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Relationship between the mean platelet volume values and tilt-table test results in patients with vasovagal syncope

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Abstract

Impaired sympathovagal balance, the main pathophysiological mechanism under the vasovagal syncope (VVS), may play a role on platelet sizes. Although it has been shown that mean platelet volume (MPV) is increased in patients with vasovagal syncope, its nature in syncope subgroups is unknown. Herein, we aimed to compare MPV values among patients with different head-upright tilt-table (HUTT) test results. Patients who underwent HUTT test were analyzed retrospectively. Patients' demographic data and their complete blood count samples within the 24h of test were obtained from hospital data network. Patients were divided into 4 groups according to their HUTT test results; group I: cardioinhibitory type, group II: mixt type, group III: vasodepressor type and group IV: negative result. There were no statistical differences regarding the age and gender between the groups. There was statistically significant difference between groups, regarding the values of MPV, platelet distribution width (PDW), hemoglobin and hematocrit. In patients with vasodepressor type response, MPV was statistically significantly higher compared with control and other groups ($p<0.001$), whereas hemoglobin and hematocrit values were significantly lower compared with the control group. We showed that MPV is increased in vasodepressor type syncope group, whereas it is decreased in cardioinhibitory and mixt type response group. However, further randomized prospective studies are warranted.

Keywords: Vasovagal Syncope, Tilt-Table Test, Mean Platelet Volume

Introduction

Syncope is temporary loss of consciousness due to global cerebral hypo perfusion [1]. The most common cause is vasovagal syncope (VVS) [2].Although the pathophysiological mechanisms are not fully understood, autonomic nervous system dysfunction is essential. Autonomic nervous system response at varying degrees leads to different types of vasovagal responses.

Increased mean platelet volume (MPV) indicates large-sized hyper aggregable platelets, which are metabolically and enzymatically more active than normal-sized platelets, and associated with many diseases [3-6]. Although there is no clear association between syncope and MPV, in a previous study in our clinic, we have shown that increased sympathetic activity in patients with vasovagal syncope may be associated with an increase in MPV [7]. Herein, we aimed to compare MPV values among patients with different HUTT test results.

Material and Method

Patients referred to our Cardiology Clinic for evaluation and treatment of unexplained syncope during the period of January 2012 and April 2016 and who underwent HUTT test were screened retrospectively and meeting the following criteria were enrolled in the study: history of two or more episodes of syncope; normal neurological evaluation; absence of structural heart disease; absence of supraventricular or ventricular arrhythmias; and no history of any chronic disease. Complete blood count analyzes of the patients performed within 24 hours before HUTT test were obtained from hospital database.

After an overnight fasting period, HUTT test was conducted in the morning in a silent, softly lighted room. A peripheral intravenous access was obtained for emergency intervention before starting the test. Patients laid down on an electrically driven table and strapped. The ECG was monitored continuously and blood pressure was recorded noninvasively, at 3-minute intervals and promptly in case of any clinical symptoms. The HUTT test protocol started with baseline recordings acquired at the end of a 10-minute resting period in a supine position. Afterwards, patients were tilted to 60° for 20 minutes. In case of negative response, a puff of sublingual nitrate spray (Nitrolingual Pump Spray, G. Pohl-Boskamp GmbH, Germany; 400 mcg/puff) was administered and the test was extended for another 15 minutes at 60° tilt angle. The test was ended after 45 min, if no loss of consciousness or no symptoms such as dizziness, chest discomfort or nausea were observed. The test result was accepted as positive if sudden development of syncope occurred or if there was presyncope associated with hypotension (systolic blood pressure <70 mm Hg or diastolic blood pressure

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<40 mm Hg), bradycardia (<75% of resting heart rate during), or both. Vasodepressor response was defined as marked fall in systolic blood pressure without bradycardia. The cardioinhibitory response was defined as asystole with a duration of 3 seconds or longer. Patients were divided into 4 groups according to their tilt-table test results; group I: cardioinhibitory type, group II: mixt type, group III: vasodepressor type and group IV: negative result.

Statistical Analysis

The categorical variables were defined as percentages whereas the continuous variables were reported as the mean±standard deviation (SD) and were compared using the Student t-test in case of normal distribution.

The normality of the continuous variables was tested using the Kolmogorov-Smirnov test. Data without normal distribution were presented as median (25th-75th) percentiles and compared by Mann-Whitney U test. Chi-square test was used to evaluate categorical variables. One-way ANOVA test was used for comparison between groups, and Tukey test was used for post-hoc analysis. Statistical significance was defined as $p<0.05$. All statistical analyses and calculations were conducted using the SPSS 20.0 Statistical Package Program for Windows (SPSS, Chicago, IL, USA).

Results

A total of 271 patients [196 male (72.3%),75 female (27.7%)] were evaluated in this study. The baseline demographic and laboratory findings of patients according to HUTT test results are shown in Table 1. There were no statistical differences regarding the age and gender between the groups. Of the 271 patients, 26 (9.5%) had cardioinhibitory type, 68 (25.0%) had mixed type, 62 (22.8%) vasovagal type and 115 (42.4%) had negative HUTT test response. There was statistically significant difference between groups regarding the MPV, platelet distribution width (PDW), hemoglobin and hematocrit values whereas neutrophil/ lymphocyte ratio and other parameters were not significantly different. In post-hoc analysis, MPV values were significantly higher in patients with vasovagal syncope group compared to control and other two groups ($p<0.001$) (Table 2).

Hemoglobin was lower in patients with vasovagal syncope group compared to control group (14.33±1.33 vs.15.02±1.66, p= 0.039), however there was no statistically significant difference between the cardioinhibitory type/ mixed type responses and the control group. There was also statistically significant difference between groups regarding to hematocrit values (p=0.026). PDW was higher in mixed type response group compared to patients with vasovagal syncope and control group (p=0.010).

Table 1. Baseline demographic and laboratory findings of patients according to head-upright tilt-table test results

	Cardioinhibitory type (n=26)	Mixed type (n=68)	Vasodepressor type (n=62)	Negative response (n=115)	P value
Age, (years)	24 (18-31)	27 (19-37)	26 (17-36)	28 (18-36)	0.399
Gender, (male)	21 (%80.8)	50 (%73.5)	33 (%53.2)	92 (%80.0)	0.634
Leukocyte count (103 µL)	7.12±1.99	6.51±1.66	6.75±1.52	6.74±1.54	0.437
Neutrophil count, (103 µL)	4.24±1.81	3.67±1.29	3.76±1.23	3.69±1.23	0.250
Lymphocyte count, (103 µL)	2.12±0.76	2.14±0.58	2.20±0.67	2.29±0.62	0.369
Monocyte count, (103 µL)	0.52±0.17	0.49±0.19	0.50±0.16	0.52±0.18	0.580
Eosinophil count, (103 µL)	0.15±0.12	0.15±0.10	0.16±0.15	0.17±0.10	0.751
Basophil count, (103 µL)	0.04±0.03	0.05±0.05	0.018±0.08	0.04±0.03	0.387
Neutrophil / Lymphocyte ratio	2.28±1.63	1.86±1.01	1.88±0.98	1.73±0.79	0.089
Erythrocyte count (103 µL)	5.20±0.45	5.10±0.57	5.04±0.48	5.19±0.52	0.246
Hemoglobin (g/dL)	15.10±1.43	14.61±2.07	14.33±1.33	15.02±1.66	0.039
Hematocrit (%)	44.86±3.97	43.11±6.61	43.22±3.59	45.02±4.50	0.026
MCV (fL)	86.98±3.21	85.37±5.95	85.97±5.70	86.66±5.94	0.439
MCH (pg)	29.28±1.68	28.59±2.67	28.70±2.41	28.99±2.08	0.500
MCHC (g/dL)	33.64±0.97	33.44±1.36	33.18±1.75	33.36±1.26	0.419
RDW (%)	12.23±1.21	13.12±1.03	12.88±0.82	13.07±1.70	0.272
Platelet count (n /µL)	236.20±41.02	264.12±58.96	240.65±62.39	248.79±58.65	0.083
PCT (%)	0.21±0.05	0.24±0.05	0.24±0.06	0.23±0.05	0.150
PDW (fL)	14.30±2.76	14.73±2.94	13.25±2.81	13.52±2.63	0.010
MPV (fL)	8.91±1.31	9.22±1.36	10.13±1.09	9.57±1.12	<0.001

MCV: Mean Corpuscular Volume;
MCH: Mean Corpuscular Hemoglobin;
MCHC: Mean corpuscular hemoglobin concentration;
PCT: Plateletcrit;
PDW: Platelet distribution width;
MPV: Mean platelet volume;
RDW: Red blood cell distribution width

Table 2. MPV values of each group according to head-upright tilt-table test results

	Cardioinhibitory type (n=26)	Mixed type (n=68)	Vasodepressor type (n=62)	Negative response (n=115)	Comparison Group	Post hoc P value
MPV (fL)	8.91±1.31	9.22±1.36	10.13±1.09	9.57±1.12	Cardioinh. vs. Mixed	0.774
					Cardioinh. vs Vasodep.	0.017
					Cardioinh. vs Neg. Resp.	0.015
					Mixed vs Vasodep.	0.038
					Mixed vs Neg. Resp	0.225
					Vasodep. vs Neg. Resp.	0.012

MPV: Mean platelet volume

Discussion

In our study, we found that MPV was lower in the cardioinhibitory and mixed type syncope groups whereas it was higher in the vasodepressor type syncope group compared to control group. We did not come across a study in the literature comparing MPV in vasovagal syncope types. Our study is novel in this respect.

The pathophysiology of vasovagal syncope has not been fully understood. Short-term inappropriate responses of cardiovascular reflexes that regulate circulation, and consequently hypotension and/or cerebral hypo perfusion due to bradycardia is the basic mechanism [1]. During early phase of vasovagal syncope cardiac output decreases as a result of reduced venous return, and the sympathetic system becomes active [8]. In terminal vasodilatation phase, suppression of the sympathetic system and slowing of heart rate occurs [9,10]. In contrast, Vaddadi et al. suggest that parasympathetic system is active and sympathetic activity of muscle nerve did not decrease in this phase [11]. Regardless of the pathophysiological mechanism, the sympathovagal balance is altered in favor of parasympathetic system in this phase. In vasovagal syncope, distinct inhibition or activation patterns of the autonomic nervous system result in different syncope responses. It is defined 'vasodepressor type' if hypotension, due to a loss of upright vasoconstrictor tone, predominates. 'Cardioinhibitory' is used when bradycardia or asystole predominate, and 'mixed' is used if both mechanisms are present. Alteration of sympathovagal balance in favor of parasympathetic system is more pronounced in patients with cardioinhibitory and mixed type syncope.

Sympathetic activity may have a significant impact on MPV, either by peripheral activation and splenic release of platelets or depending on the increased thrombocytopoiesis in bone marrow [12]. Increased plasma adrenaline levels may alter platelet shape and increase volume. The volume of platelets in the spleen is greater than in the systemic circulation, and sympathetic system activation after exercise, if necessary, enhances systemic circulation release of these large volume platelets [13,14].

Increased MPV indicates large-sized hyper aggregable platelets, which are metabolically and enzymatically more active than normal-sized platelets, and associated with many disorders including cardiovascular diseases [15-17]. Özdemir et al. showed that MPV is increased in patients with myocardial infarction and concluded that it is associated with sympathetic activity [18]. In a previous study of our clinic, we found that increased sympathetic activity in patients with vasovagal syncope is associated with increased MPV [7]. In this study, we investigated whether there was any difference regarding MPV values between different types of vasovagal syncope and found that MPV values are decreased in cardioinhibitory and mixed type syncope groups in which sympathovagal balance was altered in favor of vagal activity. These findings suggest that decreased MPV values may play a role in predicting increased vagal response in cardioinhibitory and mixed-type response pathophysiology. Although we showed that MPV is decreased in patients with syncope, an analysis of heart rate variability, which we can evaluate autonomic nervous system activity, will provide more detailed information about the sympathovagal balance of these patients.

The retrospective design and small sample size could be considered as two of the limitations of this study. Another limitation of study was that most of the study population consisted of male patients. However, further randomized studies are needed to assess the prognostic effect of MPV.

Conclusion

We showed that MPV is increased in vasodepressor type syncope group, whereas it is decreased in cardioinhibitory and mixt type response group. Decreased MPV values may play a role in predicting increased vagal response in cardioinhibitory and mixed-type response pathophysiology. However, further randomized prospective studies are warranted.

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