, delusions, and cognitive symptoms that affect almost all aspects of mental activity, including perception, attention, memory, and emotion [1]. Cardiovascular diseases are more common in schizophrenia patients than the general population, and mortality rate is higher than the general population [2]. The increase in platelet activity is an explanation of increased cardiovascular events in schizophrenia patients [3, 4]. Platelets are small, anucleotide cytoplasmic cells without genomic DNA, and they play essential roles in the progression of atherosclerotic lesions, plaque destabilization, and thrombus formation by releasing mediators for coagulation, inflammation, and atherosclerosis [5, 6]. Platelet activation including change in platelet shape, platelet aggregation and the release of platelet constituents has been associated with the pathogenesis of a number of diseases, which include atherosclerosis, coronary vascular disease, cerebrovascular disease, and also neuropsychiatric disorders [7, 8].

Mean platelet volume (MPV) is a measure of platelet size and a good marker of platelet function and activation [8]. Increased MPV levels are accepted as an indication of increased platelet activity [7]. Studies show that increased MPV is an independent risk factor for cardiovascular and atherosclerotic diseases [9, 10]. MPV has been found to be elevated in various mental disorders. The relationship between anxiety disorders, bipolar disorder, schizophrenia, major depression and increased platelet activity has been reported by several studies [11-15].

The platelet count has been used as a platelet concentration parameter. Platelet concentration is crucial for the maintenance of hemostatic function [16]. Low platelet concentration indicating decrease in platelet count can be observed in numerous cases including increased peripheral platelet destruction, increased splenic sequestration, decreased bone marrow platelet production [17]. The relationship between MPV and PC is unclear [18]. Several studies report an inverse association between platelet volume and number of platelet while a few study reports both increase during cardiovascular events [17, 19-21].

The aim of the present study was to evaluate MPV values and platelet count (PC) of patients with schizophrenia, and support the recent studies about using platelet parameters as an alternative strategy to monitor for cardiovascular diseases in schizophrenic patients.

Methods

This retrospective study included 132 consecutive patients at the age of 18-65 who were admitted to psychiatry inpatient clinic of Konya Training and Research Hospital with the diagnosis of schizophrenia and fullfilled the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) criteria between January 2015 and January 2017. Data from 100 (59 female, 41 male) patients were finally analyzed after excluding 32 patients with missing data. The control group consisted of 37 (20 female, 17 male) age and gender matched healthy volunteers with no personal history of psychiatric disorder. The study protocol was approved by the Institutional Review Board of Selcuk University Faculty of Medicine, Konya and adhered to the tenets of the Declaration of Helsinki (24.05.2017; 2017/163). Informed consent was obtained from all subjects prior to their participation in the study.

Criteria for the exclusion of a subject from the study were as follows; (1) coronary artery disease/myocardial infarction/heart valve disease, (2) pulmonary disease, (3) rheumatic disease, (4) liver disease, (5) neurological deficit/mental retardation/autism, (6) iron deficiency anemia, (7) pregnancy, (8) infection, (9) kidney disease, (10) alcohol/substance use, (11) antiplatelet-anticoagulant drug use, (12) bone marrow disease/myelodysplastic syndrome.

Sociodemographic and Clinical Data Form: Semi-structured sociodemographic and clinical data form was developed by the researchers of the study. Medical records including patient socio-demographic, clinical variables and complete blood count analysis, and reports from relatives and/or caregivers used as information sources.

Statistical analyses

Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) 20.0 for Windows (SPSS, Inc., Chicago, IL, USA). Descriptive parameters are expressed as mean, standard deviation or percentage. Once the normality of the data was determined via Kolmogorov Smirnov test; two-sided t-test and Pearson Chi-square test were used for comparison of normally distributed variables of patients with schizophrenina and healthy volunteers. Abnormal distributed variables were compared with Mann–Whitney U-test. While investigating the associations between MPV and other variables, correlation coefficients and their significance were calculated using Pearson test. For all evaluations, a p value of less than 0.05 was considered as statistically significant.

Results

Data of 100 (59 female, 41 male) patients with schizophrenia and 37 (20 female, 17 male) healty control were analyzed in this study. The ratio of females was 59.00% in the schizophrenia group and 54.10 % in the control group. There were no significant differences between the patient group and control group in the terms of age (mean age patient group vs control group: 37.72 vs 35.03, p=0.081) and sex (p=0.603). Body mass index (BMI) was found to be significantly different between groups, higher in the patient group (p=0.001). Sociodemographic and clinical characteristics of the patient and control groups are given in Table 1.

Table 1. Characteristics of patients with schizophrenia and the control group participants

Characteristics	Schizophrenia (n=100), (%), ±SD	Control (n=37), (%), ±SD	*p value*
Sex			
Female, n (%)	59 (59.00%)	20 (54.10%)	0.603
Male, n (%)	41 (41.00%)	17 (45.90%)	
Age	37.72±9.42	35.03±7.28	0.081
Duration of illness, years	13.56±8.05	_	
BMI	29.02±7.48	25.34±4.37	**0.001**

Values are mean n: number; ± SD: Standard Deviation; Bold values indicate statistical significance; BMI: Body Mass Index

Ninety-seven (97.00 %) patients were on antipsychotic treatments. Forty-five patients were treated with depot antipsychotics as monotherapy, 15 patients were treated with oral antipsychotics as monotherapy, 37 patients were treated with both depot and oral antipsychotics as combination therapy and 3 patients were drug naïve on admission. There were no significant differences between the monotherapy group and combination therapy group in the terms of MPV (mean MPV monotherapy group vs combination therapy group: 10.34 vs 10.38, p=0.834) and PC (mean PC monotherapy group vs combination therapy group: 240.43 vs 226.79, p=0.305). There were no significant differences between the typical depot antipsychotics as monotherapy group (n=19) and atypical depot antipsychotics as monotherapy group (n=26) in the terms of MPV (mean MPV typical depot antipsychotics monotherapy group vs atypical depot antipsychotics group: 10.44 vs 10.40, p=0.893), and PC (mean PC typical depot antipsychotics monotherapy group vs atypical depot antipsychotics monotherapy group: 231.16 vs 250.00, p=0.405) (Table 2).

Table 2. Mean platelet volume and platelet count in patients with schizophrenia according to typical or atypical depot antipsychotic monotherapy

Parameters	Typical Depot Antipsychotics Monotherapy (n=19) ±SD	Atypical Depot Antipsychotics Monotherapy (n=26) ±SD	*p* value
MPV (fL)	10.44±0.99	10.40±1.00	0.893
PC (K/uL)	231.16±72.20	250.0±75.61	0.405

Values are mean n: number; ± SD: Standard Deviation; MPV: Mean Platelet Volume; PC: Platelet Count;

According to the comparison of blood count values, MPV was found to be significantly higher (MPV patient group vs control group: 10.34 fL vs 9.97 fL p=0.041), and PC was significantly lower (PC patient group vs control group: 234.36 vs 267.38, p=0.008) in the schizophrenina group. The laboratory findings for the two study groups are presented in Table 3.

Table 3. Laboratory findings for the patients with schizophrenia and control group participants

Parameters	Schizophrenia (n=100), ±SD	Control (n=37), ±SD	*p value*
MPV (fL)	10.34±0.93	9.97±0.97	**0.041**
PC (K/uL)	234.36±63.48	267.38±65.92	**0.008**
Cholesterol	190.10±44.99	195.97±42.54	0.493
AST	19.59±7.80	20.57±7.45	0.510
ALT	17.56±12.93	21.32±11.85	0.124

Values are mean n: number; ± SD: Standard Deviation; Bold values indicate statistical significance; MPV: Mean Platelet Volume; PC: Platelet Count; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase

There was no correlation between MPV and BMI in the patient group (p=0.354, r=0.10), and in the control group (p=0.273, r=0.2). There was no correlation between MPV and duration of illness in the patient group (p=0.530, r=0.06). Also, there was no correlation between MPV and age in the patient group (p=0.398, r=-0.08).

When patients with schizophrenia were evaluated according to sex, PC was significantly higher in females than in males (PC female group vs male group: 245.12 vs 218.88, p=0.041). However, there were no statistically significant differences in terms of MPV (p=0.190) (Table 4).

Table 4. Mean platelet volume and platelet count in patients with schizophrenia according to sex

Parameters	Female (n=59) ± SD	Male (n=41) ± SD	*p* value
MPV (fL)	10.24±0.88	10.49±0.99	0.190
PC (K/uL)	245.12±62.83	218.88±61.91	**0.041**

Values are mean n: number; ± SD: Standard Deviation; Bold values indicate statistical significance; MPV: Mean Platelet Volume; PC: Platelet Count

Discussion

The present study found higher MPV levels and lower PC in a group of patients with schizophrenia when compared with the healthy controls. Patients with schizophrenia are reported to be at higher risk for cardiovascular diseases, and they have shorter life spans than the general population [2, 22]. Although several risk factors such as genetic vulnerability, smoking, lifestyle factors including an unhealthy diet, lack of exercise, and treatment with antipsychotic drugs have been identified for the association between schizophrenia and cardiovascular diseases, the exact mechanisms that increase cardiometabolic risk factors and metabolic syndrome in schizophrenic patients remain unclear [22-25].

Platelets play an important role in cardiovascular diseases. The increase in platelet activity is one of the explanations proposed for increased cardiovascular events in schizophrenic patients [3, 4]. MPV has been used as a peripheral marker of platelet activity, and increased MPV levels are accepted as an indication of increased platelet activity [7]. The relationship between schizophrenia and increased platelet activity has been previously reported by several studies. Our study results showing an increase in MPV and a decrease in PC in schizophrenia are consistent with previous studies. One of these studies, by Semiz et al., assessed the effect of treatment with antipsychotics on platelet volume [26]. They found significantly higher MPV levels in patients who were on atypical antipsychotic drugs than in patients who were not using any drug and also higher than control group. Furthermore, they reported that patients who were not using antipsychotics had higher MPV than control group. Semiz et al concluded that MPV appears to be affected not only by schizophrenia itself but also by atypical antipsychotic medications.

In another study, by Wysokiński and Szczepocka, which assessed the platelet parameters in patients with schizophrenia, unipolar depression and bipolar disorder found significant differences in platelet parameters between study groups. Patients with schizophrenia had significantly higher MPV levels and had significantly lower PC than other study groups [12]. Wysokiński and Szczepocka have also analyzed differences in platelet parameters between sex and age-subgroups. They found significant sex and age differences for PC and MPV in schizophrenia patients. Our results does not include analyzes comparing sex and age sub-groups. Investigating the associations between age, sex and platelet-releated parameters may help understanding the increased risk better for cardiovascular diseases in psychiatric disorders.

Lee et al. revealed that increase in MPV were found to be independent of antipsychotic treatment in their study. They concluded that there were no differences between antipsychotic types, and the MPV and PC were not significantly altered after 1 year of clozapine treatment [11]. In our study, we also compared patients receiving typical depot antipsychotic medications with atypical depot antipsychotic medications as monotherapy in order to investigate whether the changes in platelet parameters was due to typical or atypical antipsychotic therapies. Concordant with study reported by Lee et al., we found no significant differences between the typical and atypical depot antipsychotic medication group in the terms of MPV and PC. These results indicate that increase in MPV and decrease PC in schizophrenia might be related to the underlying disease process.

Body mass index is reported to have an increasing effect on MPV levels [27]. Coban et al. aimed to evaluate the effect of weight loss on the MPV in obese patients. The results of this study indicated that MPV levels decreased after a three month diet treatment in the obese group. They found a positive correlation between weight loss and reduction in MPV. We compared BMI of patients with schizophrenia with healthy controls. BMI was found to be significantly different between groups, higher in the patient group. Although there was no correlation between MPV and BMI in the patient group and in the control group, elevation in MPV levels in schizophrenia group may be attributed to higher BMI of patient group.

A number of limitations should be considered for our study. The heterogeneity of patients in terms of disease progression (i.e. acute/chronic), in terms of symptom severity and in terms of treatments received (i.e. type of antipsychotics, antidepressants etc.) are some of the limitations that make it difficult to generalize the results to all sub-groups.

Conclusion

In conclusion, the measurement of platelet volume and activity is thought to be a predictor of cardiovascular disease in the general population, and may be used as an alternative strategy to monitor for cardiovascular diseases in schizophrenic patients. The mechanism underlying the differences in platelet-related parameters is still not understood. There is need for further studies establishing the association of platelet activity and platelet-related parameters with cardiovascular diseases in patients with schizophrenia and other psychotic disorders.

Preliminary results of this study were presented in oral sessions in “9th International Congress on Psychopharmacology & 5th International Symposium on Child and Adolescent Psychopharmacology”

Conflict of Interest: None.

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