Artifact Hyperfibrinolysis in Thromboelastography With the Use of a Heparinase Cup

To the Editor.—The thrombelastograph (TEG) hemostasis analyzer TEG-5000 series (Haemonetics, Braintree, Massachusetts) is a noninvasive diagnostic instrument designed to measure primary and secondary hemostasis in whole blood. The TEG is increasingly used in the settings of liver transplantation, trauma, and cardiac surgery.1 At Texas Children’s Hospital (Houston) the TEG is used to monitor patients on ventricular assist devices and extracorporeal membrane oxygenation systems (ECMO) in addition to the commonly used settings. The TEG parameters that are automatically calculated by the instrument can determine the course of anticoagulation therapy and management of bleeding in these settings. At Texas Children’s Hospital, the TEG is run using citrated whole blood with commercially provided kaolin (Haemonetics) in a plain cup and/or a heparinase cup, which is used to monitor heparin therapy. On occasion we have observed substantial hyperfibrinolysis in multiple patients’ samples in the heparinase cup but not with the same sample in the plain cup. Also, this effect is seen in samples from patients not on heparin therapy. Figure 1, a and b, shows a nonhepa-

Figure 1. Thrombelastograph (TEG) run on a patient not on heparin therapy using the same specimen at the same time with (a) citrated kaolin in a heparinase cup and (b) citrated kaolin in a plain cup.

rinalized patient’s lysis of 6.2% (LY30) with the use of a heparinase cup and 0.5% with the use of a plain cup.

We hypothesized that the substantial hyperfibrinolysis observed with the heparinase cup was due to an artifact and did not always reflect in vivo hyperfibrinolysis. In order to prove this effect, TEG samples from a patient on heparin therapy were run in parallel with 2 different antiheparin reagents: protamine 10 mg/mL diluted to a concentration of 0.033 mg/mL and Dade Hepzyme (Siemens, Deerfield, Illinois). Hepzyme is an enzyme that cleaves heparin molecules and is able to remove up to 2 IU/mL of heparin in a sample. The heparinase cup is coated with the same enzyme at a concentration that can reverse up to 6 IU/mL of heparin per sample. The TEG was performed using 20 μL of 0.2 M calcium chloride, 20 μL of protamine or saline, and 320 μL of kaolin-citrated whole blood. Saline was added to heparinase cups and the run using Hepzyme to keep the volumes consistent across all samples and to compensate for the addition of protamine solution. Figure 2 shows a representative sample of a patient on heparin therapy in whom this effect was shown.

The TEG tracing showed a 6.5% lysis (Figure 2, a) in the heparinase cup. It shows substantial hyperfibrinolysis, which can lead to possible treatment with antifibrinolytic agents. However, no lysis was seen with protamine or Hepzyme trials (Figure 2, b and c). Similar results were observed in multiple heparinized samples in which substantial hyperfibrinolysis was seen with the use of heparinase cups and not in the plain cups with protamine or Hepzyme.

Therefore, we conclude that the hyperfibrinolysis observed when using a heparinase cup is in fact an artifact. The reason for the artifact hyperfibrinolysis seen with only the heparinase cup is unknown.

To be noted, the patient shown in Figure 2 was on an ECMO at the time of the TEG assay and had a heparin level of 0.66 IU/mL.

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