Heparinase-guided thrombelastography in an anticoagulated parturient

D. C. ABRAMSON, E. I. ABOULEISH, E. G. PIVALIZZA, S. L. LUEHR, T. MYERS AND M. D. PHILLIPS

Summary
We describe the use of heparinase-guided thrombelastography in the assessment of a parturient who had been anticoagulated with heparin for suspected thromboembolic disease. Reversal of the heparin effect in the heparinase-treated sample facilitated administration of protamine and successful subarachnoid analgesia for delivery. (Br. J. Anaesth. 1996;77:556–558)

Key words

Case report
A 35-yr-old gravid 1 para 0 presented at 29 weeks’ gestation with right upper extremity weakness, scintillating scotomata of her right visual fields and drooping of her left facial muscles. She had a significant smoking history and family history of paternal cerebrovascular accident (CVA) at 27 yr of age, followed by three further CVAs and death from myocardial infarction at 46 yr. Her sister, 32 yr, had recently had a CVA with documentation of an abnormal mitral valve.

Magnetic resonance imaging (MRI) revealed an ischaemic injury in the distribution of the right middle cerebral artery without evidence of cortical venous or sinus thrombosis. Prothrombin time (PT) was 12.4 s (normal 10.5–13.1 s) and accelerated partial thromboplastin time (aPTT) was 29.9 s (normal 25–34 s). Heparin 1500 u. h⁻¹ s.c. was started i.v. and her aPTT was 70 s before transfer to our hospital.

On admission, the fetus was active and the patient was not in labour. History and examination were otherwise unremarkable. Transoesophageal echocardiography (TEE), performed to elucidate a possible thromboembolic source, demonstrated an 8-mm mobile mass on both mitral valve leaflets. Magnetic resonance angiography (MRA) revealed right middle cerebral artery occlusion suggestive of embolic origin.

Carotid arteriogram, 24-h Holter monitoring and lower extremity Doppler examination for venous thrombosis were negative. Serial blood cultures were negative for infection, as were tests for connective tissue disorders and homocysteinuria. Although protein C concentrations were normal, functional protein S was reduced at <10% (normal 65–140%), but total and free protein S fractions were normal.

The test for functional protein S was repeated and a more appropriate result of 116% was obtained. Activated protein C resistance testing was negative. Serum cholesterol concentration was marginally increased and triglycerides were twice normal. Haematological variables, including antithrombin III and D-dimers, were normal.

As the patient had no biochemically definable coagulopathy present, a presumptive diagnosis of familial valvulopathy was made. Heparin was infused i.v. for 5 days to maintain an aPTT of 50–80 s, followed by heparin 2000 u. h⁻¹ s.c. which was continued for the duration of her confinement.

The patient was readmitted 3 months later, at 39 weeks’ gestation, for planned induction of labour. Repeat echocardiography revealed no masses on her mitral valve. Her aPTT on admission was >100 s. Heparin was discontinued 8 h before the intended placement of an extradural catheter for analgesia during labour. Nine hours later prothrombin time (PT) was 13.0 s (normal 11.1–13.1 s), packed cell volume 33.6% and platelet count 154 000 ml⁻¹ (normal 133 000–333 000 ml⁻¹). However, aPTT was prolonged at 84.5 s (normal 25–34 s). Thrombelastography (TEG) with native blood (fig. 1A) confirmed a heparin-like effect, evidenced as a prolonged r (reaction) time, prolonged k time and decreased angle (suggesting poor clot formation), and a narrow maximum amplitude (MA), implying poor platelet function. Simultaneously, a TEG was performed on a heparinase-treated sample (fig. 1B), which revealed a normal trace.

The demonstrated heparin effect was then reversed in vivo with protamine 50 mg, given slowly i.v. The repeat TEG trace after protamine was normal (fig. 2), although the aPTT remained prolonged at 46.1 s.

As labour had begun with the fetus in the occipito-posterior position and considerable maternal discomfort, regional anaesthesia was considered desirable. With TEG evidence of adequate coagulation,
sufentanil 10 μg and bupivacaine 2.5 mg were given into the subarachnoid space via a 27-gauge Whitacre needle by an experienced operator (E. A.) at the first attempt. Analgesia was effective, labour progressed rapidly, and a healthy 3.8-kg female was delivered with low forceps 1 h after intrathecal drug administration.

Post-partum TEG (1 h after delivery) showed no evidence of coagulopathy, heparin therapy was recommenced, and mother and child were discharged 3 days later with planned haematology follow-up for management of maternal warfarin.

Discussion

This report describes several issues in the preoperative haematological management and assessment of obstetric patients for regional anaesthesia.

Heparin is the currently favoured agent for anticoagulation in the parturient. This patient with suspected thromboembolic disease required substantial doses (2000 u. h⁻¹ s.c.) for optimal effect, as measured by aPTT. Although a lower dose of unfractionated s.c. heparin has a half-life of 3–4 h, the anticoagulant response of heparin increases disproportionally at increased doses. In our patient, a minimum of 8 h was anticipated to allow for waning of the anticoagulant effect before proposed extradural catheter insertion. However, 9 h after discontinuation, the prolonged aPTT suggested a heparin effect. Monitoring of the clinical heparin effect using the activated clotting time may be unreliable (in the presence of low heparin doses), and not representative of in vivo activity with plasma heparin concentrations. As heparinase-guided thrombelastography has been introduced into cardiac surgery and orthotopic liver transplantation, we used this method to assist clinical decision making in this patient.

Thrombelastography is enjoying widespread use in obstetrics. While value ranges for healthy parturients have not corresponded, they have all tended towards hypercoagulability compared with healthy non-pregnant patients. Investigation continues into TEG changes during preeclampsia and the HELLP syndrome, and the TEG is useful in the algorithm for the thromboticopentatic patient requiring assessment for extradural analgesia. The availability of heparinase, isolated from Flavobacterium heparinum, further extends the usefulness of this test, as the enzyme degrades heparin and heparin-like linkages even in the presence of the large doses of heparin required for cardiopulmonary bypass.

The native TEG trace in this patient showed marked prolongation of the r and k times and a narrow angle and MA, compatible with a heparin effect. Addition of heparinase to the sample restored the trace to that of the typical parturient. With this evidence of a heparin effect, systemic administration of protamine to the patient was followed by return to normal of the native trace.

Although safe neuraxial access has been described in anticoagulated patients, correction of the anticoagulation in this patient (in the presence of normal platelet number and function) significantly improved the risk–benefit ratio of regional analgesia. As labour was progressing adequately, it was felt that single-shot spinal analgesia would provide the necessary analgesia for completion of the second stage of labour without the risk of an indwelling extradural catheter. The addition of bupivacaine 2.5 mg to sufentanil 10 μg prolongs subarachnoid analgesia.

The normal TEG trace obtained with native blood represents a heparin effect. Monitoring of the clinical heparin effect using the activated clotting time may be unreliable (in the presence of low heparin doses), and not representative of in vivo activity with plasma heparin concentrations. As heparinase-guided thrombelastography has been introduced into cardiac surgery and orthotopic liver transplantation, we used this method to assist clinical decision making in this patient.

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