Author's response to reviews

Title: Should colloid boluses be prioritized over crystalloid boluses for the management of dengue shock syndrome in the presence of ascites and pleural effusions?

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Version: 3 Date: 23 November 2010

Author's response to reviews: see over
The editor,

BMC Infectious Diseases

Dear Sir,

I have addressed all the comments raised by reviewers and highlighted in the text. In addition, I have included some of my views below to some of the referees comments which I have not included in the text.

Many thanks

Yours Faithfully

Prof. Ranjan Premaratna
Corresponding author

Second revision: Paper entitled Crystalloid or colloid boluses for the management of dengue shock syndrome in the presence of ascites and pleural effusions? Premaratna R et al.

The title of the paper was changed to address some comments made by reviewer Po-Liang Lu to read as Should colloid boluses be prioritized over crystalloid boluses for the management of dengue shock syndrome in the presence of ascites and pleural effusions?

Reviewer: Siripen Kalayanarooj

Background – the author had used the references 3, 4 and 5 as the recommendation for IV fluid therapy in DSS patients. In fact reference 3 and 4 more or less the same recommendation but reference 5 recommend a larger amount of IV fluid which is dramatically different from the previous WHO guidelines.

Agreed. We have quoted the three references in appropriate areas of the text. We agree that reference 3 and 4 are more or less the same and the intravenous fluid recommendation in reference 5 is greater than the previous ones and needs to be studied carefully in the future.

Case 1 – The patient received 2.5 L of IV fluid before critical period. WHO guidelines do not recommend IV fluid during the febrile phase except only those who has moderate to severe dehydration and cannot have oral intake. This
patient had 1.5 L of oral intake so this patient’s treatment was not following the WHO guidelines.

This patient received iv fluids during the pre shock stage because she could not tolerate oral fluids and she had intermittent high fever, and intermittent vomiting during this period. Administration of iv fluids at this stage was purely on clinical grounds and / or based on Hb and PCV.

Also she developed profound shock: absence of peripheral pulse with increasing PCV from 42.3 to 55% (about 30% hemoconcentration) and no investigation and correction of possible abnormalities in metabolic (hypoglycemia); her sugars remained normal (included in the text), acid-base (acidosis) (blood gases could not be performed during acute DSS; this was included in the revised text) (hypocalcemia) so that she did not improve very well with only IV fluid and this may lead to more volume is needed for her. Although she did not have frank clinical bleeding, she might have concealed bleeding which is more common. (I agree that she may have developed concealed bleeding into the third space but this was not reflected in the haematological investigations)

We have re-revised the manuscript highlighting the fluids given with durations of boluses.

Case 2 – This woman also had profound shock on arrival to the hospital and no metabolic, acid-base and electrolyte investigation and correction were done so she needed more volume for resuscitation. (We agree that most of the investigations could not be done on the patient on admission, as she presented in a profound shock; furthermore, although the basic essential investigations were carried out, the results were only available after a considerable delay) The total volume of fluid resuscitation was 3,150 ml in 3 hrs, which was too much and this might cause acute pulmonary congestion and/or heart failure. This too much volume are not in the WHO recommendation. If the patient does not response to the 1-2 bolus of IV fluid, the clinician should investigate the laboratory abnormalities at least repeated the PCV and if it is dropping, blood transfusion is indicated. The treatment of this patient also not follow the WHO guidelines.

We have re-revised the manuscript highlighting the fluids given with durations of boluses.

Case 3 – The treatment of this patient seemed to be OK during initial resuscitation. But at 24 hour after shock, she developed profound shock and at this time enormous amount of Iv was given to resuscitate her, i.e. 3,250 ml in 3 hours! This is not the WHO recommendation. About 24 hours after the first shock, the plasma leakage is minimal and IV fluid should be tapered. If she developed shock, only small bolus is recommended and then stop quickly. Probably the shock at this stage might be due to volume overload and diuretic
might be indicated at this time? (There was no detail of her intake and output at this time to help differentiate the cause of shock at this time).

The manuscript has been revised highlighting the fluids given with durations of boluses.

Conclusion – the authors did not follow exactly the WHO (only reference 3 and 4) recommendation for IV fluid management so they cannot conclude that when they follow the WHO guidelines and the patients develop complications.

We hope our current revisions have addressed the referee’s comments.

Reviewer: Po-Liang Lu

Major Revisions

1. All three cases had both colloid and crystalloid fluid (different from the statement in the abstract, case presentation, the first line, …..received boluses of crystalloids), it is hard to suggest the pulmonary edema is due to crystalloid. Then it is hard to draw a conclusion about colloids rather than crystalloids would prevent development of recovery phase pulmonary oedema.

We agree. However what we wanted to highlight is that, these patients were managed according to the WHO guidelines; first with crystalloids and when the patients showed no sustained clinical response, they were treated with colloids. We do not conclude that colloids would be more beneficial than crystalloids. What we highlight with these cases is whether we should consider colloids over crystalloids in patients who develop severe DSS in the presence of significant third space fluid loss. We agree that this concept should be tested by a randomised controlled trial. (We have changed the title and the respective areas of the text in order to address this issue “Should Colloid boluses be prioritized over crystalloid boluses…..”)

2. The authors may consider the following article as a reference. Comparison of three fluid solutions for resuscitation in dengue shock syndrome. New England Journal of Medicine, 2005, 353:877–889. In the double blinded RCT, the clinical fluid overload percentages did not differ between cases using colloid and crystalloid fluid.

We agree with the referees comments, but would like to draw attention to the contents of the article.

In the randomization of the above study,
“No children in the group with severe shock received a crystalloid because of concerns about the potential development of critical fluid overload without access to advanced respiratory support. Children with shock of moderate severity (pulse pressure, >10 and ≤20 mm Hg) constituted group 1 and were randomly assigned to receive Ringer’s lactate, dextran, or starch.

Group 2 consisted of those with severe shock (pulse pressure, ≤10 mm Hg); these children were randomly assigned to receive either dextran or starch.”

Patients whose cardiovascular status did not improve after administration of the study fluid (i.e., those who had further narrowing or no response in pulse pressure, together with persisting or worsening peripheral shutdown, a rising hematocrit, or both) received infusions of 5 to 10 ml per kilogram of rescue colloid (usually dextran) at the discretion of the clinician. Similarly, if after an initial favorable response, the pulse pressure subsequently narrowed again to 20 mm Hg or less with peripheral vasoconstriction, a rising hematocrit, or both, rescue colloid could be given.

Furthermore, in this study there is no mention about the presence of third space fluid loss at the time of recruitment. They have analysed only the occurrence of them following resuscitation. Therefore, it is difficult to interpret which fluid would be beneficial in patients who already have third space fluid loss at the time of severe DSS.

3. Did the case 2 have evidence of pulmonary oedema? Could it be possible that she died of cardiovascular disease related with dengue shock syndrome.

When she was admitted, she had no pulmonary oedema. However she developed pulmonary oedema in addition to pleural effusions while she was resuscitated (I have added this in the text). It is possible that she had dengue related cardio-vascular disease as she had wide spread T wave inversions in the ECG. However, at the time of DSS, she had a good cardiac ejection fraction of 55%. Therefore, it may be that she died of severe respiratory distress/ fluid overload during recovery phase or as part of DSS itself.

Minor essential revisions
1. For abbreviations, please provide the full name when they appeared in the first time, such as CPAP. Done
2. May check the presentation of figures and units. For example, 26yrs to be 26 yrs. Done

Responses to Reviewer: Aysha Almas

2. In section of case presentation; case 1 presentation is satisfactory. In the
second case it should not astart with "the patient who died". remove the comment in bracket in line 5. Done

Also in the same para "he" has been used instead of she. Done

Remove " The serum calcium and cholesterol levels could not be carried out in this patient." Remove the above line also from the third case. In the third case mention the outcome of the patient (We have left this for the editors to decide as this was a requirement of one of the editors for the previous revision).

3. Is it conclusion or discussion? the third heading (check format) also second para should actually be the first one in this section. In the end of this para mention the concept you want to highlight about fluids. We have re-arranged the paragraphs as suggested and the concept was included as the last sentence in the same paragraph.