The effect of continuous-flow automated plateletpheresis on fibrinolytic activity of donor plasma

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SUMMARY. Blood circulating in extracorporeal circuit of the apheresis set has a contact with an artificial surface. The data on the influence of plateletpheresis on fibrinolytic activity are very limited and difficult to interpret. The aim of our study was to estimate the effect of plateletpheresis on the activation of fibrinolysis. Plateletpheresis was performed in 17 healthy blood donors using continuous-flow cell separator COM.TEC (Fresenius, Bad Homburg, Germany). Before and after plateletpheresis, blood samples were taken and markers of fibrinolysis (PAP, t-PA, PAI-I) as well as factor XII activity have been measured. We observed statistically significant decrease in t-PA and factor XII activities after plateletpheresis. There were no significant changes in concentrations of t-PA, PAI-1 and PAP as well as PAI-1 activity after plateletpheresis. Plateletpheresis performed by COM.TEC cell separator has very little, if any, effect on the activation of fibrinolysis. The mechanism of the inhibition of t-PA activity needs further investigations.

Key words: COM.TEC, factor XII, fibrinolysis, PAI-1, PAP, plateletpheresis, t-PA.

MATERIALS AND METHODS

Seventeen healthy donors, aged 21–40 years, who had not taken any drugs for at least 2 weeks prior to blood sampling, underwent standard thrombapheresis procedure. The automated continuous-flow cell separator...
The concentration and activity of toPA were measured using COALIZA High-molecular-weight kininogen, prekallikrein, factor Xa and COATEST toPA, respectively from Chromogenix-Instrumentation Laboratory SpA, Italy.

**PAP**

Concentration of PAP was measured using Immulclone PAP Elisa kit (American Diagnostica, Greenwich, CT, USA).

**Factor XII activity**

Coagulation factor XII deficient plasma (human) (Dade Behring, Marburg, Germany) and activated partial thromboplastin assay has been applied for the measurement of factor XII activity. The results were expressed in percentage of the norm.

**Statistics**

The data are presented as mean value ± standard deviation (SD). For statistical evaluation of the results Wilcoxon's test was used.

Changes in measured parameters were corrected for haemodilution.

**RESULTS**

We observed significant decrease of t-PA and factor XII activity after thrombapheresis, whereas its concentration remained unchanged. There were no significant changes in the concentrations of PAP and PAI-I as well as PAI-I activity. The data of the measured parameters are presented in Table 2.

**DISCUSSION**

High-molecular-weight kininogen, prekallikrein, factor XII and factor XI recognized as the ‘contact system’ require contact with artificial, negatively charged surfaces for zymogene activation in vitro.
These surfaces are thought to be a substitute for possible physiological receptors on the biological activating surface. The 'contact proteins' have been ascribed to have a role in the initiation of acute inflammatory responses following tissue injury as well as in the activation of plasma fibrinolysis (Niewiarowski & Prou-Wartelle, 1959; Colman et al., 1975; Colman & Schmaier, 1997). Factor XIIa and kallikrein cleave plasminogen directly, but less efficiently than t-PA or u-PA (Colman, 1969; Goldsmith et al., 1978; Mandle & Kaplan, 1979). Bradykinin selectively induces t-PA release from endothelial cells (Smith et al., 1985). However, not only the electronegativity of the surface but also other physicochemical parameters could influence the activation of the contact phase system of plasma (Renaux et al., 1999). The 'damage' to the blood is also directly related to the duration of extracorporeal circulation.

Extracorporeal circulatory systems applied in cell separators differ depending on the principle of the apheresis method (e.g. constant or intermittent flow) and on the material of the disposable set. The plateletpheresis performed on blood separator CS 3000 induced a significant activation of coagulation, decrease of α2-antiplasmin concentration and had no effect on plasmin-plasmin inhibitor complex (Kobayashi et al., 1993). Unfortunately, in that study, t-PA and PAI-1 had not been measured. Another published report revealed no effect of extracorporeal circulation of blood separators: AMICUS and MCS 3p on the activation of coagulation, on the concentration of plasmin-plasmin inhibitor complex as well as on the PAI-1 concentration (Stohlawetz et al., 1999). However, these two studies are not comparable. They used different cell separators and there were differences in the whole blood: anticoagulant (ACD-A) ratios, blood volume processed and the time of extracorporeal circulation. In the study of Stohlawetz et al. (1999), markers of coagulation were measured in blood taken from the inflowing and outflowing blood of cell separator after processing a certain flow volume. Kobayashi et al. (1993) in their study measured the effect of thrombapheresis in blood drawn from collection line of donor immediately after the start and just before the end of apheresis. In our study, we investigated the effect of plateletpheresis performed with continuous-flow blood separator COM.TEC on t-PA and PAI-1 concentration and activity and plasmin-antiplasmin complex in platelet donors. We detected decreased factor XII activity, but did not detect significant changes in PAP, PAI-1 and t-PA concentrations as well as PAI-1 activity after plateletpheresis. The mechanism of the observed decreased activity of t-PA is difficult to explain. In our opinion, it may be due to the inhibitory effect of citrate infusion on t-PA activity/release. Nevertheless, thrombapheresis performed with COM.TEC presents a save procedure for the donor in terms of activation of fibrinolysis.

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REFERENCES


