CHARACTERIZATION OF PLATELET ACTIVATION AND COAGULATION INDICES IN AN IN VITRO DIALYSIS MODEL

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Introduction and Objective

The VIVIA Haemodialysis System differs from traditional haemodialysis equipment in that it uses a pneumatically controlled diaphragm blood pump and a rigid cassette in the blood flow path. During haemodialysis, blood is chronically exposed to the extracorporeal circuit (ECC) consisting of the blood flow path and the dialyser. Blood components interact with the ECC potentially eliciting changes in platelets and coagulation factors. Platelet activation has been identified as a risk factor for cardiovascular events. Therefore, it is of clinical relevance to characterize the biocompatibility characteristics of the VIVIA ECC.

Methods

In vitro **studies using the VIVIA ECC were performed to analyze biocompatibility during simulated dialysis in a perfusion model. Treatments were performed using freshly donated heparin-anti-coagulated human blood at a blood flow of 400 ml/min for 2 hours. Blood incubated in a polypropylene tube on a rocker at 37°C served as a control. Blood samples were removed, mixed with sodium citrate or EDTA at 15, 30, 60, 90 and 120 minutes and processed for analysis of platelet activation (CD62) and counts, thrombin activation (prothrombin fragment F1+2) and heparin concentration. For all assays, samples (n=5) were assayed in duplicate.**

<u>Platelet activation</u> : CD62 expression on platelet surface was measured by flow cytometry and the increase in soluble CD62 level in the plasma.

<u>Thrombin activation :</u> Thrombin activation was measured with an EIA that detects the activation fragment released in the conversion of prothrombin to active thrombin.

<u>Contact Activation</u>: A Western blot analysis was used to detect activated Factor XIIa fragments.

Results: Platelet Activation and Coagulation Indices

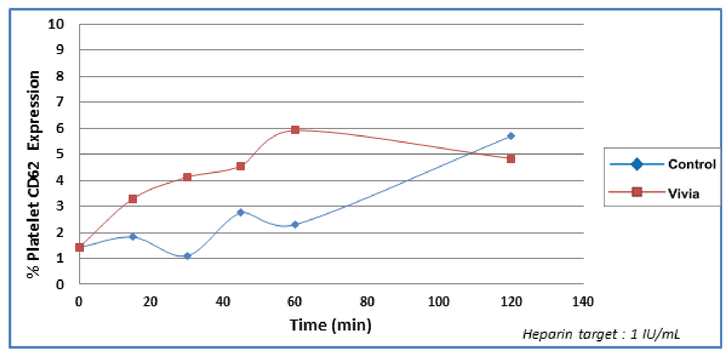

Figure 1: Platelet surface CD62 expression

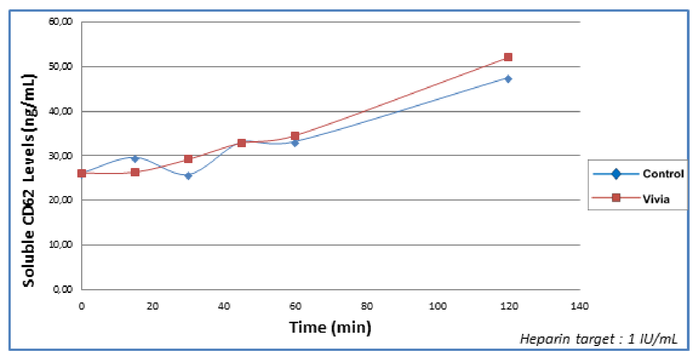

Figure 2: Soluble CD62 levels

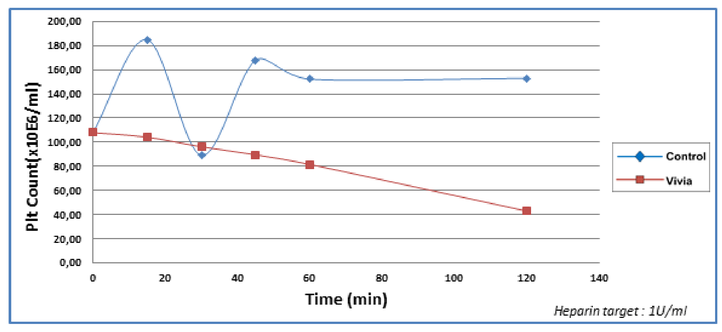

Figure 3: Platelet count: The decrease noted with VIVIA is consistent with an in vitro test model system with a large surface to volume ratio (ref. 1).

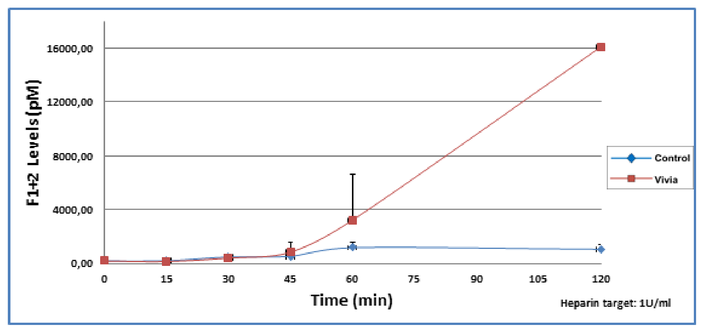

Figure 4: F1+2 levels. The magnitude of increase in F1+2 with VIVIA is consistent with reported data when corrected for higher surface to volume ratio (ref. 1,2).

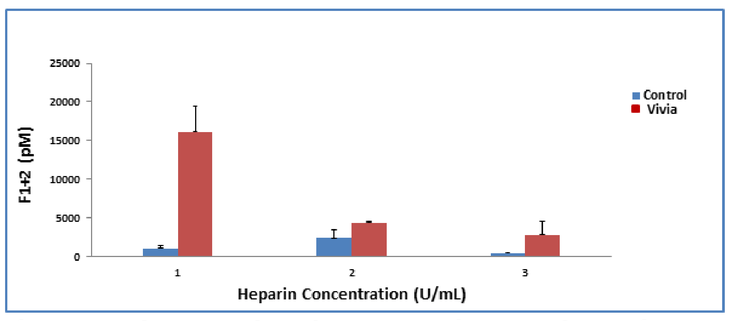

Figure 5: The F1+2 levels at 120 min were heparin dependent: a 73% and 82% reduction in F1+2 levels was observed at 2 and 3 U/ml, respectively

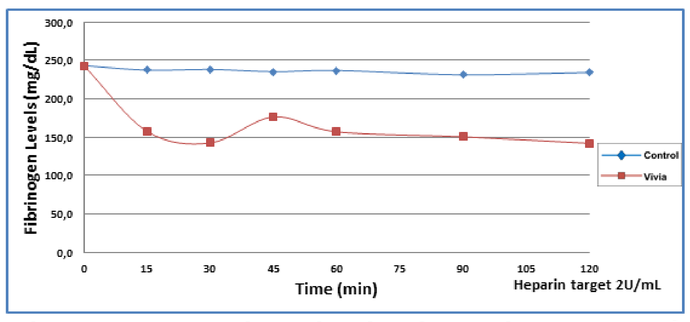

Figure 6: Thrombin activation (heparin target 2U/mL)

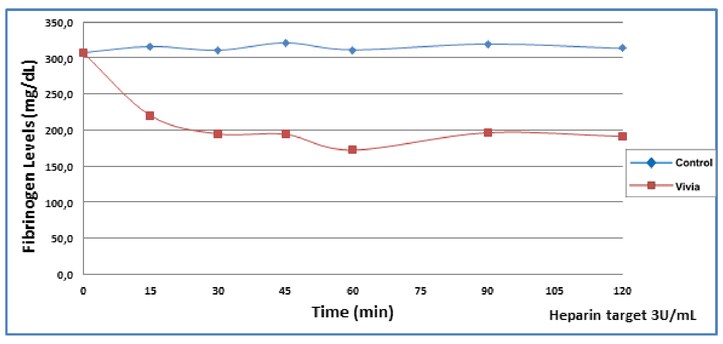

Figure 7: Thrombin activation (heparin target 3U/mL)

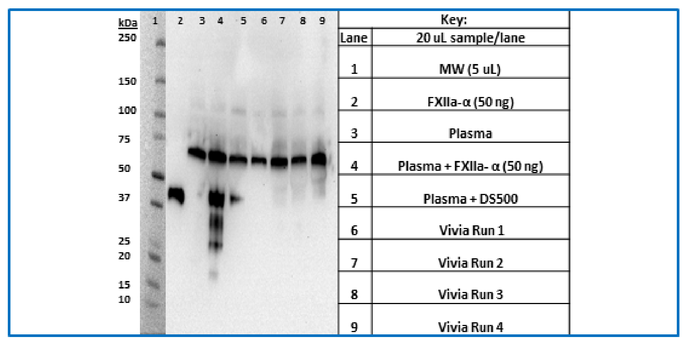

Figure 8: Western blot analysis of Factor XII

SUMMARY AND CONCLUSION: Platelet activation remained low and stable throughout the treatment as assessed by CD62 expression. Thrombin activation was low initially, but increased after an hour of perfusion to levels comparable to other published studies, an effect that could be largely reversed by increasing heparin levels. Therefore, the VIVIA Haemodialysis System ECC showed excellent biocompatibility with respect to platelet activation and coagulation indices.

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