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A Study of Leukocyte and Platelet Activity in Patients with Suicide Attempt Related to Acute Stres Reaction

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ÖZET:

Akut stres reaksiyonu ile ilişkili olarak intihar girişiminde bulunan hastalarda lökosit ve trombosit aktiviteleri üzerine bir çalışma

Amaç: Akut stres reaksiyonu (ASR) sıklıkla depresyonla birlikte görülür ve stresle ilişkili hormonlar trombosit birikimiyle ilişkili arteriyel trombozda önemli rol oynarlar. Bilgimize göre ASR ile ilişkili bir intihar girişimi sonrasında lökosit ve trombosit sayımını değerlendiren çalışma yoktur.

Yöntem: Bu çalışmada kan lökosit, trombosit ve ortalama trombosit hacim (MPV) düzeyleri incelendi. İlave olarak, bu parametreleri etkileyen etmenler değerlendirildi. Acile başvuran ve intihar girişimi sonrasında aynı psikiyatrist tarafından değerlendirilen hastalara ait veriler toplandı. Aynı bölgede yaşayan sağlıklı örneklem grubu kontrol grubu olarak kabul edildi. Vaka-kontrol çalışması olarak dizayn edilen bu çalışmada 30 intihar girişimi vakası ve yaş ve cinsiyet olarak uygun 33 kontrol vakası analize tabi tutuldu.

Bulgular: İntiharla ilişkili ASR tanısı olan 30 kişinin kontrollerle karşılaştırılmasında kan sonuçları artmış lökosit düzeyi saptanırken trombosit sayısı ve MPV düzeyleri benzer bulundu. Takipte, trombosit düzeyi hasta grubunda daha düşük düzeylerde bulundu (p=0.001) ve bu düşüklük intihar amaçlı antidepresan kullanımı ile ilişkiliydi (p=0.003).

Sonuç: ASR sonrasında trombosit sayısı veya MPV düzeyi artmadı, fakat lökosit sayısında artış gözlemlendi. İlaveten, çalışmamız antidepresan ilaçlarla ilişkili anti-trombosit etkinin varlığını da desteklemekteydi.

Anahtar sözcükler: akut stres reaksiyonu, intihar, trombosit, lökosit, ilaçlar, anti-depresan, analjezik

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ABSTRACT:

A study of leukocyte and platelet activity in patients with suicide attempt related to acute stres reaction

Aim: Acute stress reaction (ASR) is often seen with depression, and stress-related hormones may play an important role in acute arterial thrombosis by increasing platelet aggregation. To the best of our knowledge, no study has examined leukocyte and platelet counts following a suicide attempt with ASR.

Method: The present study examined blood leukocyte, platelet and mean platelet volume (MPV) levels. In addition, we examined the factors affecting these parameters. Data for patients who were admitted to the emergency room and evaluated by same psychiatrist after a suicide attempt were obtained from the health registries. Controls were selected from all residents living in the same area. Using a case-control design, we examined 30 suicide cases and 33 controls matched for gender and age.

Results: The 30 subjects diagnosed with ASR related suicide showed increased white blood cell counts but similar platelet counts and mean platelet volume compared with controls. At follow-up, the platelet count was lower in patients than in controls (p= 0.001), which was related to suicide attempts by using anti-depressants (p= 0.003).

Conclusion: ASR did not increase platelet count or MPV, but we found an increase in leukocyte counts following ASR. Additionally, our study supported the antiplatelet effect of antidepressant medications.

Key words: acute stress reaction, suicide, platelet, leucocyte, drugs, antidepressant, analgesic

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INTRODUCTION

Depression and acute stress reaction (ASR) are the most common diagnoses for suicide attempts (1,2). ASR is a diagnosis given immediately following the experience of an exceptional mental or physical stress (1). ASR increases suicide risk, and subjects with ASR and coexisting depression or substance abuse have elevated suicide rates than expected based on the independent effects of these conditions (3,4). Increases in circulating leukocytes in response to acute psychological stress or short-term intensive exercise is a well-documented phenomenon (5). The effects of stress on circulating white blood cells (WBCs) have been experimentally studied in a number of animal species and or general increases in total WBCs, has been occasionally used as a measure of stress (6,7).

Altered platelet function is observed in patients with depression (3). Platelet aggregation and mean platelet

volume (MPV) are increased in patients with depression (8-10). ASR is often seen with depression, and stress-related hormones may fulfil an important role in acute arterial thrombosis by increasing platelet aggregation (2,4,11).

To the best of our knowledge, no study has examined the association between ASR and hematological changes. Therefore, the current study aimed to examine the association between ASR and the number of leukocytes and platelets in a hospital-based population. We hypothesized that ASR would be associated with a higher number of leukocytes compared with healthy adults without a diagnosis of ASR. The second objective was to examine MPV, which is a practical indicator of platelet activity and platelet count, in patients with ASR in comparison with healthy volunteers (12,13). Additionally, we examined medications taken following suicide attempts as modifiers of these associations.

MATERIALS AND METHODS

Patients

The study was conducted in an emergency clinic from June 2009 to June 2010. Thirty patients (22 women and 8 men) meeting the ICD-10 criteria for an acute stress reaction (ASR) (1), but not for a current episode of major depressive disorder and 33 physically and mentally healthy, aged 18 years or older comparison subjects (23 women and 10 men) who were similar in age and sex to the patients with acute stres reaction were recruited. Controls were screened for DSM-IV (14) Axis I disorders. Patients with ASR were ineligible to participate in the study if they met any of the following exclusion criteria: 1-Existence of any other mental disorders i.e. depression, psychosis, conversion; 2-Treatment with any drugs such as anti-thrombotics within 2 weeks before entry; 3-Pregnancy, or history of severe drug allergy or hypersensitivity; 4-History of hematological problem or malignancy; 5-Treatment with anti-depressants within 4 weeks before entry; and 6-Suicide attempt 3 hour after admission to hospital. Clinically significant abnormalities on the baseline physical examination, electrocardiogram, or laboratory test results were also criteria for exclusion from study participation. All the patients were newly diagnosed as ASR in emergency room, and were followed up for 3 to 5 days. The agents used for suicide attempts were recorded. They have taken only supportive therapy. Written, informed consent was obtained for each patients. The study was conducted in accordance with the Declaration of Helsinki. The study was approved by the Local Ethics Committee of Duzce University, Medical School.

ASR Diagnosis

The diagnosis of ASR was assessed through a semi-structured clinical interview. According to the ICD-10 Classification, the symptoms of acute stress reaction must be present within 1 hour of the stressful or traumatic event and include one autonomic arousal symptom (e.g. sweating, heart palpitations or shaking). In addition, symptoms from three of the following categories must be present: chest and abdomen symptoms (e.g. difficulty in breathing, feeling of choking or chest pain), brain and mind symptoms (e.g. feeling dizzy, feeling that objects are unreal or fear of dying), general symptoms (e.g. numbness or chills), muscle and mental tension symptoms and other non-specific symptoms (e.g. being easily startled, difficulty concentrating or irritability).

Biochemical Measurements

Blood samples were drawn within 3 hours after ASR i.e. suicide. Soon after, acute treatment protocols were applied in emergency rooms. After 3 to 5 days, blood samples were redrawn from the patients. Blood samples of patients in 2nd measurements and controls were drawn after a fasting period of 12 hours. We measured leukocyte count, MPV and platelet count in a blood sample collected in citrate (1:4 vol/vol) to avoid the platelet swelling induced by EDTA. The expected values for leukocyte count, platelet count, and MPV in our laboratory ranged from 3.8 to 10.2 x10^3/uL, from 140 to 450 x10^3/uL, from 7 to 11 fL respectively.

Statistical Analysis

Statistical analysis was done by SPSS statistical software (SPSS 11 for Windows). Data were tested for normal distribution using the Kolmogorov-Smirnov test. All data showing uniform distribution and baseline parameters of patients and normal controls were compared by t test, others by Mann-Whitney test. In

comparison of three or more variables, One-Way ANOVA or Kruskal-Wallis tests were used. Paired t test was used to determine whether there was a significant difference between basal and posttreatment variables. Pearson correlation was used to see correlations. Data are expressed as mean ± SD. Statistical significance was defined as $p<0.05$.

RESULTS

The mean age of patients and controls were 24.97±8.13 and 27.21±6.34 years, respectively (p=0.22). Our patients attempted suicide for seeking relief from feeling ashamed, guilty, or like a burden to others (n=12) and feelings of rejection, loss, or loneliness (n=18). They also reported that their suicidal behaviors were triggered by emotional trauma (n=15), dependence on alcohol or other drugs (n=5), unemployment or financial problems (n=5), death of a loved one (n=3), and serious physical illness (n=2). Ten patients used anti-depressants (5 sertraline, 3 citalopram, 2 paroxetine), 9 patients used different analgesics (6 paracetamol, 2 diclophenac sodium, 1 naproxene sodium), and 11 patients used different agents (3 insecticides, 3 patient antipsychotics, 2 people proton pump inhibitors, 2 people antiepileptics) for suicide attempt. Those drugs reported above were belong to people in his/her family. In admission, all patients had decreased consciousness, i.e. 4 people had stupor, 10 people had deep sleep, and others had confusion. The clinical and laboratory parameters of the study population are reported in Table 1. The effect of anti-depressants and analgesics were evaluated in statistical analysis as seen in Table 2. At first measurements, mean leukocyte count was significantly higher in group with ASR (p=0.003) than in controls. This significancy was

Table 1: The comparison of WBC and platelet counts, and MPVs in each measurement

	Variable	Grup	N	Mean	Std. Deviation	Std. Error Mean	p value
FIRST MEASURE	WBC count	Patients	30	9.71	3.80	.718	**0.003**
		Controls	33	7.48	1.58	.27	
	Platelet count						
		Patients	30	268.10	76.56	14.21	0.092*
		Controls	33	289.12	57.84	10.06	
	MPV						
		Patients	30	8.41	1.36	.25	0.783*
		Controls	33	8.33	1.63	.28	
SECOND MEASURE	WBC count	Patients	30	7.76	2.61	.48	0.609
		Controls	33	7.48	1.59	.27	
	Platelet count						
		Patients	30	239.07	49.74	9.23	**0.001**
		Controls	33	289.12	57.85	10.06	
	MPV						
		Patients	30	8.30	1.11	.20	0.783*
		Controls	33	8.33	1.63	.28	

t-test, Mann-Whitney*

Table 2: The comparison of WBC (White Blood Cell) and platelet counts, and MPVs (Mean Platelet Volumes) in order to see the effects of anti-depressant and analgesics used for suicidal aim

Variables	Controls (n=33)	Patients took analgesics (n=9)	Patients took anti-depressants (n=10)	p value
1st WBC count	**7.48±1.58**	9.55±3.22	**10.51±5.19**	**0.01**
2nd WBC count		8.56±2.95	7.29±2.04	0.29
1st Platelet number	**289.12±57.84**	306.22±103.89	241.4±58.01	0.10*
2nd Platelet number		256.33±48.52	**221.50±39.55**	**0.03**
1st MPV	8.33±1.63	8.06±0.71	9.36±1.78	0.28*
2nd MPV		8.35±0.87	8.73±1.54	0.68*

ANOVA, Kruskal Wallis*

related especially to antidepressants (Table 2, p=0.01). However, statistically significant difference of leukocyte count between the groups disappeared at the 2nd measurements. No significant difference was observed between the groups regarding MPV and platelet count at the 1st results. The change of laboratory parameters in patients with ASR during the study period are given in Table 2. At the 2nd measurements, the platelet count was lower in patients as seen in Table 1 (p=0.001). The platelet count was found to be significantly decreased compared with the value of controls after the 2nd measurements in patients who took anti-depressants for suicide (p=0.003). There was also a significant decline in platelet count of patients who took antidepressants for suicide in comparison of 2 measurements (p=0.028).

DISCUSSION

Blood cells are sensitive indicators of physiological and pathophysiological responses in humans. In our study, we found that leukocyte (WBC) counts increased in ASR patients compared with controls. Although mean MPV values were higher and platelet counts were lower in patients, they were statistically indifferent in comparison to controls. Patients who took antidepressants following a suicide attempt showed decreased platelet counts at follow-up ($p<0.05$). This effect was independent of the dosage and the type of selective serotonin reuptake inhibitor (SSRI) administered. Similarly, MPV tended to decrease when compared with the initial measurement ($p>0.05$). In our patients we assessed WBC (leukocyte) count as an indicator of ASR. We have found that leukocytosis was apparent in 1st measurements. Leukocytosis is a well-known response to acute psychological stress (5,15,16). Both psychological stress and exercise have significant effects on cellular expression of adhesion molecules leading to increases in the number of circulating leukocytes and lymphocyte subsets. Maes and colleagues demonstrated that academic examination stress was accompanied by signs of immune activation, such as an increase in leukocytes (5,15,16).

Patients with major depressive disorder exhibit alterations in multiple platelet parameters, including a reduction in serotonin transporter [3H]-imipramine binding sites in platelets (17) and increases in 5HT2-receptor binding sites on the platelet surface (18). In other words, patients with depression exhibit increased platelet activation. Because ASR may occur together with depression, we looked for changes in platelet function in patients with ASR. Pozzi and colleagues revealed that stress-related hormones might increase platelet aggregation in patients with ASR (11). In contrast, De Jong and colleagues reported that low platelet count was related to increases in serum cortisol, and they concluded that low pH/bicarbonate and low platelet count as well as increased disease severity and organ failure were predictors of a subnormal increase in serum cortisol upon ACTH stimulation in a large series of critically ill patients (19). Furthermore, steroids may inhibit platelet aggregation induced by arachidonic acid, which may result in a dose-dependent decrease in the magnitude of aggregation (20). In the present study, we found normal platelet function (platelet count and MPV). Our findings were similar to some reports in the literature (21,22). Gupta and colleagues showed that steroids did not affect platelet count (21). Additionally, Schuerholz and colleagues reported that hydrocortisone mediated the immunomodulating effects of therapy in patients suffering from septic shock, without involvement of specific platelet receptors in vitro (22).

Several reports have suggested an antiplatelet effect of antidepressant medications, although the exact mechanisms are still uncertain (4,23-26). SSRIs have anti-thrombotic and fibrinolytic activity (27). Nearly all serotonin in the body is stored within platelets, and peripheral serotonin plays important roles in platelet aggregation and the regulation of vascular tonus. Furthermore, SSRIs increase central nervous system serotonin, while reducing serotonin within the platelets, and this release reduces platelet aggregation (28). Inhibition of platelet aggregation by SSRIs in response to ADP followed by inhibition of the reuptake of serotonin into platelets results in reduced platelet aggregability (28-30). In our study, we assessed platelet activity by measuring platelet count and MPV. Our findings were similar to previous studies suggesting that antidepressant treatment reduces platelet (hyper)activity (10,24,31,32). The results of the present study also indicate that high-dose SSRIs cause a decrease in the size and number of platelets in patients with ASR. Our findings provide evidence that high concentrations of SSRIs inhibit platelet activity within a short time period (within 3-5 days).

In summary, we believe we are the first to use MPV and platelet count as indicators of platelet activity in patients with ASR. We found that patients with ASR did not exhibit increased platelet activity, but our findings supported the antiplatelet affects of antidepressants, and this effect continued during subsequent days.

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