Author's response to reviews

**Title:** Administration of fibrinogen concentrate for refractory bleeding in massively transfused, non-trauma patients with coagulopathy A retrospective study with comparator group

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**Version:** 6  
**Date:** 27 August 2014

**Author's response to reviews:** see over
Seville, August 28, 2014.

Dear Sir,

Please, find enclosed our revised version of the manuscript entitled “Administration of fibrinogen concentrate for refractory bleeding in massively transfused, non-trauma patients with coagulopathy” which we would like to be considered for publication in BMC Anesthesiology.

According with your recommendations, we have performed the following changes:

1. Point by point response to the most recent comments of the referees. Please, see below

2. We have included the full name of the committee that approved your study in this statement.

Please, let me know if any additional information is needed

We appreciate the opportunity for our manuscript to be peer-reviewed and look forward to your decision at your earlier convenience.

Sincerely,

S. R. Leal-Noval, MD, PhD

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**Point by point response to the most recent comments of the referees**

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Prepublication History

Reviewer's report
Title: Administration of fibrinogen concentrate for refractory bleeding in massively transfused, non-trauma patients with coagulopathy A retrospective study with comparator group
Version:4

**Reviewer number:1**
Referee's comments to the author(s)
Do not comment in this section on the interest/importance level of the manuscript, or whether or not the manuscript should be accepted.
Revision is appropriate

Answer:

No an additional response is needed

Reviewer's report
Title: Administration of fibrinogen concentrate for refractory bleeding in massively transfused, non-trauma patients with coagulopathy A retrospective study with comparator group
Version: 4

Reviewer number: 2
Referee's comments to the author(s)
Do not comment in this section on the interest/importance level of the manuscript, or whether or not the manuscript should be accepted.

All reviewer's comments have been addressed satisfactorily.

Answer:

No an additional response is needed

Reviewer's report
Title: Administration of fibrinogen concentrate for refractory bleeding in massively transfused, non-trauma patients with coagulopathy A retrospective study with comparator group
Version: 4

Reviewer number: 3
Referee's comments to the author(s)
Do not comment in this section on the interest/importance level of the manuscript, or whether or not the manuscript should be accepted.

Some improvements have definitely been made to the manuscript. Still the main issue - namely a somewhat more hypothesis specific methodology and data analysis - is still pronounced. This may improve the general interest of your work. The downsides of retrospective observational design are (as always) obvious. The number of statistical analyses you perform does not compensate for this fact.

The revised hypothesis stated in the manuscript is still relatively clear, but in my opinion the message is lost in a number of sidetrack analyses, that does not add any important information.

Answer
The downsides relative to the retrospective design of this manuscript are inherent to all observational studies, and they are clearly acknowledged into the limitation section.

On the other hand, the adjusted analyses clearly establishes that the late administration of low dosage of fibrinogen concentrate (25 mg/kg) to massively transfused bleeding patients with coagulopathy, neither decreases blood transfusion requirements nor increases plasmatic fibrinogen level to an optimal level of 2 g/l.

Given that many centers worldwide prescribe fibrinogen concentrate as an adjuvant therapy to bleeding patients who have already been massively transfused, the results of this paper suggest that both earlier administration and higher doses could improve fibrinogen concentrate effectiveness. The authors do believe that this is new and important information.