

Artificial normocoagulant colloid solutions (ANCS): A solution for plasma free management of severe perioperative bleeding?

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Background and Goal of Study

Volume therapy by cristalloid or colloid solutions is responsible for dilutional coagulopathy in severe perioperative bleeding. This often leads to plasma transfusion as volume therapy in simultaneously hypovolemic and coagulopathic patients to avoid further deterioration of clot formation. Fresh frozen plasma based therapy of Rotem detected factor deficits is still a widely used strategy. However plasma free management might be superior as suggested by recent prospective clinical studies^{1,2}. We would like to present a plasma free colloid solution based on human albumin enriched with coagulation factor concentrates (CFC) which shows physical clot formation properties comparable to whole blood when combined with washed platelets.

Materials and Methods

- Stem solution (SS): Human albumin 5% (Grifols, Spain) in Viaflo Plasmalyte® 148 (Baxter, Spain), enriched with Ca++ gluconate (0,9 mmol/l) was titrated with TRIS buffer 2M to pH 7,3 -7,4 and heated to 37°C.
- Starting from this SS we created an enriched SS by adding:
 - Fibrinogen concentrate (FC) to get a final concentration of 4g/L
 - Protrombin Complex Concentrate (PCC) to get a final concentration of 1IU/ml
 - FXIII was added to reach a final concentration of 1IU/ml
- In a final step this plasma free procoagulant colloid solution was further enriched with washed platelets from a healthy donor to a final concentration of 200 x 10³/µl.
- This platelet and coagulation factor enriched solution was analyzed for viscoelastic properties with the EXTEM S and FIBTEM S subtests on a ROTEM® delta machine.

Results and Discussion

Our plasma free colloid solution showed the following values in Rotem key parameters:

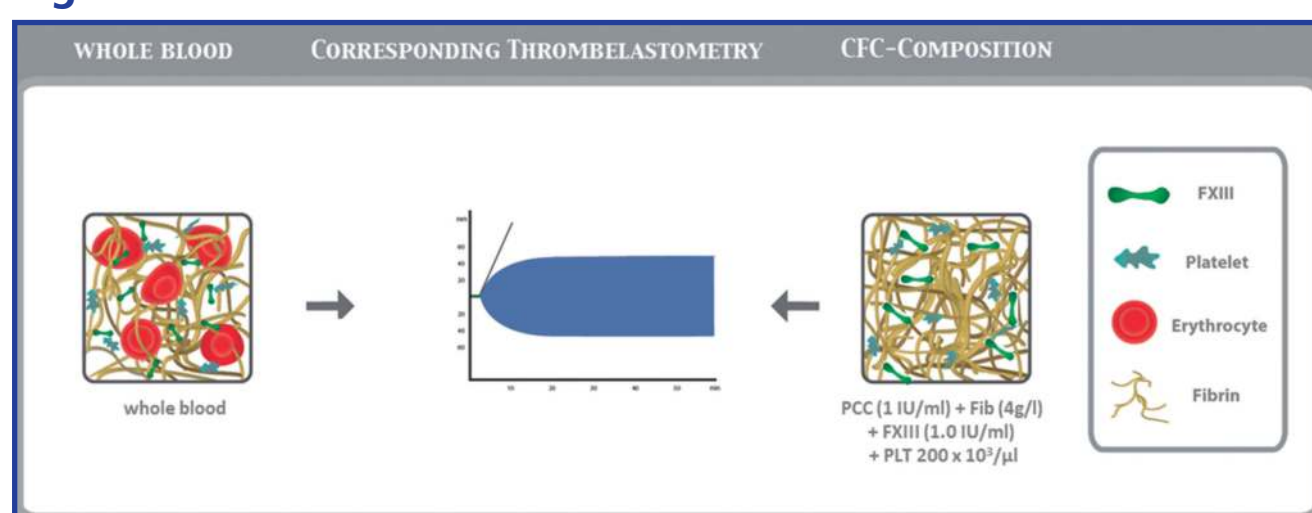
Extem:

	ANCS mean (SD), n=5	normal range whole blood
CT (sec)	73 (7,9)	38 - 79
A 10 (mm)	44 (3,1)	43 - 65
MCF (mm)	58 (3,2)	50 - 72

Fibtem:

	ANCS mean (SD), n=5	normal range whole blood
CT (sec)	74 (4,1)	na
A 10 (mm)	17 (1,3)	7 - 23
MCF (mm)	19 (2,2)	9 - 25

Figure 1:

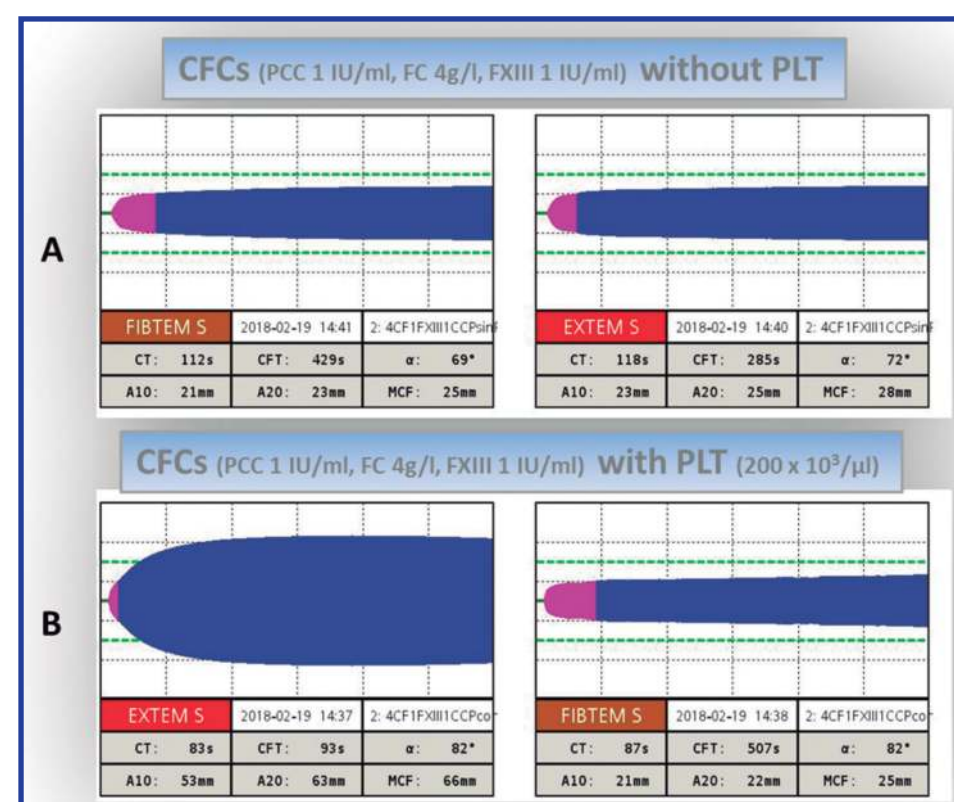


Restoring normal whole blood thrombelastometry parameters with CFC combination in an albumin based colloid fluid under presence of platelets.

Conclusions

The tested ANCS showed normal values for all ROTEM key parameters when combined with platelets. These kind of solutions might be an alternative to plasma or single Rotem based factor replacement especially in clinically "stressful" situations of massive bleeding. Further analysis is necessary to study the procoagulant qualities of ANCS.

Figure 2:



Original Rotem-graphs:

- A: CFC combination of 1IU/ml PCC, 4 g FC, 1 IU FXIII without platelets. Normal clot strength is achieved when compared to plasma.
- B: When adding platelets to the upper CFC combination normal values are achieved for all relevant ROTEM parameters when compared to whole blood.

References:

1. Innerhofer et al., P., (2017). Reversal of trauma-induced coagulopathy using first-line coagulation factor concentrates or fresh frozen plasma (RETIC): A single-centre, parallel-group, open-label, randomised trial. *The Lancet Haematology*, 3026(17), 1–14.
2. Ranucci, M., Baryshnikova, E., & Hemmings, H. C. (2016). Fibrinogen supplementation after cardiac surgery: Insights from the Zero-Plasma trial (ZEPLAST). *British Journal of Anaesthesia*, 116(5), 618–623.

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