Choice of fluids for resuscitation in children with severe infection and shock: systematic review

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CRD summary
The authors of this review concluded that there was insufficient evidence on choice of resuscitation fluid for treatment of children with severe infection and shock. They recommended further research. This was a generally well-conducted review and the authors’ cautious conclusions appear appropriate.

Authors’ objectives
To compare the efficacy of crystalloids and colloids for fluid resuscitation in children with severe infection and shock.

Searching
MEDLINE (1950), EMBASE (1980), PubMed and The Cochrane Library were searched up to September 2008 for relevant articles published in any language. Reference lists of retrieved articles were searched. Studies included in a previous Cochrane meta-analyses were reviewed.

Study selection
Randomised controlled trials (RCTs), controlled trials, quasi-randomised trials and cohort studies that compared different intravenous fluids (administered as boluses) for the treatment of shock caused by severe infectious illness in children aged between one month and 12 years were eligible for inclusion. The main outcomes of interest were efficacy in the treatment of shock, mortality and adverse events. Studies were excluded if they reported fluid resuscitation in diarrhoeal disease, burns and trauma or injury cases and in situations where fluid was given for a surgical procedure or for anaesthesia purposes.

Included studies were conducted in Kenya and Asia. Children were aged between one month and 15 years and had malaria, dengue shock syndrome or sepsis. Studies compared crystalloids versus colloids, crystalloids versus crystalloids or colloids versus colloids. Some studies included a control group (no bolus). Treatment of shock was reported as resolution of shock and achievement of haemodynamic stability, but definitions varied across studies.

Two reviewers screened studies for inclusion. Disagreements were resolved through referral to a third reviewer.

Assessment of study quality
Two reviewers independently assessed study quality based on study design, adequacy of randomisation, allocation concealment, blinding and follow-up. Disagreements were resolved through referral to a third reviewer.

Data extraction
Two reviewers extracted data.

Methods of synthesis
Where clinical or methodological heterogeneity was judged to be present, findings were reported narratively. Studies in which clinical or methodological heterogeneity was judged not to be present and in which at least one death was reported, a fixed-effects model was used to calculate Peto odds ratios (ORs) and 95% confidence intervals (CIs). Statistical heterogeneity was assessed using the $X^2$ test. Subgroup analysis was undertaken by type of illness.

Results of the review
Nine studies (n=1,189 reported and 1,231 calculated, range 27 to 512) were included in the review: six RCTs and three quasi-randomised trials. Three studies in children with dengue shock syndrome were of low risk of bias and one was at high risk of bias; all studies in children with severe malaria and the one study in children with sepsis were at high risk of bias. None of the studies were specifically designed or adequately powered to assess mortality as a primary outcome.
There was no evidence of statistical heterogeneity, but due to clinical heterogeneity odds ratios and 95% CIs were not pooled. The authors stated that three out of six studies that reported at least one death showed greater survival in children resuscitated with colloids compared to crystalloids (Peto OR ranged between 0.18, 95% CI 0.02 to 1.42 and 0.48, 0.06 to 3.99). However, the forest plots suggested that only one study showed a statistically significant difference in favour of colloids and the remaining five showed no statistically significant differences. Three studies that assessed the effect of human albumin solution on survival in children with severe malaria showed conflicting results. One study of children with sepsis found no statistically significant difference in the risk of mortality with fluids used (saline versus gelatin polymer).

There were no statistically significant differences in recovery from shock in children with sepsis or malaria who were resuscitated with different fluids. Studies in children with dengue shock reported greater efficacy of colloids compared to crystalloids for resolution of severe shock.

There was no evidence of publication bias using a funnel plot (data not presented).

**Authors’ conclusions**
Existing evidence was not sufficiently robust to allow definitive conclusions to be made regarding the choice of resuscitation fluid; a definitive trial was needed to address this.

**CRD commentary**
The review question and inclusion criteria were clearly stated. An appropriate search was undertaken in any language, but no attempts were made to locate unpublished data so potentially relevant studies may have been missed. The authors acknowledged this and there did not appear to be evidence of publication bias. The authors assessed the generally poor study quality. Each stage of the review process was undertaken in duplicate, which reduced potential for reviewer error and bias. A narrative synthesis was appropriate given the variability among studies. The authors acknowledged certain limitations with the included studies, such as the small number of trials and small sample sizes, potential for bias and lack of mortality data. One consideration in the review related to the inclusion criteria, which stated that only studies of children up to the age of 12 were eligible for inclusion, while some studies included in the review appeared to include children up to the age of 15 (this may explain the difference in reported and calculated numbers). This was a generally well-conducted review and the authors' cautious conclusions seem appropriate.

**Implications of the review for practice and research**
**Practice:** The authors stated that the focus of the review was on fluid responsiveness rather than fluid refractory shock and the relevance of the findings to children who needed inotropic support was uncertain. They also stated that due to the variation in disease among the studies and variation in approaches to management of shock, the findings could not be generalised across the paediatric population.

**Research:** The authors stated that broad-based trials were needed to assess the efficacy of fluid expansion of colloids and crystalloids in children, taking into account the safety concerns of certain colloids.

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