Reviewer's report

Title: Citrate prevents heparin induced complement activation and neutrophil degranulation, when used for anticoagulation during continuous venovenous haemofiltration in critically ill patients.

Version: 2 Date: 17 August 2013

Reviewer: Heleen M Oudemans-van Straaten

Reviewer's report:

The authors have addressed most of the comments. However, in the revised version raises some new issues.

1. The new title “Citrate prevents heparin induced complement activation and neutrophil degranulation, when used for anticoagulation during continuous venovenous haemofiltration in critically ill patients” is not precise. The same concerns the conclusion “Regional citrate anticoagulation prevents potentially harmful complement activation and neutrophil degranulation in the filter induced by heparin, during CVVH in the critically ill”

The study does not show that citrate prevents heparin-induced complement activation because citrate and heparin were not used together. I would suggest use of citrate anticoagulation for CRRT confers less complement activation and neutrophil degranulation than heparin or something alike.

2. “The sieving coefficient was low and lower in group 3 than the other groups (no anticoagulation 0.49 (0.05-9.45), heparin 0.35 (0.12-11.2), citrate 0.10 (0.02-0.62), P<0.001) nd decreased in time in all groups (P<0.001).”

The difference in sieving coefficient between groups is remarkable because the same filter was used. A lower sieving coefficient could be due to more clogging, but this is likely not the case with citrate. The higher sieving coefficient might also indicate higher production at the filter membrane and subsequent direct removal by filtration. To my opinion this is the most likely explanation. Could the authors please comment on this?

The sentence in the discussion referring to this result: “Due to higher ultrafiltration flows, concentrations of C5a in the ultrafiltrate were lowest in the citrate group, as was the sieving coefficient,” should be adjusted.

The lower C5a concentrations in the ultrafiltrate of the citrate group can have several causes: 1. less production at the membrane (most likely), 2. dilution due to higher UF flows (marginal difference), 3. lower permeability of the membrane due to more clogging (very unlikely).
3. The suggestion of the first reviewer to replace the annotations of group numbers into group names is not consequently performed. Please adjust.

4. Please add "in" before "study" in the following sentence of the discussion: “The time course of the release of elastase and MPO seems to be dissimilar our study” (page 10)

5. Please adjust the conclusions of abstract and main text (see 1.)

**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I have no competing interests.