Reviewer's report

Title: Thromboelastographic Evaluation of the Effects of Recombinant Factor VIIa on Dilutional Coagulopathy

Version: 1 Date: 18 October 2004

Reviewer: Andreas Hillarp

Reviewer's report:

General

There have been conflicting results whether haemodilution produce a hyper- or hypocoagulable state or not. The mechanisms for the conflicting results of diluted blood on various coagulation parameters are not understood but methodological problems are likely to be involved. An important tool to study the dynamics of whole blood clotting is thromboeleastography and haemodilution usually results in changes suggestive of impaired coagulation with this type of analysis.

In the paper by Engstrom et al., the authors have used rotational thromboelastography (ROTEG) to study haemodilution and the effect of recombinant factor VIIa (rFVIIa). Haemodilution was performed ex vivo by mixing two parts of blood from healthy volunteers with one part hydroxy ethyl starch. In order to monitor the effect of rFVIIa, 6 µg rFVIIa was added to some of the diluted samples before analysis. A lowered Hb and increase of INR were seen as a result of dilution. The ROTEG analysis was performed with activating reagents (INTEG and EXTEG) as recommended by the manufacturer of the system. The parameters obtained were clotting time, clot formation time and the strength of the clot after 15 minutes after addition of reagent. With the contact activator (INTEG), haemodilution resulted in impaired clot formation time and clot strength. Addition of rFVIIa had no effect on the impaired parameters. Diluted samples that were activated with tissue factor reagent (EXTEG) also resulted in impaired clot formation time and clot strength compared to undiluted blood. However, addition of rFVIIa resulted in a further impairment of these parameters. The authors conclude that the observed effect of rFVIIa on the ROTEG parameters may be related to methodological problems and not to be a true impairment of coagulation. Thus, it is likely that the commercially available EXTEG reagent is inappropriate for monitoring rFVIIa in situations of dilution.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1. Page 3, 5th line from bottom: In the text it says that “build-up and lysis of a clot” is shown in figure 1. Figure 1 does not show the lysis stage.
2. Page 3, third line from bottom: It looks like a reference number should replace the word “ref” within the brackets.
3. Page 7, second paragraph: The authors discuss dysfunctional fibrinogen as one possible explanation for the unexpected finding of further impairment of the EXTEG parameters after addition of rFVIIa. This is difficult to understand as the INTEG parameters are unaffected by rFVIIa.
4. Page 8, first paragraph: The authors make the interesting, and probably important, observation that the tissue factor concentration is relevant for the outcome of the ROTEG analysis. It would have been interesting to see if the effect of rFVIIa will be differently traced after activation with diluted...
EXTEG reagent. Do the authors have data from titrations of EXTEG reagent?
5. Page 8, second paragraph: The discussion of TFPI generation in the test tube is difficult to understand. How can rFVIIa lead to generation of TFPI in the test tube?
6. Table 1: PT should replace “PK” in the third row.
7. Figure 1: In order to make figure 1 easier to understand it would be better if the scales are indicated in the figure.

Discretionary Revisions (which the author can choose to ignore)

What next?: Accept after minor essential revisions

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:

None