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Original Article

Is mean platelet volume a predictor of atherosclerosis in hemodialysis patients?

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Abstract

Aim: Cardiovascular (CV) mortality accounts for the 45% of all mortality in dialysis. Carotid intima-media thickness (CIMT) is a preclinical marker for CV disease. Activated platelets pose important part of the cellular component in the pathophysiology of atherothrombosis. Mean platelet volume (MPV) is a parameter that indicates the activation of platelets and assessed by studies in various patient groups in atherosclerosis. The aim of this study is to determine the relation of MPV with CIMT in haemodialysis (HD) patients without a history of atherosclerosis.

Material and Methods: Eighty two HD patients and 20 healthy individuals were enrolled in this cross-sectional study. Ultrasonographical B-mode imaging of bilateral carotid arteries was performed with a high resolution real-time ultrasonography with 12MHz linear-assay transducer (Mindray DC7). The value was expressed as an average of the maximal CIMT. MPV was measured by automated devices.

Results: CIMT was found to be higher in study population when compared to control group. MPV was not different between groups (8.40±0.85 vs 8.4±0.81; P>0.05). In correlation analysis CIMT was found to be positively correlated with age(r=0.326; P=0.003), ALP(r=0.309; P=0.005) and MPV(r=0.26; p= 0,017). Patients were grouped according to median levels of MPV. The patients having higher MPV values were found to have higher PTH (533.9 ± 458.3 vs 845.8 ± 860.2; P<0, 05) and CIMT (0.8 ± 0.1 vs 0.9 ± 0.2; P<0. 05) values.

Conclusions: MPV was found to be correlated with CIMT in HD patients. MPV can be used as a marker in HD patients for determining atherosclerosis.

Keywords: Atherosclerosis; Hemodialysis; Mean Platelet Volume.

INTRODUCTION

Chronic kidney disease (CKD) is an important problem for a public health and the mortality is higher than normal population. Approximately annual mortality in dialysis patients is 21.2 %. In uremic process many organ systems are affected but cardiovascular (CV) mortality accounts for the 45% of all mortality in dialysis (1).

Atherosclerosis is a multifactorial, chronic, progressive process that affects all arteries and begins with the increase in intima-media thickness (2). The femoral artery or carotid intima-media thickness (CIMT) observed by Ultrasonography (USG), can be helpful in detecting atherosclerosis. Carotid arteries are most commonly used due to the ease of visualization. CIMT is a preclinical marker for cardiovascular disease (CVD) that is used for evaluating severity and progression of atherosclerosis (3).

Activated platelets pose important part of the cellular component in the pathophysiology of atherothrombosis. Platelets are not only a component of a thrombus formation, but also contribute to the formation of atherogenesis as an inflammation inducer (4). Mean platelet volume (MPV) is a parameter that indicates the activation of platelets and investigated by studies in various patient groups in atherosclerosis (5-8). However in the literature few studies exist in uremic population. The aim of this study is to determine the relation of MPV with CIMT in hemodialysis patients without atherosclerosis history.

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MATERIAL and METHODS

The study was initiated after the approval of local ethic committee of Diskapi Yildirim Beyazit Research and Training Hospital and informed consent was obtained from all participants.

Eighty two HD patients and 20 healthy individuals were enrolled in this cross-sectional study. Patients were eligible for inclusion in the study if they were treated with HD for at least 6 months. Exclusion criteria were the presence of malignancy, history of trauma, surgery or burn in the past month, presence of acute infection, chronic liver disease, and history of CVD or using acetyl salicylic acid.

Pre-dialysis blood samples were drawn and routine laboratory assessments were performed by standard laboratory techniques. Data on demography, cause of renal failure, diabetes mellitus (DM), dialysis vintage and treatment parameters were collected. The control group consisted healthy volunteers from the internal medicine outpatient clinic who applied for a routine check-up.

Ultrasonographic B-mode imaging of bilateral carotid arteries was performed with a high resolution real-time ultrasonography with 12MHz linear-assay transducer (Mindray DC7). Evaluations were performed by a single trained medical doctor who was not aware of patients clinical status with the patients lying in the prone position with the head extended and turned to the opposite direction.

Carotid arteries, carotid bulb and internal carotid arteries were examined by two different longitudinal projections. At each longitudinal projection CIMT was conducted from the site of the greater thickness. CIMT was defined as the distance between the leading edges of the lumen interface at the far wall in plaque-free arterial segments. The value was expressed as an average of the maximal CIMT.

Statistical analysis was performed by using statistical package SPSS version 19.0 (SPSS Inc., IL, USA). All variables were expressed as the mean±SD unless otherwise indicated. The Kolmogorov-Smirnov test was used to analyze the normality of distribution. Pearson's correlation analysis was used to clarify the relation between CIMT, inflammatory parameters and MPV.

RESULTS

Eighty two hemodialysis patients and 20 controls were included in the study. There was no difference between groups in terms of age and sex. BMI was not different between groups (Table 1). When biochemical parameters are observed urea, creatinine, uric acid, total protein, albumin, alkaline phosphatase (ALP), calcium, phosphate and hemoglobin levels were different between groups (Table 1).

CIMT was found to be higher in study population when compared to control group. MPV was not different between groups (8.40±0.85 vs 8.4±0.81; P>0.05) (Table 1). In correlation analysis CIMT was positively correlated with age (r=0.326; P=0,003), ALP (r=0.309; P=0.005) and MPV (figure 1) (table 2). When patients are grouped in two according to median values of MPV, the patients having higher MPV values are found to have higher PTH (533.9 ± 458.3 vs 845.8 ± 860.2; P < 0.05) and CIMT (0.8 ± 0.1 vs 0.9 ± 0.2; P < 0.05) values (Table 3).

Table 1. Comparison of patient and control group

	Patient (N=82)	Control (N=20)	p
Female /male	46/36	9/11	>0.05
Age(years)	55.67±15,5	50.95±8,32	>0.05
BMI(kg/m²)	25.6±14.4	25.3±3.7	>0.05
Glucose(mg/dl)	102.3±38.05	89.45±10.4	>0.05
Urea (mg/dl)	130.9±29.1	24.9±4.3	<0.05
Creatinine(mg/dl)	7.1±2.07	0.85±0.1	<0.05
Uric acid(mg/dl)	5.7±1.37	4.7±1.2	<0.05
Total protein(g/dl)	6.8±0.6	7.5±0.43	<0.05
Albumin(g/dl)	3.6±0.5	4.4±0.1	<0.05
Alkaline phosphatase(IU/l)	168.4±213.7	74.6±25.6	<0.05
Calcium(mg/dl)	8.7±0.8	9.3±0.3	<0.05
Phosphate (mg/dl)	5.3±1.1	3.09±0.3	<0.05
Hemoglobin(g/dl)	10.6±1.3	14.6±1.5	<0.05
CIMT(cm)	0.87±0.19	0.62±0.1	<0.05
Mean platelet volume(fl)	8.40±0.85	8.4±0.81	>0.05

CIMT: Carotid intima-media thickness

Table 2. Correlation analysis

Parameters (n=82)	r	p
Age	0.326	0.003
Body mass index	0.046	0.682
Alkaline phosphatase	0.309	0.005
Calcium	0.029	0.798
Phosphate	-0.26	0.817
Parathyroid hormone	0.213	0.055
Mean platelet volume	0.26	0.017

Table 3. Comparison of groups according to mean platelet volume values

N=82	MPV(fl)≤0,85	MPV(fl)≥0,85	p
Age(years)	53.8±16.03	57.92±15.12	>0.05
BMI(kg/m²)	27.6±19.9	23.6±4.1	>0.05
Calcium(mg/dl)	8.7±0.8	8.7±0.7	>0.05
Phosphate (mg/dl)	5.1±1.1	5.6±1.2	>0.05
CIMT(cm)	0.8±0.1	0.9±0.2	<0.05
Alkaline phosphatase (IU/l)	116.2±56.5	223.7±296.4	<0.05
Parathormon (pg/ml)	533.9±458.3	845.8±860.2	<0.05

CIMT: Carotid intima-media thickness

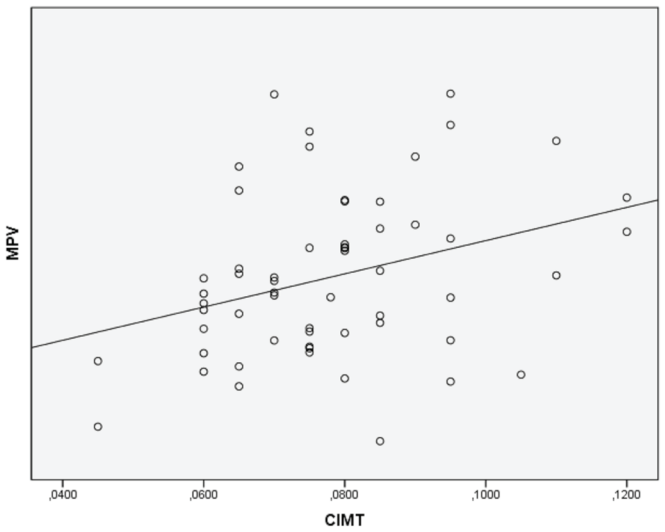

Figure 1. Correlation of MPV with CIMT

DISCUSSION

The main finding of this study is the positive correlation of MPV and CIMT. In uremic patients changes in CV system are the main predictor of prognosis. In CKD patients CVD pathogenesis is complex. Higher CV complication risk cannot be explained by the presence of classical risk factors. The obtained data suggest chronic inflammation, oxidative stress, anemia, uremic toxins, insulin resistance, platelet dysfunction, decreased fibrinolytic activity and the uremic process -related factors, such as calcium - phosphorus abnormalities involved in pathogenesis of CVD (9). The presence of CKD is an independent risk factor for CVD (10). In a study in asymptomatic HD patients, more than half of patients undergoing coronary angiography had coronary artery stenosis (11). In another study, 23% of the HD patients had latent ischemia determined by ambulatory monitoring (12). Therefore, early determination of CVD may decrease the mortality and morbidity in this patient group. In our study we aimed to investigate the relation of MPV which is an easy and inexpensive method, with CIMT is used as a reliable indicator of atherosclerosis (13). CIMT was shown to be an independent predictor of coronary artery disease (CAD) in CKD patients (14). In our study CIMT used as a predictor of subclinical atherosclerosis and it was higher in patient group when compared with study group and this was compatible with the studies.

The clinical and epidemiological studies in uremic patients, high phosphorus and ALP levels have been proven to be associated with calcification in the coronary arteries, increased CVD risk and total mortality (15). In a study conducted in 3-4 CKD patients, increased serum phosphate concentration of 1 mg/dl was associated with an increase in adjusted all-cause mortality risk of %23 (16). Additionally hypophosphatemia was related to poor CV outcome independently. (17). In our study CIMT was correlated with ALP but not with phosphate level. This may be caused by the usage of ohosphate binders.

Aging is a risk factor for atherosclerosis. CIMT increases by aging and this change is 0.005-0.01 mm/year approximately (18). Also in HD population CIMT increases with age (19). In our study CIMT was found to be positively correlated with age. Correlation between BMI and CIMT was statistically significant in some studies (20) while insignificant in others (21). There was no correlation in our study and this may be caused because of the lower incidence of obesity in our population.

Activated platelets are important in the pathogenesis of atherothrombosis. Platelets are not only components of thrombosis formation but also involved in the induction of inflammation (9). Earlier studies demonstrated that platelet reactivity is increased in larger platelets (22). This may be caused because of increased thromboxane A2 produced by larger platelets (23). Previous studies demonstrated platelets to play a critical role in carotid atherosclerosis. P-selectin is stored in secretory granules and may be important in the development of atherosclerosis by affecting plaque maturation and calcification (24). Platelet reactivation is related to thrombogenic activation and increased CVD risk (25). In patients with CAD who had coronary stent implantation, MPV was found to be higher in patients having stent restenosis (26). In The Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT), MPV was higher in patients having end organ damage with hypertension (HT) (27). In patients with HT MPV was found to be correlated with the severity of end organ damage (28). In another study independent relation was detected between peripheral arterial disease prevalence and MPV (29). Additionally in male patients without CVD, DM, HT or hyperlipidemia independent relation was determined between MPV and CAD (30). A relationship between MPV and coronary and carotid atherosclerosis has been reported in other studies (5-8). MPV was used in determining the severity of CAD and is associated with adverse CV outcomes in patients with CVD (31,32). Also in a study of Kalkan et al. they measured the thoracic-aortic media thickness and assessed its relationship between MPV. As a result MPV was correlated with the extend of thoracic-aortic atherosclerosis (33). In a study MPV was found to be correlated with microvascular complications of type 2 DM (34). In a study in type 2 DM, MPV was found to be positively correlated with creatinine and proteinuria (35). Number of studies related to MPV is not much in uremic population. In a study in South Korea, MPV was found to be increased with decreasing GFR (36). In a cross sectional study in HD patients with higher MPV had higher incidence of CAD history (37). In a study of Bal et al. they investigated 149 consecutive ESRD patients, MPV and age were found to be independent predictors of extend of CAD. These findings are compatible with our findings (38). As a result data of this study suggests a possible relation between atherosclerosis and MPV in HD population. But this is a cross-sectional single center study and made with a small number of patients. Because of the cross-sectional design of the study we can only talk about a numerical relationship. So well-designed prospective studies are needed.

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