Effects of a new modified balanced hydroxyethyl starch preparation (Hextend) on measures of coagulation

Editor—We read with interest the study by Boldt and colleagues. This was an important report, addressing some interesting issues especially relating to the electrolyte content of i.v. fluids, as well as the type and formulation of hydroxyethyl starch (HES). Recent work has shown that the modern, medium to low molecular weight HES compounds with lower substitution ratios, are associated with fewer side-effects than those previously reported with the older highly substituted high molecular weight HES products, such as the incidence of HES retention, bleeding diatheses and coagulopathies.

On the other hand, a growing body of evidence points to the benefit of using buffered, balanced electrolyte formulations rather than saline-based preparations for fluid therapy, and especially volume resuscitation. This is seen both with crystalloids and colloids. It has been suggested that improved renal, gastrointestinal and bleeding variables are associated with balanced electrolyte fluid therapy.

What makes the Boldt study particularly interesting is that a medium molecular weight tetra starch in a saline-based formulation (130/0.4, Voluven<sup>®</sup>, Fresenius-Kabi) is compared with Ringer’s lactate solution (crystalloid), and a high molecular weight hetastarch in a balanced electrolyte solution (Hextend<sup>®</sup>, Abbott Laboratories). The results indicate that the balanced salt hetastarch is associated with increased bleeding, deranged coagulation variables, and the use of more blood and blood products.

We have performed in vitro and in vivo studies, examining various aspects of crystalloid and colloid fluid therapy, as well as the role of electrolyte content. We would like to ask the authors to address a few questions to assist us with the interpretation of these data.

(i) Citrated blood
Camezind and colleagues have reported the use of citrated blood in thrombelastography. They found a significant change in the TEG<sup>®</sup> variables over time from sampling. We have also performed a study, examining the use of fresh whole vs citrated blood on TEG<sup>®</sup> variables with haemodilution. Our results indicated that citrated blood was inadequate for such a study. We would like to enquire what the rationale was to use citrated blood, especially as the time from sampling to TEG<sup>®</sup> measurement was so short (10 min). Are there data-validating ROTEG<sup>®</sup> (Pentapharm, GmBH) measurements made on citrated blood after this very short period of storage?

(ii) ROTEG
What type of validation work has been performed on the ROTEG<sup>®</sup> for this type of study, as this instrument functions in a different manner from the existing TEG<sup>®</sup> (Haemoscope Corp)?

(iii) Small numbers
Because of the numbers in the study (n=21 per group), would the authors comment if any outliers were apparent in these data, and report the median and range of the bleeding and blood transfusion data? What was the power of the study to detect any differences in estimated blood loss reliably?

(iv) Surgical vs non-surgical bleeding
This is a notoriously difficult issue. Were there any problems with intraoperative surgical bleeding, as most of the blood loss difference between groups seemingly occurred intra-operatively? For example, we have in previous studies tried to equate clinically significant surgical bleeding with non-surgical bleeding suggesting a coagulopathy that requires treatment with blood and blood products. No details are given as to the technique of measurement of blood loss. As this is also notoriously difficult and inaccurate we would be interested to know how blood loss was estimated in this study. The authors also comment that there was no significant correlation between blood loss and ROTEG<sup>®</sup> measurements, but no details of the regression analysis are provided. How then do they explain the finding of increased blood loss and impaired ROTEG<sup>®</sup> measures in the balanced salt hetastarch group, if the two were not related?

(v) Blinding
What steps were taken to blind the intraoperative part of the study? We have found this to be a challenge as the study fluids are often different colours, as is the case here.

(vi) Inotropic support
The authors refer to the use of epinephrine if the MAP was <50 mm Hg, with adequate volume status. They then continue by describing the use of norepinephrine if volume therapy and dopamine did not keep the MAP >50 mm Hg. Which inotrope was used first, dopamine or epinephrine? This may be of relevance, given the effects of catecholamines on the initiation of the coagulation process.

This was clearly an important study, addressing a relevant clinical question. We would find the authors’ response of value in assisting us to power and plan future studies at our institutions.

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