

# Correcting Dilutional Coagulopathy in Haemophilia



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## ■ Introduction

During the management of severe intra-operative bleeding plasma expanders are used to maintain circulating volume. This can induce a dilutional coagulopathy, resulting in the formation of weak, unstable clots.

Patients with severe haemophilia A are undergoing surgery more frequently, exposing them to the risk of intra-operative bleeds and dilutional coagulopathy.

Standard treatment is with FVIII replacement to 100% normal levels. Once haemodiluted it is unclear if this treatment is sufficient to normalise clot formation and stability compared to individuals without haemophilia who undergo a similar degree of haemodilution.

The aims of this study were to examine the impact of 50% dilution on clot stability in haemophilia plasma (HP) versus normal plasma and examine the effect of adding FVIII to diluted HP.

## ■ Hypotheses

- 1) Haemodilution causes impairment in clot stability in control plasma and to a greater extent in HP
- 2) Addition of FVIII to HP fails to normalise clot stability

## ■ Method

Commercially available plasma (FVIII deficient plasma, Factor deficient plasma spiked with FVIII (1IU/ml) and normal control, Technoclone) were undiluted, diluted 50:50 with Gelofusin or 0.9% NaCl.

Clotting was triggered with tissue factor 1:40,000 plus calcium and turbidity recorded (FLUOstar Omega). The endpoint reported is clotting time (CT).

To examine clot stability tissue plasminogen activator (*t-PA* 0.75nM) was added simultaneously. Area under the turbidity curve was recorded as a measure of clot stability.

## ■ Results

Dilution with both Gelofusin and NaCl caused significant decrease in clot stability in control and HP from baseline (Mann-Whitney  $p < 0.05$ ) (Figure 1).

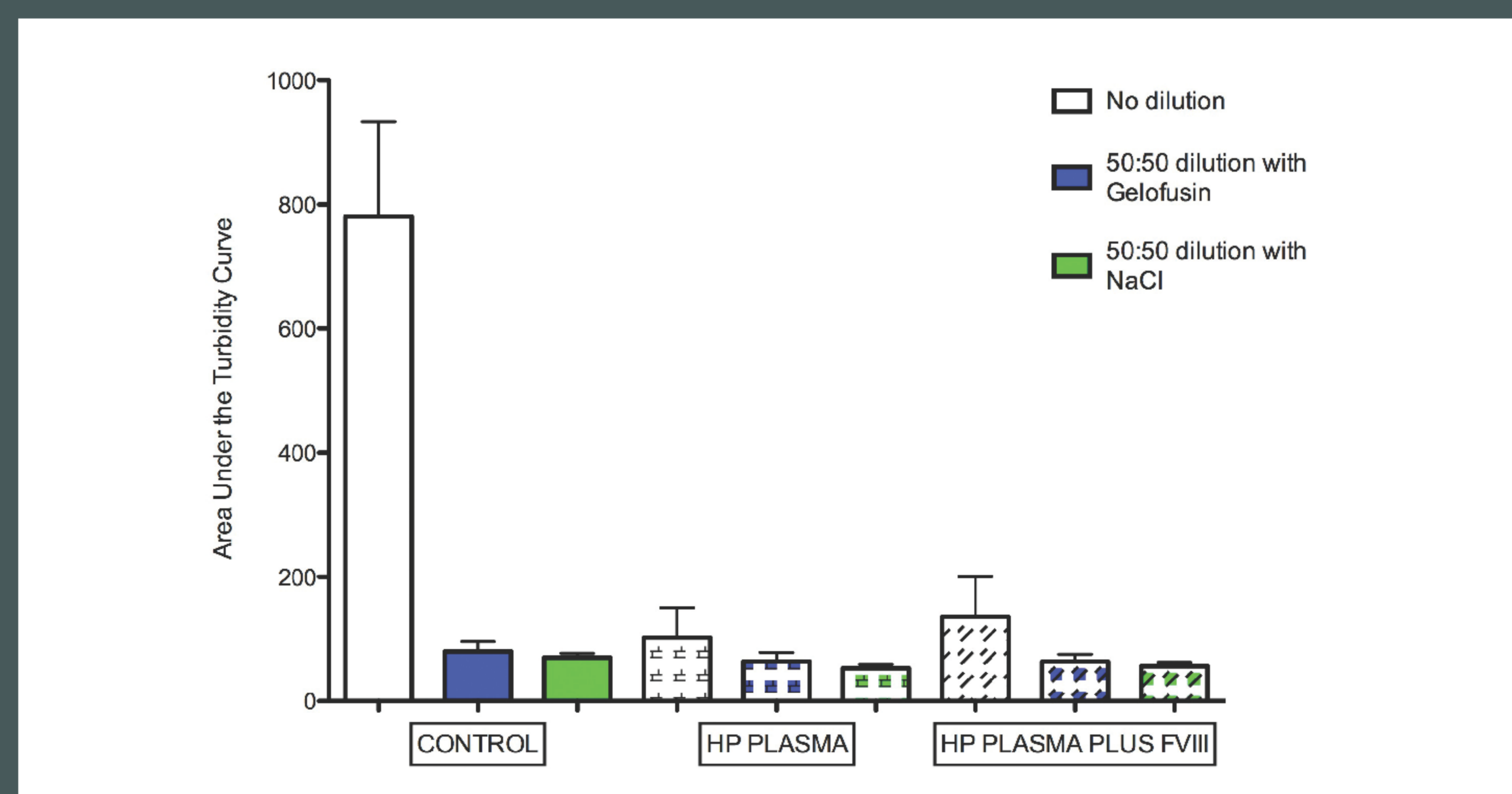
The effect of Gelofusin on clot stability did not differ between the control and haemophilia group. However, diluting with NaCl caused a greater impairment in clot stability in the HP (Mean AUC HP:55, C:69,  $p < 0.001$ ).

Addition of FVIII to HP failed to normalise clot stability compared to undiluted control plasma and plasma diluted 50:50 with NaCl (Figure 1).

## ■ Conclusions

In this pilot study, FVIII failed to correct clot stability in diluted HP compared to the normal control, suggesting that when haemophilia patients undergo major surgery, FVIII alone is insufficient and haemodilution itself should additionally be monitored for and treated.

■ Figure 1: AUC Turbidity



The figure demonstrates the effect on clot stability (AUC) of haemodilution on normal plasma, FVIII deficient plasma and FVIII deficient plasma with FVIII replacement.



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