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Original Article

Platelet distribution width can be a useful marker of decreased platelet activity after percutaneous mitral balloon valvuloplasty

Trombosit dağılım genişliği, perkütan mitral balon valvüloplasti sonrası azalmış trombosit aktivitesinin yararlı bir göstergesi olabilir

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Abstract

Aim: Increased platelet activity and elevated mean platelet volume (MPV) has been demonstrated in patients with rheumatic mitral stenosis (RMS). However, platelet distribution width (PDW) and the impact of percutaneous mitral balloon valvuloplasty (PMBV) on PDW has never been studied. Therefore, we aimed to investigate whether PMBV decreases PDW in patients with RMS.

Material and Methods: Symptomatic patients with severe RMS undergoing PMBV were included. Echocardiographic characteristics and hematologic parameters was measured just before and 1 month after the PMBV procedure.

Results: A total of 30 patients (24 female, mean age: 49.8±13.2 years) were included the study. Mean transmitral pressure gradient, pulmonary artery pressures and left atrium diameter decreased but mitral valve area increased significantly after PMBV. PMBV procedure significantly decreased PDW in patients with RMS (13.5±2.3 vs 12.4±1.9 fL, before and after procedure, respectively; $p<0.0001$). MPV was decreased after PMBV but it was not statistically significant (10.9±0.8 vs 10.6±0.9 fL, $p=0.056$). Platelet count was significantly increased after procedure (250±62.6 vs 273.5±78.6 x103/ul, $p=0.035$). In linear regression analysis, an independent relationship was found in magnitude of PDW decrease and magnitude of increase in mitral valve area (ß:0.491, $p=0.046$).

Conclusion: PMBV is associated with a significant decrease in PDW 1 month after the procedure. There was a significant correlation between the magnitude of decrease in PDW and magnitude of increase in mitral valve area after PMBV.

Keywords: platelet distribution width; platelet activity; percutaneous mitral balloon valvuloplasty

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Öz

Amaç: Romatizmal mitral darlığı (RMD) olan hastalarda artmış trombosit aktivitesi ve yüksek ortalama trombosit hacmi (MPV) gösterilmiştir. Bununla birlikte, trombosit dağılım genişliği (PDW) ve perkütan mitral balon valvüloplasti'nin (PMBV) PDW üzerindeki etkisi hiç çalışılmamıştır. Bu nedenle, RMD'lı hastalarda PMBV işleminin PDW üzerine etkisini araştırmayı amaçladık.

Gereç ve Yöntemler: PMBV uygulanan ciddi RMD'lı semptomatik hastalar dahil edildi. Ekokardiyografik özellikler ve hematolojik parametreler PMBV işleminden hemen önce ve bir ay sonra ölçüldü.

Bulgular: Çalışmaya toplam 30 hasta (24 kadın, ortalama yaş: 49,8 ± 13,2 yıl) dahil edildi. Ortalama transmitral basınç gradyanı, pulmoner arter basınçları ve sol atriyum çapı azaldı, ancak mitral kapak alanı PMBV'den sonra anlamlı olarak arttı. PMBV prosedürü RMD'lı hastalarda PDW'yi anlamlı şekilde azalttı (sırasıyla 13.5 ± 2.3 vs 12.4 ± 1.9 fL, prosedürden önce ve sonra; p <0.0001). MPV, PMBV'den sonra azaldı, ancak istatistiksel olarak anlamlı değildi (10.9 ± 0.8'e karşılık 10.6 ± 0.9 fL, p = 0.056). Trombosit sayısı işlem sonrası anlamlı olarak arttı (250 ± 62.6 vs 273.5 ± 78.6 x 103 / ul, p = 0.035). Lineer regresyon analizinde, PDW azalmasının büyüklüğü ile mitral kapak alanındaki artışın büyüklüğü arasında bağımsız bir ilişki bulundu (ß 0.491, p = 0.046).

Sonuç: PMBV, işlemden 1 ay sonra PDW'de belirgin bir azalma ile ilişkilidir. PMBV'den sonra PDW'deki düşüşün büyüklüğü ile mitral kapak alanındaki artışın büyüklüğü arasında anlamlı bir ilişki vardır.

Anahtar kelimeler: trombosit dağılım genişliği; trombosit aktivitesi; perkütan mitral balon valvüloplasti

Introduction

Rheumatic mitral stenosis (RMS) is still a serious cause of mortality and morbidity in developing countries and systemic thromboembolism is a major complication of RMS [1]. Increased platelet activity that has been demonstrated in rheumatic mitral stenosis significantly contributes to prothrombotic state [2-3]. Previous studies have shown that percutaneous mitral balloon valvuloplasty (PMBV) decreases the risk of systemic embolism and platelet activity in patients with RMS [4-7]. Although the mechanism of reduced platelet activity by PMBV remains unclear, alterations in the hemodynamic and echocardiographic factors such as increased mitral valve area (MVA), reduced left atrial area, left atrial pressure, and pulmonary artery systolic pressure after PMBV might have a role in reduced platelet, thrombin, and fibrinolytic activities after PMV [4-7].

Platelet activity can be measured by using different laboratory tests. Platelet indices are frequently used and easy available markers to measure platelet activity [8] but only a few studies in the literature have measured platelet indices in RMS [9-11]. These studies showed increased mean platelet volume (MPV) in patients with RMS [9-10] and decreased MPV after PMBV [11]. However, platelet distribution width (PDW) which is known as more specific marker of platelet activation than MPV has not been evaluated in RMS yet. Therefore, the aim of our study is to evaluate the effect of PMBV on PDW in patients with RMS.

Material and Methods

Study population

This retrospective study included thirty patients who underwent successful PMBV due to symptomatic RMS. Patients included in the study were carefully checked for conditions that might increase platelet activity from their medical records (hypertension, diabetes mellitus, renal failure, hepatic failure, other valve diseases, acute or chronic infection, malignancy, etc.). The patients with incomplete information and patients who were not followed up after the procedure were excluded from the study. PMBV had been performed by the transseptal approach using INOUE balloon catheter. Written consent was obtained from all patients and the study protocol was approved by the local ethic commitee

Echocardiography

The echocardiographic examinations were performed with System V and a Vivid T8 from GE Ultrasound (G E Medical Systems, Wisconsin, USA) with a 1.7/3.4 MHz harmonic transducer and a multiplane 6.7 MHz transesophageal probe. Measurements of MVA, transmitral pressure gradient, pulmonary artery pressure, left atrial diameter were recorded from echocardiographic

reports of the studied patients that has performed before and one month after procedure. MVA had been calculated using Doppler pressure half-time method. Two dimensional examination was done to assess Wilkins score [12].

All patients had been underwent transesophageal echocardiography (TEE) examination to confirm absence of left atrial thrombus before valvuloplasty. For TEE, all patients were studied in the fasting state beginning five hours before examination. The oropharynx was anaesthetised by topical application of lidocaine spray. When needed light sedation with 2.5–5.0 mg midazolam was given intravenously. After introduction of the multiplane transducer probe and adjustment of gain and compression settings a standardised examination was performed. The left atrium and the left atrial appendage were closely inspected for the presence of thrombi.

Blood sample analysis

Platelet activity has been measured by using MPV, PDW and platelet count derived from whole blood count of the patients that were done just before and one month after procedure. The same sampling method was used before and after procedure.

Statistical analysis

All statistical analyses were performed using the SPSS 20 (SPSS INC, Chicago, Illinois, USA). Continuous variables are presented as mean ± Standard deviation. Categorical data were presented as number (%). Variables, before and after the procedure, were compared using paired t-test. The relationships between PDW and MVA, pulmonary artery systolic pressure, left atrial diameter, mean transmitral pressure gradient were performed using the Pearson correlation analysis. Linear regression analysis was used for evaluating independent association between PDW decrease and change in echocardiographic parameters. A calculated difference of $p<0.05$ was considered to be statistically significant.

Results

Thirty patients with symptomatic RMS undergoing PMBV were included. The baseline characteristics of the study group are summarized in Table 1. The mean age of the patients included in this study were 49.8±13.2 years and 24 of the 30 patients (80%) were female. All patients presented with severe RMS with mitral valve area of 1.02 ±0.3 cm2 and echocardiographic score of 6.9 + 1.2. At entry into the study, 8 patients (26.7%) were in atrial fibrillation. The medications most frequently used were beta-blockers (80% of cases) followed by aspirin (73%) and diuretics (60%).

Table 1: Demographic characteristics and medication of the study group.

Variables	Values
Patients, n	30
Age, years	49.8±13.2
Male/female, n (%)	6/24 (20/80)
Rhythm (Sinus/AF)	22/8
Hemoglobin (g/dl)	13.3±1.8
Hematocrit (%)	40.7±4.9
Platelet count (x103/ul)	251.7±64.8
Mean platelet volume (fL)	10.9±0.8
Platelet distribution width (fL)	13.5±2.31
Medications, n (%)	
Aspirin	22 (73.3)
Warfarin	8 (26.6)
Beta Blockers	24 (80)
Diuretics	18 (60)

AF, atrial fibrillation

Changes after percutaneous mitral balloon valvotomy

Changes in echocardiographic characteristics and hematologic parameters of the overall patients before and after PMBV procedure are summarized in Table 2. Mean transmitral pressure gradient, pulmonary artery pressures and left atrium diameter decreased significantly after PMBV. Mitral valve area increased significantly after PMBV. PMBV procedure significantly decreased PDW in patients with RMS (13.5±2.3 vs 12.4±1.9 fL, before and after procedure, respectively; $p<0.001$) (Figure 1). MPV was decreased after PMBV but it was not statistically significant (10.9±0.8 vs 10.6±0.9 fL, $p=0.056$). Platelet count was significantly increased after procedure (250±62.6 vs 273.5±78.6 x103/ul, $p=0.035$).

Table 2: Comparison of echocardiographic findings and hematologic parameters before and after mitral balloon valvuloplasty.

	Before PMBV	After PMBV	p
Mitral valve area (cm2)	1.2±0.14	2.0±0.2	<0.001
Mean transmitral pressure gradient (mmHg)	10.5±3.7	4.8±2.5	<0.001
Left atrium diameter (cm)	4.7±0.61	4.5±0.65	0.003
Pulmonary artery systolic pressure (mmHg)	39.1±14.4	28.1±7.6	<0.001
Mean platelet volume (fL)	10.9±0.87	10.6±0.95	0.056
Platelet distribution width (fL)	13.5±2.3	12.4±1.9	<0.001
Platelet count (x103/ul)	250±62.6	273.5±78.6	0.035

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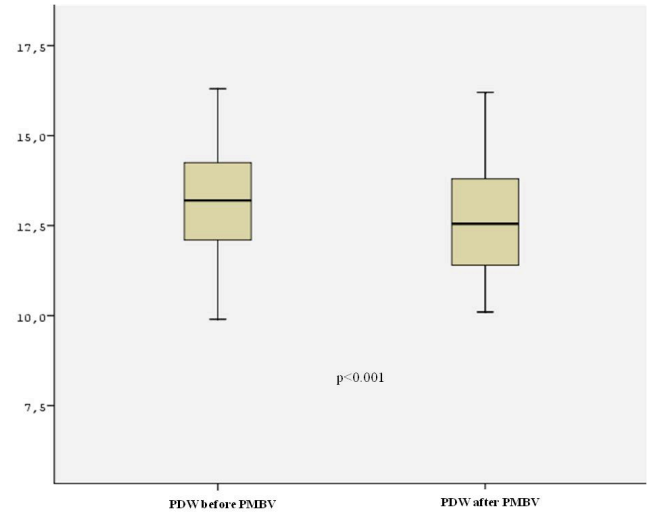

Fig 1. Platelet distribution width (PDW) before and after percutaneous mitral balloon valvuloplasty (PMBV).

Pearson correlation analysis demonstrated that there was a significant correlation between the magnitude of decrease in PDW and magnitude of increase in MVA after PMBV (r=0.515, p=0.024) (Figure 2). However, there was no significant correlation among the magnitude of decrease in PDW and magnitude of decrease in the left atrium diameter (r= 0.228, p=0.380), magnitude of decrease in mean transmitral pressure gradient (r=0,92, p=0,701) and magnitude of decrease in pulmonary artery pressure (r=0,346, p=0.206). In linear regression analysis, an independent relationship was found in magnitude of PDW decrease and magnitude of increase in MVA (β0.491, p=0,046). There was no relationship between magnitude of PDW decrease and change in other echocardiographic parameters. Results of the regression analysis are showed in Table 3.

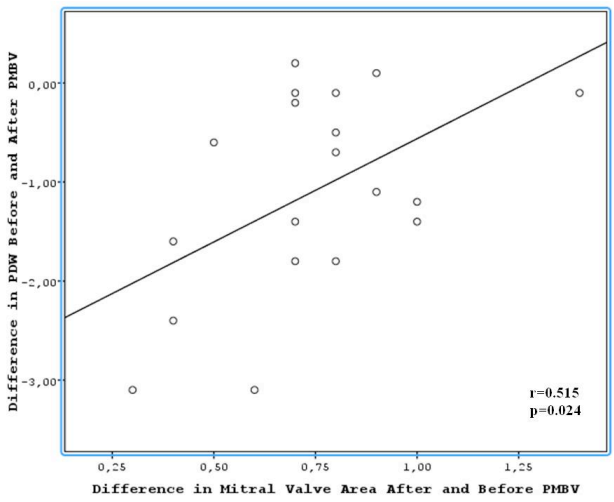

Fig 2. Correlations between the change in mitral valve area (MVA) and platelet distribution width (PDW).

Table 3: Relation between magnitude of PDW decrease and echocardiographic parameters in lineer regression analysis.

Variables	B coefficient	SE	T-value	P
ΔPASP (mmHg)	0.351	0.029	1.464	0.174
ΔLAdiameter (cm)	0.303	1.071	1.357	0.205
ΔMVA (cm2)	0.491	1.096	2.162	0.046
ΔMean gradient (mmHg)	0.249	0.105	1.052	0.318

Abbreviations: Δ, change before and after PMBV

Discussion

The main finding of our study is that PDW was significantly decreased after PMBV, reflecting platelet activity in patients with RMS. In our study, we found that the mechanism of PDW decrease after PMBV was increase in MVA.

Platelets participate the process of coagulation, inflammation and thrombosis. Several laboratory tests including platelet number and size, secretory substances of platelets (PF4 and beta-thromboglobulin), surface P-selectin are used to estimate platelet activity [13]. However, MPV and PDW are simple platelet indices, which are increased during platelet activation. Platelet activation causes morphologic changes of platelets and PDW represents the heterogeneity of platelet size [8]. Clinical use of MPV is more extensive but PDW is a more direct marker to represent platelet reactivity than MPV [14, 15].

RMS is associated with embolic complications and increased platelet activity [2,3]. Previous studies demonstrated that platelet activation occurs in peripheral blood of patients with RMS both in atrial fibrillation and sinus rhytm [16, 17]. The mechanism of platelet activation in RMS could be explained by increased shear stress against turbulent flow in and around the stenotic mitral valve (18,19). Another factor is blood stasis in the left atrium.

PBMV is a successful intervention in patients with MS that provides hemodynamic and symptomatic improvement [20]. Chiang et al. [7] reported that patients with previous PMBV had a lower incidence of thromboembolism. Several studies demonstrated that platelet activity significantly decreased after optimal PMBV [11]. In our study we demonstrated a significant decrease in PDW levels 1 month after PMBV revealing decreased platelet activity after PMBV. Chen et al.[4] described the mechanism of reducing platelet activity after PMBV due to increase in MVA by PMBV instead of hemodynamic and echocardiographic factors. In contrast to Chen, Hasan-ali et al. [21] found a significant improvement in left atrium diameter and pulmonary arterial systolic pressure after PMBV which significantly predict the decrease in the platelet activity. In our study, we found a positive correlation between the increase of MVA and decrease of PDW levels. However, in our study we could'nt find any relationship between PDW decrease and other echocardiographic parameters after PMBV similar to Chen and colleagues [21].

MPV decrease after PMBV has been assesed by Erdoğan et al.[11] and they found a significant decrease in MPV 1 month after the procedure. In our study we found a decrease in MPV but it was not statistically significant. Our study showed that

MPV and PDW were both decreased after PMBV, but PDW was more sensitive and useful test reflecting decreased platelet activity after PMBV.

Study limitations

Several limitations of our study should be noted. As this was a retrospective, single-center study, which included a relatively small sample of patients, potential cause-effect relationship could not be determined. The use of another assays such as soluble p-selectin or soluble CD40L would provide a more sensitive and accurate evaluation of the platelet activation status before after PMBV.

Conclusion

Larger platelets are haemostatically more active and a risk factor for developing thromboembolic events and patients with increased MPV and PDW, could be easily identified during routine haematological analysis. RMS is associated with increased platelet activities that decrease after PMBV. Altered hemodynamics play a possible role in these changes. PDW is more sensitive and specific than MPV for the detection of reduced platelet activities after PMBV.

Declaration of conflict of interest

The authors received no financial support for the research and/or authorship of this article. There is no conflict of interest.

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