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The change of mean platelet volume and mean platelet volume to platelet count ratio one year after iniation of peritoneal dialysis

Ortalama trombosit hacmi ve ortalama trombosit hacmi/trombosit sayısı oranının periton diyalizi başlandıktan bir yıl sonraki değişimi

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ABSTRACT

Aim: Cardiovascular diseases are the most common cause of mortality in patients undergoing peritoneal dialysis. Thrombocyte indices which are indicators of platelet activation are predictors of cardiovascular events. We aim to examine the change in platelet count, mean platelet volume, and mean platelet volume to platelet count ratio one year after initiation of peritoneal dialysis in patients with end-stage renal disease.

Materials and Methods: This retrospective study included 28 patients. Demographic and clinical characteristics of the patients at the time of initiation of peritoneal dialysis were recorded from the patient files. Laboratory data within the last month before the initiation of peritoneal dialysis and in the first year were recorded from the patient files. The mean platelet volume to platelet count ratio was calculated as mean platelet volume (femtolitres) divided by platelet count (number of thousand platelets/microliter).

Results: The mean age was 51.1 ± 14.6 years, and 42.8% of the patients were male. Diabetic nephropathy and hypertensive nephropathy were the most common causes of end-stage renal disease. One year after the initiation of peritoneal dialysis, the urea level decreased significantly, and C-reactive protein level increased significantly. Platelet count increased from 240 ± 55 x10 3 /µL to 274 ± 53 x10 3 /µL (p=0.003) and mean platelet volume decreased from 10.7 ± 1.0 fl to 10.2 ± 0.8 fl (p<0.001). There was a significant decrease in mean platelet volume to platelet count ratio (p=0.001).

Conclusion: Mean platelet volume and mean platelet volume to platelet count ratio, which are risk factors for cardiovascular diseases, decreases one year after initiation of peritoneal dialysis. This finding may be associated with the improvement of the uremic environment.

Keywords: C-reactive protein level, mean platelet volume, mean platelet volume to platelet count ratio, peritoneal dialysis

ÖZ

Amaç: *Periton diyalizi yapan hastalarda en sık ölüm nedeni kardiyovasküler hastalıklardır. Trombosit aktivasyonunun göstergesi olan trombosit indeksleri ile kardiyovasküler olaylar arasında ilişki olduğu gösterilmiştir. Amacımız, son dönem böbrek hastalığı olan hastalarda periton diyalizi başlandıktan sonra trombosit sayısı, ortalama trombosit hacmi ve ortalama trombosit hacmi/trombosit sayısı oranının değişiminin incelenmesidir.*

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Gereç ve Yöntemler: *Bu retrospektif çalışmaya 28 hasta dahil edildi. Hastaların periton diyalizi başlandığı sıradaki demografik ve klinik özellikleri hasta dosyalarından kaydedildi. Periton diyalizi başlanmadan önce son bir ay içindeki ve başlandıktan sonra birinci yıldaki laboratuvar verileri kaydedildi. Ortalama trombosit hacmi/trombosit sayısı oranı, ortalama trombosit hacminin her mikrolitrede 1000 trombosit sayısına bölünmesi (ortalama trombosit hacmi/trombosit sayısı oranı=ortalama trombosit hacmi/her mikrolitrede 1000 trombosit sayısı) ile elde edildi.*

Bulgular: *Hastaların yaş ortalaması 51.1 ± 14.6 idi. Hastaların %42.8' i erkekti. Diyabetik ve hipertansif nefropati en sık son dönem böbrek hastalığı nedeniydi. Periton diyalizi başlandıktan bir yıl sonra C-reaktif protein düzeyi anlamlı olarak yükseldi. Periton diyalizi başlandıktan bir yıl sonra, trombosit sayısı 240 ± 55 x103/μL' den 274 ± 53 x103/μL' e yükseldi (p=0.003), ortalama trombosit hacmi 10.7 ± 1.0 fL' den 10.2 ± 0.8 fL' ye düştü (p<0.001), ortalama trombosit hacmi/trombosit sayısı oranında anlamlı azalma oldu (p=0.001).*

Sonuç: *Periton diyalizi başlandıktan bir yıl sonra C-reaktif protein düzeyi arttığı, trombosit sayısının arttığı, ortalama trombosit hacminin azaldığı ve ortalama trombosit hacmi/trombosit sayısı oranının azaldığı gösterilmiştir. Kardiyovasküler hastalıklar için risk faktörü olan ortalama trombosit hacmi ve ortalama trombosit hacmi/trombosit sayısı oranındaki azalma üremik ortamın düzelmesi ile ilişkili olabilir.*

Anahtar Sözcükler: *C-reaktif protein düzeyi, ortalama trombosit hacmi, ortalama trombosit hacmi/trombosit sayısı oranı, periton diyalizi.*

INTRODUCTION

Peritoneal dialysis (PD) is one of the kidney replacement therapies for patients with end-stage renal disease (ESRD). Cardiovascular diseases (CVD) are the most common cause of mortality in PD patients (1).

Platelets are involved in the pathogenesis of atherosclerotic lesions that cause CVD (2). Platelet indices, which are indicators of platelet activation and inflammation, have been shown to be independent risk factors for CVD and mortality (3, 4). Two of these risk factors are mean platelet volume (MPV) and mean platelet volume to platelet count ratio (MPR) (5-7). For patients with cardiovascular disease, high MPV was associated with thrombotic complications and mortality (6). In hemodialysis patients, all-cause and cardiovascular mortality were found to be higher in patients with high platelet count and MPV (8, 9). The number of studies evaluating platelet indices in PD patients is limited and the results are inconsistent. Peng et al. showed that mortality was higher in patients with high platelet count, but MPV was not associated with high mortality (10). MPV was found to be high in patients with chronic kidney disease who did not undergo renal replacement therapy (11). MPR has been shown to be an independent risk factor for mortality in PD patients (12). Most patients with chronic kidney disease have platelet dysfunction which may improve with renal replacement therapy (13). However, there has been no study that evaluated the change of MPV and MPR after the initiation of PD. Our study aims to evaluate the changes in MPV and MPR in the first year after initiation of PD.

MATERIALS and METHODS

This is a retrospective cohort study. Thirty-nine adult patients started PD between 1 January 2015 and 31 August 2020 for the treatment of ESRD. Exclusion criteria included 1- the patients with kidney transplantation (n=1), 2- the patients who started PD due to a vascular access problem during hemodialysis treatment (n=2), 3- the patients who switched to another kidney replacement therapy within one year after initiation of PD (n= 5), 4- the patients lost to follow-up within one year after initiation of PD (n=3). The study included 28 patients. The Local Ethics Committee approved this study (Number: 21-11T/22, Date: 04.11.2021).

Demographic and clinical data (age, gender, height, weight, cause of ESRD, comorbidities, blood pressure, type of PD) and medications at the time of initiation of PD were obtained from the patient files. The weekly total Kt/V_{urea} performed between 3-6 months after the initiation of PD were recorded. Laboratory data (urea, creatinine, sodium, potassium, calcium, phosphorus, uric acid, albumin, C-reactive protein (CRP), parathormone, ferritin, total cholesterol, triglyceride, low-density lipoprotein (LDL), leukocyte count, hemoglobin, platelet count, and MPV were recorded from patient files. MPR was calculated as mean platelet volume (femtolitres) divided) by platelet count (number of thousand platelets/microliter). Body mass index (kg/m^2) was obtained by dividing body weight (kg) by the square of height (m).

Continuous variables were presented as mean ± standard deviation or median (25th-75th percentile) and compared with Mann-Whitney U

test or t-test. Categorical variables were presented as percentages and compared with the chi-square test. The correlations were conducted by using the Spearman correlation test. The changes in the descriptive variables in the first year were evaluated with a t-test and a Wilcoxon test. The change of categorical variables was evaluated with the McNemar test; $p < 0.05$ was considered statistically significant. Data were analyzed with Statistical Package of Social Science (SPSS) software version 14.0 for Windows.

RESULTS

A total of 28 incident PD patients were enrolled in this study. Baseline demographic and clinical characteristics and laboratory data of the patients are shown in Table-1. The mean age was 51.1 ± 14.6 years and 42.8% of the patients were male. The most common causes of ESRD were diabetic nephropathy and hypertension. The cause of ESRD was unknown in 25% of the patients. Most of the patients (78.6%) were treated with continuous ambulatory PD. At the initiation of PD, anti-hypertensive drugs (82.1%), diuretics (71.4%), and phosphate-binding agents (89.3%) were the most commonly used drugs. Ten patients received erythropoietin, and three patients received antiplatelet therapy (acetylsalicylic acid and/or clopidogrel). Total weekly Kt/V_{urea} was 2.46 ± 0.4. At the initiation of PD, urea, creatinine, hemoglobin and platelet count were 190 ± 66 mg/dL, 7.57 ± 1.85 mg/dL, 10.1 (9.5-11.4) g/dL and 240 ± 55 x 10^3 /µL, respectively.

Table-1. Demographic and clinical findings of the patients before initiation peritoneal dialysis.

Age (years)	51.1 ± 14.6
Gender (Male, n, %)	12 (42.8)
Body mass index (kg/m^2)	26.1 ± 4.3
Causes of end-stage kidney disease	
Diabetic nephropathy (n, %)	6 (21.4)
Hypertensive nephropathy (n, %)	5 (17.9)
Chronic glomerulonephritis (n, %)	3 (10.7)
Unknown (n, %)	7 (25)
Other (n, %)	7 (25)
Cardiovascular disease (n, %)	3 (10.7)
Diabetes mellitus (n, %)	7 (25)
Type of PD	
Continuous ambulatory PD (n, %)	22 (78.6)
Automated PD (n, %)	6 (21.4)
Medications	
Antihypertensive drug (n, %)	23 (82.1)
Diuretics (n, %)	20 (71.4)
Phosphate binding agent (n, %)	25 (89.3)
Vitamin D analogues (n, %)	15 (53.6)
Erythropoietin (n, %)	10 (35.7)
Anti-platelet treatment (n, %)	3 (10.7)
Systolic blood pressure (mmHg)	144 ± 17
Diastolic blood pressure (mmHg)	83 ± 15
Urea (mg/dL)	190 ± 66
Creatinine (mg/dL)	7.57 ± 1.85
Sodium (mEq/L)	140 (138-141)
Potassium (mEq/L)	4.7 ± 0.8
Calcium (mg/dL)	9.1 ± 1.1
Phosphorous (mg/dL)	6.3 ± 1.6
Uric acid (mg/dL)	6.7 ± 1.7
Albumin (g/dL)	4.1 ± 0.6
CRP (mg/dL)	0.30 (0.16-0.45)
PTH (pg/mL)	314 (167-485)
Ferritin (ng/mL)	171 (105-384)
Leukocytes (x 10^3/µL)	7.6 ± 1.5
Hemoglobin (g/dL)	10.1 (9.5-11.4)
Platelets (x 10^3/µL)	240 ± 55
Total cholesterol (mg/dL)	187 ± 53
Triglyceride (mg/dL)	158 ± 61
LDL (mg/dL)	111 ± 46
PD, peritoneal dialysis; CRP, C-reactive protein, PTH, parathormone, LDL, low-density lipoprotein	

Table-2. Laboratory data of the patients at the initiation and in the first year of peritoneal dialysis.

	Initiation of PD	First year of PD	p
Urea (mg/dL)	190 ± 66	104 ± 31	<0.001
Creatinine (mg/dL)	7.57 ± 1.85	8.23 ± 2.16	0.252
CRP (mg/dL)	0.30 (0.16-0.45)	0.37 (0.18-0.67)	0.01
Leukocytes (10^3/μL)	7.6 ± 1.5	7.6 ± 2.0	0.705
Hemoglobin (g/dL)	10.1 (9.5-11.4)	10.9 (10.3-12.8)	0.015
Platelets (10^3/μL)	240 ± 55	274 ± 53	0.003
MPV (fL)	10.7 ± 1.0	10.2 ± 0.8	<0.001
MPR (fL/ 10^3/μL)	0.047 ± 0.013	0.039 ± 0.009	0.001
Erythropoietin treatment (n, %)	10 (35.7)	5 (17.9)	0.180
Anti-platelet treatment (n, %)	3 (10.7)	3 (10.7)	1.0

PD, peritoneal dialysis; CRP, C-reactive protein; MPV, mean platelet volume; MPR, mean platelet volume to platelet count ratio (10^3/μL)

The laboratory data of the patients at baseline and in the first year after the initiation of PD are shown in Table-2. Serum urea level decreased from 190 ± 66 mg/dL to 104 ± 31 mg/dL (p<0.001) in first year. CRP level increased significantly (p=0.01). The platelet count increased from 240 ± 55 x 10^3/μL to 274 ± 53 x 10^3/μL (p=0.003) and MPV decreased from 10.7 ± 1.0 fL to 10.2 ± 0.8 fL (p<0.001) one year after the onset of PD. There was a significant decrease in MPR in the first year (p=0.001). There was a decrease in the rate of patients treated with erythropoietin at the end of the first year, but it was statistically non-significant (p=0.180).

In Spearman's correlation analysis, platelet count was negatively correlated with MPV at the time of initiation of PD (r=-0.454, p=0.015). Platelet count was not correlated with urea, creatinine and CRP (r=-0.132, p=0.502; r=-0.271, p=0.163; r=-0.145, p=0.488, respectively). MPV was not correlated with urea, creatinine, and CRP (r=0.113, p=0.566; r=-0.074, p=0.707; r=0.308, p=0.134, respectively).

The platelet count one year after starting PD was negatively associated with MPV (r=-0.385, p=0.048). One year after initiation of PD, platelet count was not associated with urea, creatinine and CRP (r=-0.258, p=0.194; r=0.222, p=0.266; r=0.162, p=0.419, respectively). MPV was not associated with urea and CRP (r=-0.222, p=0.265; r=0.040, p=0.841, respectively). MPV was negatively correlated with creatinine (r=-0.385, p=0.047).

DISCUSSION

In our study, platelet count increased, MPV and MPR decreased one year after initiation of PD in patients with ESRD. Platelet count was negatively correlated with MPV.

In ESRD, platelet dysfunction occurs secondary to abnormal glycoprotein IIb/IIIa expression, abnormal secretion of granules by platelets, disorders in prostaglandin synthesis, and structural changes in platelets (14). In addition, it has been shown that there is a decrease in nucleated platelets, which is an indicator of platelet production (15). There is a tendency to lower platelet counts in patients with ESRD when compared to normal individuals and this finding has been attributed to insufficient thrombopoietic activity (16). Studies have shown that platelet dysfunction improves with the initiation of renal replacement therapy. Previously, it was shown that platelet count increases and platelet aggregation, which leads to platelet dysfunction, improves with PD (17). Platelet functions improve after successful kidney transplantation (18). In our study, platelet count increased and MPV decreased one year after the PD initiation; therefore, MPR is reduced. In our study, MPV decreased in the first year despite the increase in CRP, which is an inflammation marker. These findings suggest that an increase in the platelet count and a decrease in MPV may be associated with the improvement of the uremic environment or the better clearance of medium molecular weight solutes by PD. As MPV and platelet count was not correlated with CRP in the presented study, the changes in platelet indices may be independent of inflammation. In our study, MPV and MPR decresed but CRP increased at the end of the first year. Platelet count may be increased secondary to increased platelet production in the bone marrow with the onset of PD.

Platelets adhere to the extracellular matrix in the damaged vessel wall, aggregate, and contribute to coagulation. Platelets are also involved in inflammation and wound healing. Platelets with larger volumes are more reactive and prothrombotic (5). MPV is determined by measuring the platelet volume with automatic blood count devices. In normal physiological conditions, MPV and platelet count are inversely proportional, and MPV decreases when platelet production increases (19). In some pathological conditions, this physiological balance is disturbed. Cytokines such as interleukin-6, which play a role in inflammatory processes, cause the release of large platelets from the bone marrow and increase MPV (20). On the other hand, MPV is found to be low in some systemic diseases because platelets are localized in the area of inflammation (21, 22).

Chronic inflammation is common in patients with ESRD and associated with malnutrition, myopathy, endothelial damage, and atherosclerosis (23, 24). Some studies showed that inflammatory markers were increased in patients treated with PD for the long term (25, 26). In our study, CRP increased significantly one year after the onset of PD. On the other hand, interleukin-6 and CRP levels did not change one year after the onset of PD in a previous study (27).

The limitation of our study is the retrospective design. Patients treated with anti-platelet drugs and erythropoietin were also included in the study. However, the rates of patients treated with these drugs at the initiation of PD and in the first year were found to be similar.

In conclusion, platelet count was increased and MPV and MPR were decreased one year after the initiation of PD. These changes in platelet indices which are risk factors for CVD may be associated with the improvement of the uremic environment.

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