ORIGINAL ARTICLE

Does calcium cause the different effects of Gelofusine and Haemaccel on coagulation?

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Emerg Med J 2006;23:193–194. doi: 10.1136/emj.2005.024034

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Accepted for publication
11 July 2005

Background: Gelofusine (which does not contain calcium) has a greater effect on coagulation than Haemaccel (which contains 6.25 mmol/l of calcium). This in vitro study was performed to assess whether calcium might be the cause of the different effects on coagulation.

Methods: Three solutions were compared; (a) Gelofusine, (b) Gelofusine with calcium added to 6.25 mmol/l, and (c) Haemaccel. Thromboelastography (Sonoclot) was used to examine whole blood coagulation, with time to peak clot weight as the primary outcome measure.

Results: There was no significant difference between the Gelofusine containing solutions. Both Gelofusine solutions gave a greater impairment of coagulation than the Haemaccel solution.

Conclusions: The different effect of Gelofusine on coagulation compared with Haemaccel does not seem to be related to the different calcium contents of the solutions.

There is little uniformity in the methods that have been used to study the effects of various resuscitation fluids on coagulation. A variety of fluids has been used, at many different dilutions. In addition, several measures of coagulation have been used, which adds to the difficulty in interpretation of results. Crystalloids have usually been reported to enhance coagulation^{1–4} or have no effect,⁵ whereas colloids have been variously reported to impair coagulation,^{4–11} to give a weak impairment of coagulation,^{12–13} to have no effect,^{14–17} or to enhance coagulation.^{18–19}

Gelofusine and Haemaccel have different effects on whole blood coagulation despite being similar types of resuscitation fluid. Gelofusine has a profound anticoagulant effect, which affects the “cellular” phase of clot formation and so is not seen on the conventional coagulation screen (international normalised ratio (INR); activated partial thromboplastin time (APTT)) as these tests examine the “plasma” phase.²⁰ In contrast, Haemaccel has a weaker effect on coagulation. Both of these colloids are derived from bovine collagen, and are similar molecules; however, one marked difference is that Haemaccel contains 6.25 mmol/l of calcium, whereas Gelofusine contains none. There is some evidence that this might cause the different effects on coagulation as calcium is central to blood clotting.²¹ This study was performed to evaluate whether the difference in calcium content between Gelofusine and Haemaccel contributes to the difference in effect on coagulation.

METHODS

Ethics review board approval was obtained. The study was powered to be 80% sure of finding a 200 second difference in the time taken to form maximum clot weight. In vitro analysis of blood from 13 healthy volunteers was performed. Three aliquots of freshly drawn blood from a free flowing cannula were taken from each volunteer. Each sample was diluted to 40% with either Haemaccel, Gelofusine, or Gelofusine to which calcium chloride had been added to give a 6.25 mmol/l solution.

A Sonoclot profile (thromboelastogram) was measured for each sample. The Sonoclot is one of several techniques available for thromboelastography, and none has been shown to be superior. All involve the measurement of the resistance

to vibration of a probe in a sample of coagulating blood. Resistance to vibration increases as clot forms and then decreases as fibrinolysis takes place.²² The endpoint for the study was the time taken to reach peak resistance to probe vibration (time to peak). Three Sonoclot machines were used in the study, with sample order being rotated to minimise any machine bias.

Statistical analysis

Analysis was carried out using the MedCalc software package (www.medcalc.be). Normality of data distribution was assessed using the Kolmogorov-Smirnov test, and the data presented as mean and 95% confidence intervals (CI) for each type of fluid.

RESULTS

As shown in fig 1, all dilutions significantly prolonged the time to peak clot weight (95% CI did not cross zero). The two Gelofusine groups were not significantly different (95% CI overlapped), but there was a trend to less disturbance of coagulation when calcium was added. Both Gelofusine groups had a significantly longer time to peak than the Haemaccel group.

DISCUSSION

These results suggest that the different effects of Haemaccel and Gelofusine on coagulation are not due to the different calcium concentrations. Gelofusine seems to impair coagulation even if calcium is added. The exact mechanism by which Gelofusine interferes with coagulation is unknown; however, in a previous study, electron microscopy of the clot formed seemed to show less cross linking of fibrin strands.⁸ As collagen has a profound effect on the coagulation system, it is not surprising that collagen derived colloid solutions have an effect on blood clotting.

An effect of collagen based colloids on blood clotting is not noticed in clinical practice; however, the conventional “coagulation screen” only measures a small part of the complex process of forming a clot. The endpoint of these tests

Abbreviations: APTT, activated partial thromboplastin time; INR, international normalised ratio

Figure 1 The effect of three test solutions on time to peak clot weight.

(such as INR and APTT) is the beginning of thrombin formation. At least 96% of thrombin formation and the whole of the cellular phase occurs after the end of these coagulation tests,²³ so false reassurance can be given by “normal” results if the impairment of coagulation occurs later in the process of clot formation. Whole blood coagulation testing by thromboelastography examines all parts of the process.

It is likely that the different effects on coagulation of Gelofusine and Haemaccel are caused by a characteristic that interferes with clot maturation. Factors that warrant further investigation are the difference in electrical charge on the molecule (Gelofusine is highly negatively charged and platelet wall interactions are dependent on negative charge) and the way that the molecular shape of the resuscitation fluid physically interacts with, and is incorporated into, the developing clot.

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Competing interests: none declared

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