Reviewer's report

Title: Exploring mechanisms of excess mortality with early fluid resuscitation: insights from the FEAST trial

Version: 1 Date: 26 October 2012

Reviewer: Emanuel Rivers

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The authors make interesting and significant conjectures regarding the results of fluid therapy in this pediatric model of sepsis. They hypothesized that boluses may cause excess deaths from neurological or respiratory events relating to fluid overload. However, some major considerations should be made that were not previous addressed.

1. Early hemodynamic optimization is a comprehensive process that includes fluid therapy. When fluid therapy is examined in isolation outside of the theater of it recommendations, the interpretation becomes problematic. According to the ACCCM hemodynamic support is a strategy aimed at early hemodynamic optimization of oxygen delivery guided by preload (central venous pressure or surrogate, fluids), afterload (mean arterial pressure, vasopressors), arterial oxygen content (packed red blood cells, oxygen), and contractility (inotropes) if ScvO2 still low.1 This strategy has been shown to improve outcomes in other pediatric outcome trials.2 Why is this study different from previous pediatric studies?

2. The therapy in this study should be contrasted to ACCCM recommendations in a flow diagram so that the reader gets a more clear view of the differences in management.

3. Almost 57% of the patient had malaria which does not represent traditional community acquired sepsis. The authors should comment of this difference and the generalizability of their findings in this study to community acquired sepsis and of other etiologies.

4. Hypotension or cardiovascular collapse after fluid administration is normally treated with vasopressors. This does not mean fluid therapy is bad because shock is reversed with appropriate monitoring. If the response to this hypotension is limited because of resources, this is a different matter.

5. Hemodynamic collapse is a frequent event in both human and animal models of sepsis and this is reversed with a comprehensive treatment algorithm.3

6. Antibiotic-induced endotoxin release has been observed in both animal and human models of sepsis after antibiotic administration.4 This is a potentially harmful event in the absence of recognition and hemodynamic optimization.
Even with this event, one does not question the evidence of antibiotic administration.5,6 When were antibiotics given?

7. In another sub-Saharan Africa study on sepsis therapy in adults, early fluid administration was associated with improved mortality.7 This should be examined, contrasted and discussed.

References


Quality of written English: Acceptable

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

Declaration of competing interests:

I have no competing or conflicts of interest.