Assessment of the Hemostatic Parameters and Platelet Function on Thromboelastometry and Impedance Aggregometry in Hemodialysis Patients Qualified for Kidney Transplantation: Preliminary Report

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ABSTRACT

Background. Chronic kidney disease is one of the medical conditions that affect hemostasis. Patients undergoing hemodialysis present both hemorrhagic and prothrombotic tendencies. Platelet adhesion to the artificial surface of the dialyzer's membrane, blood vessel endothelial wall disruption, and quantitative and qualitative changes in clothing factors are thought to be causative agents of the above-mentioned conditions. Thromboelastometry and impedance aggregometry enable precise assessment of clot formation and platelet function abnormalities, including changes related to chronic renal failure in patients undergoing renal replacement therapy.

Methods. A prospective study with control group was designed. The study group consisted of 17 adults with diagnosed chronic renal failure undergoing hemodialysis. The control group consisted of 13 healthy volunteers. EXTEM and FIBTEM tests in rotational thromboelastometry and TRAPtest in impedance aggregometry analyzer were performed.

Results. EXTEM parameter test results were comparable between analyzed groups, whereas FIBTEM test results were significantly increased in the study group. Platelet aggregation as measured by the TRAPtests was significantly decreased in patients undergoing hemodialysis.

Conclusions. In end-stage renal disease patients undergoing hemodialysis, whole-blood clot formation is not disturbed, even though platelet dysfunction occurs. Increased fibrin clot formation reflected by FIBTEM results may compensate the observed platelet disorders. The compilation of ROTEM and Multiplate may support appropriate hemostatic control and decision-making during kidney transplantation.

EARLY stages of chronic kidney disease (CKD) are typically associated with prothrombotic tendencies, whereas in its more advanced stages patients also have bleeding diathesis [1]. These multifactorial changes involve intrinsic and extrinsic pathways, natural anticoagulants, and fibrinolysis [2]. Markers of endothelial cell damage and inflammation are also present [3]. Standard laboratory tests are not sensitive enough to detect most of these changes. The usage of a point-of-care (POC) method enables diagnosis of a wider spectrum of hemostatic disorders. Thromboelastometry provides a viscoelastic measurement of clot formation in whole blood. This method is sensitive for fibrinogen and severe coagulation factor deficiencies, hyperfibrinolysis, and platelet-fibrin interaction [4]. EXTEM measures changes in the extrinsic pathway of coagulation with the use of tissue factor as an activator [5]. FIBTEM assesses plasma fibrinogen level without platelet components,

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using cytochalasin D in combination with EXTEM [6]. Thromboelastometry does not provide precise information on platelet function related to adhesion and aggregation [7] but can be utilized for the assessment of the overall interaction between platelet glycoprotein IIb/IIIa (GPIIb/IIIa) and fibrinogen [8].

Platelet abnormalities (quantitative and qualitative) are also observed among hemodialysis patients [9]. Impedance aggregometry, the POC method designed for platelets assessment, measures an increase in impedance as a result of platelet aggregation. The result is quantified as the area under the aggregation curve (AUC, [AU*min]). The activity of the platelet surface GPIIb/IIIa, which is crucial for platelet adhesion and aggregation, can be assessed by use of the TRAPtest after stimulation with thrombin receptor-activating peptide (TRAP-6). Impairment of the TRAPtest might be an indicator of global platelet function impairment [10].

Aggregometric tests combined with viscoelastic methods extend the diagnostic spectrum beyond that offered by conventional laboratory tests of coagulation [11].

The aim of this study was to assess the influence of end-stage renal disease (ESRD) requiring hemodialysis on hemostatic changes, particularly platelet function, on the basis of in vitro results of thromboelastometry and impedance aggregometry.

METHODS

After approval of Bioethics Committee of Medical University of Warsaw, 30 participants were enrolled in the prospective, control group study. The study group consisted of 17 patients with ESRD, receiving hemodialysis 3 times per week for at least 2 years. The control group consisted of 13 healthy volunteers with no history of CKD and hemostatic disorders. Patients taking antiplatelet medications were excluded from the study.

Five milliliters of blood was drawn immediately before initiation of hemodialysis. Thromboelastometry (ROTEM Delta, Tem International, Munich, Germany) and impedance aggregometry (MULTIPLATE, Roche, Basel, Switzerland) were performed according to the manufacturer's instructions.

In thromboelastometry, the amplitude of clot firmness in the 20th minute (A20) in EXTEM and FIBTEM were analyzed. Both analyses were performed for a minimum of 25 minutes. In impedance aggregometry, the measurement of platelet aggregation in the TRAPtest was done, and the area under the curve was determined.

The results are expressed as mean ± standard deviation (SD). Normal distribution was checked by use of the Shapiro-Wilk test. Statistical analysis (Statistica 10) was performed with the use of the Student t test for independent samples. A value of $P < .05$ was considered as statistically significant.

RESULTS

Baseline demographic and clinical characteristics of the participants were compared and presented in Table 1. Standard laboratory results consisting of white blood count (WBC), hemoglobin (HGB), hematocrit (HCT), platelet count (PLT), prothrombin time (PT), and activated partial thromboplastin time (APTT) were compared between groups. Statistically significant difference has been noticed in terms of the mean of HGB, HCT, and PLT, which were lower in the study group than in the control group (107 g/L vs 146 g/L, $P = .000$, 0.33% vs 0.42%, $P = .000$, 184 × 10^3/L vs 228 × 10^3/L, $P = .029$, respectively). Fibrinogen levels (FIB) were comparable between groups (3.1 g/L vs 2.9 g/L in controls, $P = .42$).

Table 1. Demographic and Clinical Characteristics of Groups (mean ± SD or percent)

	Study Group (n = 17)	Control Group (n = 13)	*P* Value
Age (years)	59.8 ± 12	44.1 ± 14	<.05
Male (%)	65	61	>.05
Diabetes (%)	47	0	<.05
Hypertension (%)	76	15	<.05
Coronary artery disease (%)	52	0	<.05
Cerebrovascular disease (%)	18	0	<.05
Months on hemodialysis	41 ± 16		
Length of hemodialysis (hours/week)	12 ± 1.5		
No. of hemodialysis sessions/week	3		
Cause of ESRD			
Diabetes (%)	30		
Hypertension (%)	22		
Glomerulonephritis (%)	18		
Other (%)	30		
Type of dialyzer			
Low-flux, polysulfone (%)	100		

Viscoelastic properties of clot measured after 20 minutes by A20 EXTEM showed no differences between analyzed groups (64.9 ± 7.5 vs 63.1 ± 3.4, $P = .45$). A20 in FIBTEM was significantly higher in the study group (22.3 ± 6.0 vs 16.7 ± 3.7, $P = .004$) (Fig 1).

ESRD patients showed significantly lower platelet activity after stimulation with TRAP (814 ± 118 vs 1130 ± 366, $P = .038$) (Fig 1).

DISCUSSION

Hemostatic changes resulting from CKD are multifactorial and multi-faceted. The severity of the disturbances depends on the stage of renal disease. Patients with ESRD have an elevated risk of developing bleeding and thrombotic complications. Darlington et al [12] showed that nearly three quarters of patients present with hyper- or hypo-coagulable status, a third of whom have both abnormalities.

Functional analyses of platelet and plasmatic systems regulating thrombotic and hemostatic processes in patients with ESRD have only been investigated separately in available studies [12]. However, impaired primary hemostasis and platelet function changes cannot be detected by means of thromboelastometry alone [13]. The combination of thromboelastometry and impedance aggregometry is preferred for POC coagulation assessment in hemodialysis patients with multifactorial hemostatic disorders.