THE EFFECT OF SELECTIVE SEROTONIN REUPTAKE INHIBITOR (SSRI) TREATMENT ON MEAN PLATELET VOLUME IN MAJOR DEPRESSIVE DISORDER (MDD) PATIENTS

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ABSTRACT

Introduction*: Patients with depression are at an increased risk for cardiovascular disease. Mean platelet volume (MPV) provides a measurement of activated platelets; increasing platelet activation is one of the mechanisms that may link depression and ischemic cardiac disease.*

Material and method*: 100 newly diagnosed patients with major depressive disorder (MDD) and 100 healthy controls admitted to our outpatient clinics. We started selective serotonin reuptake inhibitor (SSRI) treatment in the MDD patients and followed them for 3 months. Patients' laboratory tests and physical, neurological, and psychiatric examinations were performed both at diagnosis and after 3 months of treatment.*

Results*: The MDD group consisted of 90 people and the control group consisted of 88 people met the inclusion/exclusion criteria. There was no significant difference between the ages of the groups (p = 0.28). There were more males within the MDD group (55.6%). MPV was significantly greater in MDD group (p<0.001); MPV levels showed significantly decline after treatment with SSRIs (p<0.001). The platelet counts were also significantly low in MDD patients when compared with the control group, with the difference being statistically significant (p<0.001). No significant difference was observed in platelet counts after treatment. Severity of depression also declined after treatment. The average Montgomery-Asberg Depression Rating Scale (MADRS) score decreased 9.23 points; the difference was statistically significant (p<0.001).*

Conclusion*: We conclude that MPV can be an indicator of platelet activity in patients with MDD and SSRIs can be used along with MPV to help identifying and treating coronary artery disease in MDD patients. According to our findings, SSRIs may have an antiplatelet action in addition to their antidepressant effects, which may be beneficial for MDD patients with coronary artery disease.*

Key words*: Depression, mean platelet volume, coronary artery disease, SSRI.*
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Introduction

Platelets are very important in the pathogenesis of atherosclerotic process by contributing thrombus formation[(1)]. MPV (mean platelet volume) is the most commonly used measure of platelet size; it shows activated platelets. This marker is an available, simple, and inexpensive test that is easy to interpret within clinical practice. MPV levels are associated with various diseases and unhealthy habits. MPV levels are elevated in patients with diabetes mellitus[(2, 3)], myocardial infarction[(4, 5)], hyperthyroidism[(6)], chronic obstructive pulmonary disease[(7)], smoking habits[(8)], and renal artery stenosis[(9)]. MDD (major depressive disorder) have important role for cardiovascular mortality and morbidity[(10, 11)].

MDD is a major health problem that associated with morbidity and mortality..World Health Organization (WHO) reported that major depressive episode has seen 6.5 % in China, 19.2 % in USA and 21% in France[(12)]. One of every five women and one of every eight men have an episode of major depression in the course of their life[(13, 14)].

Many studies indicate that MDD is a predictor of cardiovascular disease[15, 16]. Increased platelet activation is one of the mechanisms that show a relationship between depression and ischemic cardiovascular disease[17]. Platelet activation is due to reduced plasma levels of 5-hydroxytryptamine (5-HTA) and epinephrine[18] and SSRIs (Selective Serotonin Reuptake Inhibitors) inhibit platelet activation both in nerve cells and platelets[19].

In our study, we aimed to investigate the relationship between MPV levels and the presence of MDD and compare the results with non-depressive volunteers. Our secondary goal was to determine the effect of SSRI treatment on MPV levels in patients with MDD.

Materials and methods

Participants

Our study included 100 newly diagnosed MDD patients and 100 control patients admitted to our outpatient clinics for routine examination. Our control patients consist of people who do not have our exclusion criteria and without depressive symptoms. Control group age and gender characteristics were closed. We followed these patients from September to December 2014. The patients were evaluated both at diagnosis and after 3 months of treatment. All of the patients signed consent forms to participate the study. The study design was approved by the ethics committee of Firat University, Faculty of Medicine, Elazig, Turkey. The study was conducted in accordance with the Declaration of Helsinki.

Clinical examination

All the patients were questioned for past medical history. Their laboratory tests and physical, neurological, and psychiatric examinations were done at diagnosis and after 3 months of treatment.

Biochemical measurements

Fasting venous blood samples were drawn after 8 hours of fasting. The assays were performed at the laboratory in Cagri Private Medical Center and Firat University's Faculty of Medicine using a biochemical analyzer (HORIBA ABX PENTRA DX 120). Hemograms values were measured by an autoanalyzer (Beckman Coulter LH 780 Hematology System). The blood samples were processed within 30 minutes after blood collection.

Diagnosis and exclusion criteria

The Diagnostic and Statistical Manual of Mental Disorders, 4th Edition's (DSM-IV) criteria was used to diagnose major depressive disorder (MDD). The MADRS[20] was used for assessing the severity of depression and the effectiveness of the treatment. Patients with cardiovascular disease, hepatic or renal failure, previously detected malignancies, diabetes mellitus, hyperthyroidism, pregnancy, chronic obstructive pulmonary disease, or who were smokers or using anticoagulant-antiplatelet medications, were excluded from the study.

Treatment

The MDD patients were all newly diagnosed and they did not use any drugs or co-medications. Their treatment started with SSRIs (escilatopram and sertraline) and continued for 3 months. Escitalopram and sertraline were given at a dose of 10 to 20 milligrams per day (mg/d) and 25 to 50 mg/d consecutively.

Statistical analysis

All statistical analyses were performed with the Statistical Package for the Social Sciences (SPSS) 15.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics were presented as arithmetic mean ± standard deviation. The significance of the mean differences between groups was assessed by Student's *t*-test and the Mann-Whitney *U*-test. Also, the nonparametric Wilcoxon Signed-Rank test was used to test for differences between related (paired) samples. Relationships between variables were tested using Pearson's correlation analysis. Receiver operating characteristic (ROC) curve graphics were used in the comparison of sensitivity and specificity. Two tailed *P* values of less than 0.05 were regarded as significant.

Results

100 MDD patients were evaluated; 90 patients were enrolled in our study. The control group included 88 healthy individuals. Mean age was 43.9 ± 11 in MDD patients and 40.1 ± 11.6 in the healthy group. There were no significant difference between the age distributions of the groups ($p = 0.28$). 55.6% of MDD patients and 33% of the healthy group was male. Majority of patients with MDD were male. The demographic and gender dispersions of the subjects are summarized in Table 1.

	Depression patients	Controls
Number of patients	90	88
Age (years)	43,9±11	40,1±11,6
Male (n/%)	50 / 55,6%	29 / 33%
Female	40 / 44,4%	59 / 67%

Table 1: Baseline characteristics of patients and control group.

In MDD patients, platelet count was detected as 175.34± 61 x 109 /L and MPV as 10.4±1.46 fl. In the control group, platelet counts was 228.6 ±81.4 x 109 /L and MPV was 9.33 ± 1.14 fl. MPV was found to be higher in the MDD group ($p<0.001$) and MPV levels which measured after SSRI treatment were significantly low when compared with the baseline levels ($p<0.001$). The platelet counts were also significantly lower in MDD patients when compared with control group ($p<0.001$). Severity of depression also declined after treatment. MADRS score decreased 9.23 points ($p<0.001$) (Table 2).

	Patients(n=90)	Controls(n=88)	p
MPV (fL)	10,4±1,5	9,3±1,1	**<0,001**
PLT (x103)	175,3±61	228,6±81,4	**<0,001**

Table 2: Baseline MPV (mean platelet volume) levels and PLT (platelet) counts of study groups.

The significant difference between the baseline levels of MPV in the MDD and control group was not detected after the SSRI treatment ($p<0.001$). The effect of treatment on clinical and biochemical features in patients with depression are given in Table 3.

	Before treatment	After Treatment	p
MPV (fL)	10,4±1,5	9,7±1,2	<0,01
PLT (x103)	175,3±61	188±68	0,85
MADRS	23,5±11,6	14,3±9,3	<0,001

Table 3: Before and after treatment levels of MPV (mean platelet volume) and count of PLT (platelet).

Discussion

Patients with MDD are at an increased risk for cardiovascular disease[15]. The mechanism is not clear yet. High platelet activity may be one of the reasons for this condition[17]. MDD have an impact on multiple platelet parameters, including reduction of serotonin transporters and increase of 5-HT2 receptor binding place on the platelet's surface[21]. Several studies have shown that antidepressant medications, especially SSRIs (sertraline, escitalopram, and fluoxetine), have antiplatelet effects[19, 22, 23]. Non-SSRI antidepressant medications are not effective on platelet activity[24, 25].

Atar et al. showed that escitalopram treatment blocked platelet activity in coronary artery disease and in metabolic syndrome[26]. In another study Wozniak et al. showed that SSRIs use is associated with re-infarction and mortality by inhibition of platelet aggregation[27].

The effect of escitalopram was evaluated in patients without depression in studies. Our study adds value to the literature by evaluating in vivo effects of SSRIs in MDD patients.

In this study, we examined the MPV and platelet levels in MDD patients and the effect of SSRI treatment on these parameters. The results of our study support that platelet activation increases during depression and decreases after SSRI treatment. We proved that MPV can be a biomarker of platelet activity in patients with MDD and that it can be used for determining the efficacy of SSRIs treatment..

Our study had some limitations. This study was a mid-size cross-sectional study so that we could observe an association between study parameters and depression. Only hemogram parameters were evaluated in our study; other biochemical parameters were not studied.

In conclusion, our study showed that SSRI treatment decreased MPV levels in MDD patients when compared with healthy people. We found a correlation between the decline in severity of MDD symptoms, high MPV levels, and improved MADRS score after SSRI treatment. According to our results, SSRIs may have an antiplatelet activity besides to its antidepressant effect, which may be beneficial for MDD patients with coronary artery disease.

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