Reviewer's report

Title: The role of osmotic agents in children with acute encephalopathies: a systematic review

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Reviewer: Neeraj S Naval

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The role for osmotic agents in children with acute encephalopathies: A systematic review.

This paper by Dr Gwer et al is a concise, limited review of hyperosmolar therapy for elevated ICP in encephalopathic children. Its scope is well-defined and the stated inability to generate a meta-analysis is honest and legitimate. This is a topic is one in which there is a true lack of definitive data and a review of the data that is available is a valuable addition to medical literature. In general, the paper is well written and thought-provoking.

There are several concerns though.

General comments:

• The age covered is 0-16 but there is no mention made within analysis of each study of the age group encompassed or if subgroups defined by age were given within any of the studies. As there is a potentially large difference between neonates and adolescents, such data would be a valuable addition to this paper. If this was not available or no additional information was given by such subgroup analysis, this would bear mentioning if only to show it was considered.

• When available, the dosing of the agents used, particularly those with positive results, would be beneficial.

Specific points:

• Please provide a p value for the decreased mortality seen with hypertonic saline compared to mannitol for study Reference 32

• Page 3, PP 1: “Therefore, management of raised ICP aims to reduce ICP, …” Recommend rewording – e.g. Management of elevated intracranial pressure involves optimizing CPP and oxygen supply to the brain in addition to reduction of ICP

• Page 3, PP1: “Besides standard management such as correction of hypoglycemia and electrolyte imbalances…” This sentence implies that this is therapy for ICP management – would reword to clarify management of the critically ill.
• Page 6, PP1 and Figure 1: DexGlycerol is referred to in the figure and glycerol and dexamethasone is referred to in the text – that these are the same should be stated.

• Figure 1 lists heterogeneous agents and associated relative risk – listed as “rate ratio” – the assumption being that the agent listed first has the associated RR compared to the second. Based on this, there are the following concerns:

  - Figure 1 shows glycerol had a higher mortality rate than the DexGlycerol group yet this is not referred to in the text.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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