

Original Article

Decrease in Mean Platelet Volume after percutaneous transvenous mitral commissurotomy in patients with Rheumatic Mitral Stenosis

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Abstract

Introduction: Rheumatic mitral stenosis (RMS) is associated with increased thromboembolic events, especially in the presence of concomitant atrial fibrillation. Mean platelet volume (MPV) is the marker of platelet activity as larger platelets are hemostatically active and have more propensity of thrombosis. It has also been reported that percutaneous transvenous mitral commissurotomy (PTMC) attenuates platelet activity. We aimed to investigate whether PTMC decreases MPV in patients with RMS.

Methods: In the present study, MPV was measured in 39 patients with RMS in sinus rhythm just before and one month after PTMC. Thirty four, sex and age-matched, apparently healthy controls were used for comparison. Mitral valve area (MVA), mean diastolic gradient across mitral valve (MDG) and pulmonary artery systolic pressure (PASP) were measured using transthoracic echocardiography and mean left atrial (LA) pressure measured during the procedure.

Results: As compared to apparently healthy controls, patients with RMS had higher MPV (11.51 ± 1.46 vs. 9.6 ± 0.75 fl, $p < 0.001$). All patients with RMS underwent successful PTMC. One month after the procedure, LA diameter, MVA, MDG, PASP and LA pressures were reduced significantly ($p < 0.001$). The final mean platelet volume measured in patients with RMS undergoing PTMC measured after one month also had significant reduction when compared with the initial mean MPV (11.51 ± 1.46 vs 9.55 ± 1.11 fl $p < 0.001$).

Conclusions: As compared to apparently healthy controls, patients with RMS have higher MPV reflecting increased platelet activity, and PTMC is associated with a significant decrease in MPV one month after the procedure.

Key Words: Mean platelet volume, percutaneous transvenous mitral commissurotomy, rheumatic mitral stenosis

Introduction

Rheumatic mitral stenosis is a common heart disease in developing countries and surgical and non-surgical treatments are the options¹. Cardio embolism is a common complication in patients with RMS. Number of abnormalities in parameters of both coagulation and platelet aggregation were previously reported in patients with RMS².

The mean platelet volume is considered as an accurate measure of platelet size. It is considered a marker and

determinant of platelet function since larger platelets are hemostatically more reactive than platelets of normal size hence increasing the chances of thrombosis³. Evidence from several studies has shown that shear stresses in turbulent flow as a result of stenotic valves induce platelet activation⁴⁻⁷. MPV is a simple and easy method of assessing platelet function^{8,9}. In comparison to smaller ones, larger platelets have more granules, aggregate more rapidly with collagen, have higher thromboxane A₂ level and express more glycoprotein Ib and IIb/IIIa receptors¹⁰⁻¹². Large platelets are known to be

hyperfunctional; they show greater aggregation to ADP, collagen, or adrenaline and secrete more thromboxane A_2 per unit volume of cytoplasm¹³. Elevated MPV level has been shown to be an independent risk factor for cardiovascular disease¹⁴.

PTMC is the method of dilatation of the stenotic mitral valve using Inoue balloon. The objective of this study is to compare the MPV between healthy individual and those with RMS and observe any change in MPV after PTMC in patients with RMS.

Methods

Study population

The study was conducted in Manmohan cardiothoracic, vascular and transplant center in the department of cardiology. This was a comparative cross-sectional study. We selected 39 consecutive patients with RMS and 34 consecutive healthy age- and sex-matched control subjects. Exclusion criteria were diabetes mellitus, renal failure, heart failure, hematological disorders, acute or chronic infection, cancer, and atrial fibrillation and use of anti-platelet drugs. All subjects were in sinus rhythm.

The protocol of this study was approved by the ethical committee, and written consent was obtained from every subject participating in this study.

Control group for comparison of hematology data

Thirty four, sex and age-matched, apparently healthy subjects who had normal echocardiographic findings including normal mitral valve and left ventricular ejection fraction ($>55\%$) were included as control group for comparison of MPV values. The same exclusion criterias were applied for this group.

Echocardiographic examination

Using a Vivid Seven GE ® Echocardiography System two-dimensional, M-mode, and subsequent Doppler echocardiography was performed in all patients with RMS just one day before and one month after the procedure. Left atrial diameter, mitral valve area, transmitral pressure gradient, and pulmonary artery pressure were calculated. To confirm absence of left atrial thrombus and to evaluate the degree of spontaneous echo contrast, all patients underwent transesophageal echocardiography (TEE) examination before PTMC.

PTMC procedure

PTMC was done in patients with RMS having MVA $<1.5\text{cm}^2$ who were symptomatic, as per the American college of Cardiology (ACC) guidelines.

Sheaths were inserted into the right femoral veins and femoral artery. Polymer pigtail catheter was inserted into the aortic sinus for pressure measurement. Subsequently, PTMC was performed by the trans septal approach using Inoue balloon catheter (Toray Medical Corporation; Tokyo, Japan)¹⁵. Successful dilation was defined as a final mitral valve area $> 1.5\text{ cm}^2$ with $> 50\%$ increase of the initial mitral valve area without more than mild mitral regurgitation. Each patient received a dose of 5000 U heparin soon after trans septal puncture. No thromboembolic event occurred in any patient during or after the procedure.

Hematologic measurements

Hematologic measurements were done just before and 1 month after the procedure. Blood samples were drawn from the antecubital vein by careful veinpuncture in a 21 G sterile syringe without stasis. MPV was measured in a blood sample collected in EDTA tubes. An automatic blood counter (Sysmex XS-500i) was used for whole blood counts. MPV was measured within 30 min after sampling to prevent EDTA-induced platelet swelling.

Statistical analyses

All analyses were conducted using SPSS 18.0. Data were expressed as mean \pm SD for continuous variables and as percentage for categorical variables. For continuous variables, differences between groups were compared with independent t-test. A p value < 0.05 were considered significant.

Results

Clinical characteristics of the study population

General characteristics of the patients and controls are presented in Table 1. All of the patients with RMS and controls were in sinus rhythm. The groups were similar regarding age, sex, hemoglobin concentration, white blood cell count (WBC), platelet count. MPV (11.51 ± 1.46 vs 9.6 ± 0.75 , $p < 0.001$) were statistically different between the groups.

Table 1. Demographic features and laboratory parameters of patients with rheumatic mitral stenosis and control subjects

	RMS (n=39)	Controls (n=34)	p value
Age (years)	33.74 ± 10.01	34.14 ± 1.74	0.865
Gender (M/F, %)	8 (20.5%)/31 (79.5%)	13 (38%)/21 (62%)	0.095
Hemoglobin (Hb gm%)	12.38 ± 1.66	12.92 ± 1.55	0.157
WBC (10 ⁹ /L)	8.41 ± 2.45	7.72 ± 1.26	0.144
Platelets (10 ⁹ /L)	260.23 ± 58.64	264.97 ± 711.98	0.765
MPV (fl)	11.51 ± 1.46	9.6 ± 0.75	<0.001

Relationship of mean platelet volume to hemodynamic and echocardiographic parameters

Pre PTMC mean platelet volume had significant negative correlation with mean LA pressure ($r = -0.345$, $p = 0.0310$) and pre mean diastolic gradient ($r = -0.341$, $p = 0.033$), however no significant correlation with left atrium diameter, mitral valve area and pulmonary artery pressure. Post PTMC mean platelet volume also didn't have any significant correlation with the above variables.

Changes in hemodynamic and echocardiographic parameters after PTMC

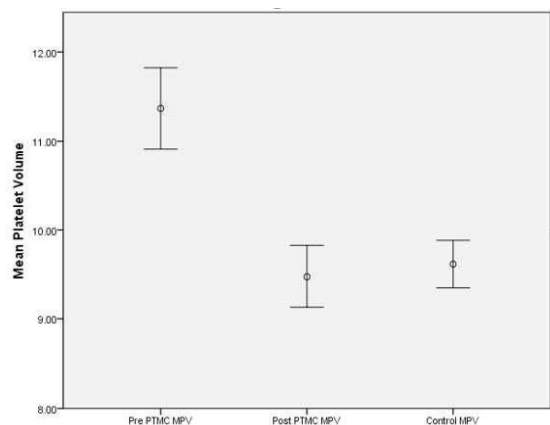
Changes in the RMS group after PTMC procedure are summarized in Table 2. Mitral valve area, transmitral pressure gradients, pulmonary artery pressures and mean left atrial pressure decreased significantly after the PTMC procedure.

Table 2. Comparison of echocardiographic findings, hemodynamic profile before and after mitral balloon valvuloplasty

Variable	Before PTMC	After PTMC	p value
LA diameter Index (mm/m ²)	30.78 ± 3.99	27.69 ± 3.40	< 0.0001
Mitral valve area by planimetry (cm ²)	0.97 ± 0.17	1.72 ± 0.15	< 0.001
Mean diastolic gradient (MDG) mm Hg	12.58 ± 3.76	5.55 ± 2.11	< 0.001
Pulmonary artery systolic pressure (PASP) mm Hg	47.58 ± 14.86	22.84 ± 5.72	< 0.001
Mean LA pressure (mm Hg)	21.64 ± 7.90	12.41 ± 5.19	< 0.001

Changes in mean platelet volume after percutaneous mitral balloon valvotomy

Percutaneous mitral balloon valvuloplasty significantly decreased MPV in patients with RMS (11.51 ± 1.46 vs 9.55 ± 1.11 fl, before and after the procedure, respectively; $p < 0.001$). Figure 1.

**Fig 1. Mean Platelet volume before and after PTMC compared with control**

Discussion

The main finding of the study are that MPV was elevated in patients with RMS and significantly decreased after PTMC, reflecting platelet activity in these patients. Our results suggest that antiplatelet or anticoagulation may be reasonable even in the absence of AF or left atrial thrombi. Patients with RMS and high MPV could benefit from early PTMC.

Several plausible mechanisms can be suggested to explain increased platelet activity and prothrombotic state in RMS. Flow turbulence and increased shear stress against this flow turbulence in and around the stenotic mitral valve result in endothelial damage⁵. Another plausible mechanism is blood stasis in the left atrium that leads to subsequent platelet activation and initiation of thrombus formation. As in our findings, mean LA pressure and MDG has negative correlation with MPV which mean that more the blood stasis due to high gradient across the valve, higher would be the MPV. This was however in contrast with the study by Dogan et al which has positive correlation with MPV but non-significant¹⁶. They fulfill the Virchow triad: endothelial/ endocardial damage or dysfunction; abnormal blood stasis; and abnormal haemostasis, fibrinolysis and increased platelet activity. Accordingly, previous studies have shown that plasma endothelin, D-dimer, platelet factor 4, beta thromboglobulin and thrombin-antithrombin III complex are higher in patients with RMS as compared to controls^{17–20}. Moreover, plasma D-dimer, platelet factor 4, beta thromboglobulin and thrombin-antithrombin III complex significantly decrease soon after successful PTMC, only in RMS patients with left atrium pressure <10mm Hg after PTMC¹⁸. In line with previous reports, we showed that MPV was significantly higher in patients with RMS than that in controls.

Chiang et al²¹ revealed that PTMC (RR: 0.37;CI: 0.18 – 0.79) was a negative predictor of systemic embolism in RMS patients with AF. This observation suggests a potential benefit from early use of this procedure in patients with mitral stenosis, though prospective studies of PTMC for this indication are lacking. Chen et al.^{22,23} proposed that venous plasma concentration of P-selectin and soluble CD40L released from platelets was rapidly reduced following PTMC in patients with moderate-to-severe RMS. Similarly, Zaki et al.¹⁸ and Kataoka et al.²⁴ demonstrated that platelet activity significantly decreased after optimal PMBV. In line with previous

reports, the present study showed that MPV decreased significantly after optimal PTMC.

Conclusion

Patients with rheumatic mitral stenosis have increased mean platelet volume as compared with healthy volunteers. The mean platelet volume decreased significantly following PTMC.

Conflict of interest: None declared

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