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ORIGINAL ARTICLE

Patients with First Episode Psychosis and Chronic Schizophrenia may not Differ in Mean Platelet Volume Affecting its Value as an Indicator of Cardiovascular Disease

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ABSTRACT

Objective: The aim of the present study was to examine differences in terms of mean platelet volume (MPV) in patients with first episode psychosis, chronic schizophrenia, and psychiatrically healthy controls and to determine the potential value of MPV for cardiovascular disorders in patients with psychotic disorders.

Methods: A total number of 32 patients with first episode psychosis, 44 patients with chronic schizophrenia, and 43 randomly selected weight- and body mass index-matched psychiatrically healthy controls who presented to the Psychiatry Outpatient Clinic were included. The Positive and Negative Syndrome Scale (PANSS) was administered to the patients group. The body mass index (BMI) was calculated and MPV was measured for each subject.

Results: The mean MPV level was 9.38±1.00 fL in patients with first episode psychosis, 9.60±1.02 fL in patients with chronic schizophrenia, and 9.2±0.94 fL in psychiatrically healthy controls group. MPV levels were not significantly different between the three groups. There were no statistically significant differences between the three groups in terms of platelet count or BMI. There were no statistically significant correlations between the MPV levels and total PANSS scores in the patients groups.

Conclusions: To the best of our knowledge, the present study was the first to evaluate the MPV levels in patients with first episode psychosis. We consider that it is not appropriate for MPV to be used as an indicator for CVDs in patients with psychosis. Better-designed and more advanced studies are necessary to determine the exact function of platelets and the importance of MPV in patients with first episode psychosis and chronic schizophrenia.

Keywords: Chronic schizophrenia, first attack psychosis, mean platelet volume

INTRODUCTION

Cardiovascular diseases (CVDs) are more commonly encountered in psychotic disorder patients when compared to the general population (1,2). Cardiovascular risk factors such as obesity, smoking, and diabetes are more common among psychotic patients when compared to the healthy controls, so the risk for cardiovascular diseases is higher in psychotic disorder (3). Also, the mortality rate due to CVDs is higher among schizophrenic patients when compared to the general population, and is frequently observed at younger ages.

The mean platelet volume (MPV), the measure of platelet size, is considered to be a determinant of platelet function. Increased MPV is thought to be firmly associated with CVDs, especially ischemic heart diseases (4), acute myocardial infarction (MI) (5), and congestive heart failure

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(6). Peripheral platelet models are widely used as indicators of central serotonin (5-HT) metabolism, as they reflect central serotonergic function (7). Serotonin is a factor in the pathophysiology of psychotic disorders and plays pivotal roles in the vascular system in the regulation of vascular tone and platelet aggregation (8) Platelets have serotonin (5-HT) receptors such as 5-HT2A, 5-HT3, and a 5-HT transporter (5-HTT) in their membranes (9,10). Experimental studies have shown that 5-HT-potentiated procoagulant responses of platelets enhance thrombogenesis on damaged vascular surfaces. MPV has been defined as a key factor in platelet function. It has been shown that platelet size, measured as MPV, correlates with platelets' reactivity (4). Some studies showed that patients with some psychiatric disorders have elevated platelet counts (6,8). Also, the relationship between increased platelet activity and psychiatric disorders such as major depressive disorder and schizophrenia has been previously reported in previous studies (8-10).

The aim of the present study was to examine differences in the mean platelet volume of patients with first episode psychosis, chronic schizophrenia, and psychiatrically healthy controls and to determine the potential value of MPV for cardiovascular disorders in patients with psychotic disorders.

METHODS

Study Participants

This study included a total number of 32 patients with first episode psychosis, 44 patients with chronic schizophrenia, and 43 randomly selected weight- and body mass index-matched psychiatrically healthy controls who presented to the Psychiatry Outpatient Clinic. Diagnoses of the patients were made schizophrenia diagnosis criteria per the Diagnostic and Statistical Manual of Mental Disorders Fourth edition (DSM-IV).

The patients with the first episode who take antipsychotics and patients with affective psychosis were excluded from the study. Individuals with any other chronic disease such as diabetes mellitus, hypertension, hyperlipidemia, or neurological disorders, who were under 18 years of age and those over 65 years of age and pregnant women in the menstrual cycle, were excluded from the study. People with any additional psychiatric conditions were excluded; also those with mental retardation and those with organic brain damage were not included in the study. A written informed consent was obtained from each participant.

The study protocol was approved by the Institutional Ethics Committee. When sufficient number of patients was reached, the sample collection process was terminated between 2014 and 2017. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Blood Collection and Clinical Laboratory Measurements

Socio-demographic data, such as age, gender, educational level, marital status, occupational status, mental status, smoking, height and weight and BMI index, were collected. The severity of schizophrenia symptoms in the patients was evaluated using the Positive and Negative Syndrome Scale (PANSS). Physical and neurological examinations were performed in all participants. Routine psychiatric examination and PANSS scale were administered on the blood collection day. Approximately 10 mL of blood was obtained from the front of the left arm after a 12-hour fasting period, and the first 2 mL of blood, which was used for the full blood count, was drawn into a vacutainer tube containing 0.04 mL of 7.5% ethylenediaminetetraacetic acid (EDTA, tripotassium salt). The remainder of the blood was drawn into a vacutainer tube without anticoagulant. To minimize the potential interference of EDTA in relation to MPV, all blood samples were analyzed 60 minutes after venipuncture. MPV and platelet count were measured using a Cell-Dyn 3500 (Abbott Laboratories, Abbott Park, Chicago, IL, USA) device. After obtaining the blood samples, MPV and platelet counts were measured. Levels of 150,000-400,000 per mm3 of blood were accepted as the normal range for platelet counts and 6.9-11.0 fL (femtoliter, a

metric unit of volume equal to 10-15 L) was used for MPV. All samples were analyzed daily at the Hospital Central Laboratory.

Statistical Analysis

Statistical analysis was performed using NCSS version 2007 software (Number Cruncher Statistical System) (Kaysville, Utah, USA). Descriptive data were expressed in mean, standard deviation, frequency, and rate. Shaphiro-Wilk test was used at compliance control of constant variables with normal distribution. Student's t-test was used for normally distributed variables in comparison of numeric variables at two independent groups, and Mann-Whitney U test was used for ones not normally distributed. One-way ANOVA test was used for normally distributed variables while comparing at more than two groups and Kruskal-Wallis test was used for the ones not distributed normally. Spearman's Rank test was used for the relationship between numeric variables, and chi-square test was used for the relationship between coefficient of correlation and categorical variables. P values of <0.05 were considered statistically significant.

RESULTS

All groups had similar demographic characteristics. The demographic and biochemical characteristics were shown in Table 1. The BMI was 24.89±5.02 kg/m^2 in patients with first episode psychosis, 26.02±4.82 kg/m^2 in patients with chronic schizophrenia and 24.53±4.02 kg/m^2 in control group, indicating no statistically significant differences were found between the three groups (p=0.300).

The mean MPV level in patients with first episode psychosis was 9.38±1.00 fL, 9.60±1.02 fL in patients with chronic schizophrenia and 9.2±0.94 fL in control group. MPV level was not statistically different between the three groups (p=0.184). In addition, there were no statistically significant correlations between the MPV levels and total PANSS scores in the patients groups (p>0.05). There were no statistically significant differences in sociodemographic variables in terms of the mean MPV levels between the three groups. MPV levels of three groups were not statistically significantly corrlated with BMI and smoking status (p>0.05).

DISCUSSION

In the present study, MPV levels were not significant different between the three groups. In addition, we found that MPV did not correlate with severity of psychotic symptoms. Some studies showed correlation between increased MPV and some psychiatric disorders such as attention-deficit/ hyperactivity disorder (11), major depressive disorder (12), panic disorder (13), bipolar disorder (14), and schizophrenia (15). One study demonstrated significant correlations between decreased MPV and panic disorder (16). Some factors such as genetic vulnerability (17), illness-related outcomes (18), unhealthy lifestyle choices (19), and antipsychotic treatment (20-22) were blamed for increasing cardiometabolic risk factors in schizophrenia. Change in

Table 1: The demographic and biochemical characteristics of all groups

Variables data	First attack psychosis group (n=32)	Chronic schizophrenia group (n=44)	Control group (n=43)	Statistic	p
Sex (female/male)	13 (19)	21 (23)	25 (18)	χ^2:0.982	0.309
Age (X±SD)	30.34±11.8	34.11±10.76	29.77±7.97	F:1.210	0.106
BMI (kg/m^2)	24.89±5.02	26.02±4.82	24.53±4.02	F:2.491	0.300
Total PANSS	101.75±17.85	95.75±21.04	-	U:301.50	0.195
PC (x10^9)	275.91±67.87	276.86±80.35	268.21±58.26	F: 6.384	0.894
MPV (fL)	9.38±1.00	9.6±1.02	9.2±0.94	F:2.272	0.184

BMI: Body mass index, PANSS: Positive and Negative Syndrome Scale, PC: Platelet count, MPV: Mean platelet volume, fL: Femtoliter, Pearson's Chi-square test, Mann Whitney U Test, One-way ANOVA Test, Kruskal Wallis Test, Adjustment for Multiple Comparisons: Bonferroni, p<0.05

platelet activity has also been reported to contribute to increased cardiovascular disease and metabolic syndrome in patients with schizophrenia (5). The platelets are considered to be a peripheral marker in major psychiatric disorders including schizophrenia (23). In the in vitro study by Dietrich-Muszalska and Olas (24), aggregation of blood platelets induced by ADP was found to be higher in schizophrenia patients than in healthy individuals. In the literature, this is the second study to evaluate MPV levels in first episode psychosis patients. In this study, we consider it is significant that MPV levels of patients both with first episode psychosis and chronic schizophrenia were the same with healthy control groups. We propose the number of platelet should be determined prior to treatment and monitored in the course of therapy to determine relationship between MPV and psychosis.

In the present study, we found no significant correlations between the MPV levels and BMI. Some studies showed significant correlation between increased MPV and BMI (25,26), while some studies (27,28) showed no significant correlations between MPV and BMI, which is similar to our findings. Antipsychotic drugs are widely used in the treatment of psychotic disorders. Atypical antipsychotics are known to induce weight gain as well as cardiovascular and metabolic abnormalities, thereby increasing the patient's risk of obesity, the metabolic syndrome, and type 2 diabetes mellitus, and associated cardiovascular morbidity (29). Increased risk of thrombotic events in schizophrenic patients treated with antipsychotic drugs has also been reported (30-32). The antipsychotic treatment may cause the modification of platelet reactivity in vivo and in vitro (33,34). The antiplatelet effects of antipsychotics have been established (30,35). Antipsychotics can alter platelet membrane lipid, receptors on the surface, intracellular messengers, and signal transduction. They may have some effects on platelet membrane structure and dynamics via lipid peroxidation caused by free radicals (35,36).

In this present study, we found no correlations between the MPV levels and total PANSS scores in the patient groups. Therefore, we concludes that there were no relationship between the severity of psychosis and MPV levels. Platelets play role in particularly serotonin synthesis, release, and reuptake of monoamines just as the one in central nervous system (37). SERTs and 5-HT2A receptor of serotonergic neurons at platelet and the brain are encoded by the same gene (37,38). İncrease of epinephrine and changes at serotonin concentration make it possible for platelets to get activated (29). There is wide a range of preclinical and clinical studies which point out those 5-HT1A receptors are responsible for cognitive changes in patients with schizophrenia (39). In genetic studies, it has been demonstrated that 5-HT1D and 5-HT1F receptors play role in schizophrenia (40). It has also been concluded that 5-HT2A and 5-HT2C receptors play a remarkable role displaying therapeutic effects of antipsychotic. It was also proposed that 5-HT2A receptor had also effect on information processing of working memory, which was impaired in patients with schizophrenia. Reduction of dopamine transmission at nucleus accumbens is the basis of effects of antipsychotics on the positive symptoms of schizophrenia. It has been showed that 5-HT2C receptor agonists reduce dopamine transmission at nucleus accumbens and ventral tegmental area (39,40). The mechanisms explaining the relationship between antipsychotics and blood platelet responses are not clear. We consider the findings significant that MPV levels were similar in chronic schizophrenia patients who were under antipsychotic treatment and the patients who did not receive antipsychotic treatment. Perhaps the patients in our study were using typical antipsychotics. Another reason might be the absence of any other underlying cardiometabolic diseases in our patients.

In the present study, we found no significant correlations between the MPV levels and smoking status. Kario et al. reported that an increase in MPV due to smoking may also contribute to the acceleration of atherosclerosis and should be considered as a risk factor for atherosclerotic disease (41). Better-designed and more advanced studies are necessary to determine relationship between the MPV and smoking.

MPV has been reported to be a determinant of platelet function. It has been previously reported that larger platelets have a greater mass, denser granules and are more active enzymatically and metabolically than smaller platelets (4,42). Additionally, larger platelets

aggregate more rapidly than smaller platelets (42). Increases in platelet volume are often associated with decreases in platelet count perhaps as a result of small platelets being consumed to maintain a constant platelet functional mass (43). We found normal platelet count and no significant correlations between the MPV levels and platelet counts in our study.

This present study has certain limitations. First, this is a cross-sectional study with a small sample size. Absence of data relating to the duration of first episode psychosis in psychotic patients is another limitation. Another limitation is lack of controlling for symptoms of depression/anxiety, lack of controlling for antipsychotics used. Therefore, we were unable to compare the effects of typical and atypical antipsychotics on MPV in patients with chronic schizophrenia.

To the best of our knowledge, the present study was the first to evaluate the MPV levels in patients with first episode psychosis. Moreover, it is also first study to compare the MPV levels of patients with first episode psychosis and chronic schizophrenia. We consider that it is not appropriate for MPV to be used as an indicator for CVDs in patients with psychosis. Better-designed and more advanced studies are necessary to determine the exact function of platelets and the importance of MPV in patients with first episode psychosis and chronic schizophrenia.

Ethics Committee Approval: The study protocol was approved by the Institutional Ethics Committee.

Conflict of Interest: The authors declared no conflicts of interest.

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