Reviewer’s report

Title: Protocol for a systematic review of the impact of resuscitation fluids on the microcirculation after haemorrhagic shock in animal models

Version: 0 Date: 24 Jul 2015

Reviewer: Kim Wever

Reviewer’s report:

A well prepared protocol for a preclinical review on an interesting topic. I have some minor concerns/remarks:

- You plan to include and analyze studies that compare different types of fluid resuscitation (rather than fluid versus haemorrhage only). I wonder if this analysis currently falls within your current research question. The first research question will be answered by the summary of overall analyses for each outcome measure. The second research question can be tested by comparing subgroups of different fluids (all with "haemorrhage only" controls). But it seems that the analysis described under "other meta-analysis details" is trying to answer a question such as "compared to crystalloid, which is better, PRBC or colloid?". It may fall within the second research question, but it is not entirely clear to me. I suggest rephrasing or adding a third question.

- add "in animal models" or "preclinical evidence for" to the title to signify that this is a preclinical review

- in line 1 of methods: SYRCLE (no S at the end)

- in research questions: add "in animal models" or "preclinical evidence for" to signify that this is a preclinical review. This also specifies the population (along the lines of PICO).

- if you plan to include all types of publication types, how are you going to handle abstracts and letters to the editor, from which essential methodological detail is likely to be missing?

- will you include animals with co-morbidities? I also noticed that you plan to include knock-out animals, but do you think these can be readily pooled with wild type animals?

- is it necessary to restrict the search to 1975? This seems a bit arbitrary.

- could you specify for which outcome measures you expect to use the mean difference / SMD? Also, I would suggest using the normalised mean difference, rather than the SMD, if possible (see the paper on MA methodology by Vesterinen et al.). The SMD often gives rise to skewed funnel plots, making an assessment of publication bias impossible.
the term clinical heterogeneity pops up in the article, but I guess pre-clinical may be more suitable here.

when performing multiple subgroup analyses using the same data, it is necessary to correct the P-value. I suggest adding how you plan to do this under subgroup analysis.

will you be assessing the impact of any study quality items on the reported treatment efficacy?

The last lines of the paragraph on other meta-analysis details are unclear to me. I guess that if the same control group is used to multiple experimental groups, the number of control animals could be corrected and the data could be used. Unless you are worried about "same study bias" resulting from including lots of comparisons from a particular study and only single comparisons from the other studies. In this respect, I also am not sure how to interpret the last line of this paragraph. Could you please clarify?

I believe the statistical approach of most tests for funnel plot asymmetry (including peter's test) assume that the data have a normal distribution. However, 10 studies may be too few to ascertain this. Also, for funnel plots of animal data, many tests are hampered by the small variation in precision (i.e. group sizes in animal models are generally very similar), and the use of the SMD. I would suggest not performing an analysis for publication bias with fewer than 20 studies.

Sincerely,

Kim Wever

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An article of importance in its field

Quality of written English
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