Title: IV Colloid Plasma Volume Expanders for Hypovolemia

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Research question: What is the clinical effectiveness of intravenous colloid plasma volume expanders for patients with profound traumatic hypovolemia in pre-hospital settings? What are the guidelines for use of IV colloid plasma volume expanders?

Methods: A limited literature search was conducted on key health technology assessment resources, including PubMed, The Cochrane Library (Issue 2, 2007), University of York Centre for Reviews and Dissemination (CRD) databases, ECRI's HTAIS, EuroScan, international HTA agencies, and a focused Internet search. Results include articles published between 2002 and the present, and are limited to English language publications only. Abstracts and Internet links are provided, where available.

Results:

Health technology assessments:


OBJECTIVES: To systematically review the evidence on the effectiveness (in terms of mortality and morbidity) of prehospital intravenous (i.v.) fluid replacement, compared with no i.v. fluid replacement or delayed fluid replacement, in trauma patients with no head injury who have haemorrhage-induced hypotension due to trauma. DATA SOURCES: Electronic databases, relevant websites, handsearching, expert contacts. REVIEW METHODS: Search strategies were defined to identify randomised controlled trials (RCTs)
and previous systematic reviews relating to the use of i.v. fluids in a prehospital (or other) setting compared to no fluids or delayed fluids. Inclusion and exclusion criteria were applied to identified studies, and key quality criteria of included studies were checked. Data were extracted independently by two reviewers. Economic evaluations were also systematically sought and appraised. RESULTS: Four relevant RCTs were identified, three of which were poorly designed and/or conducted. One good-quality RCT suggested that i.v. fluids may be harmful in patients with penetrating injuries. No evidence was found on the relative effectiveness of i.v. fluids in patients with blunt versus penetrating trauma. No reliable evidence was found from systematic reviews to suggest that a particular type of fluid is more beneficial compared to another type, although there was a trend favouring crystalloids over colloids. The relative costs of using i.v. fluids versus not using them were found to be very similar and changes in the use of fluids would therefore have no cost consequences for the ambulance service. A more detailed cost-effectiveness analysis would require further information on the relative consequences (mortality, morbidity) of different resuscitation strategies. CONCLUSIONS: The review found no evidence to suggest that prehospital i.v. fluid resuscitation is beneficial, and some evidence that it may be harmful. This evidence is however not conclusive, particularly for blunt trauma. A UK Consensus Statement, and to a lesser extent the UK Joint Royal Colleges Ambulance Liaison Committee guidelines represent a more cautious approach to fluid management than previously advocated and are therefore consistent with the limited evidence base. Further research is required on hypotensive (cautious) resuscitation versus delayed or no fluid replacement, particularly in blunt trauma. There is also a need for an improvement in the quality of data collection and analysis of routinely collected ambulance call-out data.

Systematic reviews:


Traditionally, the management of bleeding trauma patients has included early rapid fluid replacement on scene. However, evidence shows that a delay to definitive treatment (control of bleeding) may be harmful and UK policy advocates minimal delay on scene with intravenous fluids being administered in transit to hospitals. This paper systematically reviews the evidence for administering fluids in pre-hospital trauma patients with no head injury. Randomized controlled trials comparing immediate and delayed fluid replacement were sought using formal search strategies. Study selection, quality assessment and data extraction were performed independently by two reviewers using pre-defined criteria. We found no evidence to suggest that pre-hospital fluid administration is beneficial. There is some evidence that it may be harmful and that patients do comparatively well when fluids are withheld. However, this evidence is not conclusive, particularly for blunt trauma, and is not sufficient to disprove current UK policy, which recommends hypotensive resuscitation.


BACKGROUND: Colloid solutions are widely used in fluid resuscitation of critically ill patients. There are several choices of colloid and there is ongoing debate about the relative effectiveness of colloids compared to crystalloid fluids. OBJECTIVES: To assess
the effects on mortality of colloids compared to crystalloids for fluid resuscitation in critically ill patients. SEARCH STRATEGY: We searched the Injuries Group specialised register, Cochrane Controlled Trials Register, MEDLINE, EMBASE and BIDS Index to Scientific and Technical Proceedings, and checked reference lists of trials and review articles. SELECTION CRITERIA: All randomised and quasi-randomised trials of colloids compared to crystalloids, in patients requiring volume replacement. Cross-over trials and trials in pregnant women and neonates were excluded. DATA COLLECTION AND ANALYSIS: Two reviewers independently extracted data and rated quality of allocation concealment. Trials with a 'double-intervention', such as those comparing colloid in hypertonic crystalloid to isotonic crystalloid, were analysed separately. The analysis was stratified according to colloid type and quality of allocation concealment. MAIN RESULTS: Colloids compared to crystalloids Albumin or plasma protein fraction. Nineteen trials reported data on mortality, including a total of 7576 patients. The pooled relative risk (RR) from these trials was 1.02 (95% confidence interval [95% CI] 0.93 to 1.11). When the trial with poor quality allocation concealment was excluded, pooled RR was 1.01 (95% CI 0.92 to 1.10). Hydroxyethyl starch. Ten trials compared hydroxyethyl starch with crystalloids, including a total of 374 randomised participants. The pooled RR was 1.16 (95% CI 0.68 to 1.96). Modified gelatin. Seven trials compared modified gelatin with crystalloid, including a total of 346 randomised participants. The pooled RR was 0.54 (95% CI 0.16 to 1.85). Dextran. Nine trials compared dextran with a crystalloid, including a total of 834 randomised participants. The pooled relative risk was RR 1.24 (95% CI 0.94 to 1.65). Colloids in hypertonic crystalloid compared to isotonic crystalloid Eight trials compared dextran in hypertonic crystalloid with isotonic crystalloid, including 1283 randomised participants. Pooled RR was 0.88 (95% CI 0.74 to 1.05). AUTHORS’ CONCLUSIONS: There is no evidence from randomised controlled trials that resuscitation with colloids reduces the risk of death, compared to resuscitation with crystalloids, in patients with trauma, burns or following surgery. As colloids are not associated with an improvement in survival, and as they are more expensive than crystalloids, it is hard to see how their continued use in these patients can be justified outside the context of randomised controlled trials. PLAIN LANGUAGE SUMMARY: No evidence that colloids are more effective than crystalloids in reducing mortality in people who are critically ill or injured. Trauma, burns or surgery can cause people to lose large amounts of blood. Fluid replacement, giving fluids intravenously (into a vein) to replace lost blood, is used to try to maintain blood pressure and reduce the risk of dying. Blood products, non-blood products or combinations are used, including colloid or crystalloid solutions. Colloids are increasingly used but they are more expensive than crystalloids. The review of trials found no evidence that colloids reduce the risk of dying compared with crystalloids.
identified trials were contacted. The search was last updated in August 2004. SELECTION CRITERIA: Randomised controlled trials comparing albumin/PPF with no albumin/PPF, or with a crystalloid solution, in critically ill patients with hypovolaemia, burns or hypoalbuminaemia. DATA COLLECTION AND ANALYSIS: We collected data on the participants, albumin solution used, mortality at the end of follow up, and quality of allocation concealment. Analysis was stratified according to patient type. MAIN RESULTS: We found 32 trials meeting the inclusion criteria and reporting death as an outcome. There were 1632 deaths among 8452 trial participants. For hypovolaemia, the relative risk of death following albumin administration was 1.01 (95% confidence interval 0.92, 1.10). This estimate was heavily influenced by the results of the SAFE trial which contributed 91% of the information (based on the weights in the meta-analysis). For burns, the relative risk was 2.40 (1.11, 5.19) and for hypoalbuminaemia the relative risk was 1.38 (0.94, 2.03). There was no substantial heterogeneity between the trials in the various categories (chi-square = 21.86, df = 25, p =0.64). The pooled relative risk of death with albumin administration was 1.04 (0.95, 1.13). AUTHORS’ CONCLUSIONS: For patients with hypovolaemia there is no evidence that albumin reduces mortality when compared with cheaper alternatives such as saline. There is no evidence that albumin reduces mortality in critically ill patients with burns and hypoalbuminaemia. The possibility that there may be highly selected populations of critically ill patients in which albumin may be indicated remains open to question. However, in view of the absence of evidence of a mortality benefit from albumin and the increased cost of albumin compared to alternatives such as saline, it would seem reasonable that albumin should only be used within the context of well concealed and adequately powered randomised controlled trial. PLAIN LANGUAGE SUMMARY: There is no evidence that giving human albumin to replace lost blood in critically ill or injured people improves survival when compared to giving saline. Trauma, burns or surgery can cause people to lose large amounts of blood. Fluid replacement, giving fluids intravenously (into a vein), is used to help restore blood volume and hopefully reduce the risk of dying. Blood products (including human albumin), non-blood products or combinations can be used. The review of trials found no evidence that albumin reduces the risk of dying. Albumin is very expensive in which case it may be better to use cheaper alternatives such as saline for fluid resuscitation.


BACKGROUND: Colloids are widely used in the replacement of fluid volume. However doubts remain as to which colloid is best. Different colloids vary in their molecular weight and therefore in the length of time they remain in the circulatory system. Because of this and their other characteristics, they may differ in their safety and efficacy. OBJECTIVES: To compare the effects of different colloid solutions in patients thought to need volume replacement. SEARCH STRATEGY: We searched the Cochrane Injuries Group specialised register, the Cochrane Controlled Trials Register (2002 Issue 3), MEDLINE (1994-2002/07), EMBASE (1974-2002 August week 1), and the National Research Register (2002 issue 3). Bibliographies of trials retrieved were searched, and drug companies manufacturing colloids were contacted for information. The search was last updated in September 2002. SELECTION CRITERIA: Randomised and quasi-randomised trials comparing colloid solutions in critically ill and surgical patients thought to need volume replacement. The main outcomes measured were death, amount of whole blood transfused, and incidence of adverse reactions. DATA COLLECTION AND ANALYSIS: Two authors independently extracted the data and assessed the quality of the trials. MAIN RESULTS: Fifty-seven trials met the inclusion criteria, with a total of 3659 participants.
Quality of allocation concealment was judged to be adequate in 20 trials and poor or uncertain in 37. Deaths were obtained from 36 trials. For albumin or PPF versus hydroxyethyl starch (HES) 20 trials (n=1029) reported mortality. The pooled relative risk (RR) was 1.17 (95% CI 0.91, 1.50). For albumin or PPF versus gelatin four trials (n=542) reported mortality. The RR was 0.99 (0.69, 1.42). For gelatin vs HES 11 trials (n=945) reported mortality, RR was 1.00 (0.78, 1.28). RR was not estimable in the albumin vs dextran, gelatin vs dextran, and HES vs dextran groups. Thirty-six trials recorded the amount of blood transfused, however quantitative analysis was not possible due to skewness and variable reporting. Fifteen trials recorded adverse reactions, but none occurred. AUTHORS’ CONCLUSIONS: From this review, there is no evidence that one colloid solution is more effective or safe than any other, although the confidence intervals are wide and do not exclude clinically significant differences between colloids. Larger trials of fluid therapy are needed if clinically significant differences in mortality are to be detected or excluded. PLAIN LANGUAGE SUMMARY: No strong evidence to be certain of the safety of any particular type of colloid solution for replacing blood fluids. When a person is bleeding heavily, the loss of fluid volume in their veins can lead to shock, so they need fluid resuscitation. Colloids and crystalloids are two types of solutions used to replace lost blood fluid (plasma). They include blood and synthetic products. Both types appear to be similarly effective at resuscitation, but one type of colloid (human albumin) was found by another Cochrane review to increase deaths. Different colloids may have different effects. However, the review of trials found there is not enough evidence to be sure that any particular colloid is safer than any other.


**General guidelines and recommendations:**


**RCTs:**

None Found
Appendix – Further information:

Review articles:


Venous access and fluid therapy should still be considered to be essential elements of pre-hospital advanced life support (ALS) in the critically injured patient. Initiation of fluid therapy should be based on a clinical assessment, most importantly the presence, or otherwise, of a radial pulse. The goal in penetrating injury is to avoid hypovolaemic cardiac arrest during transport, but at the same time not to delay transport, or increase systolic blood pressure. The goal in blunt injury is to secure safe perfusion of the injured brain through an adequate cerebral perfusion pressure, which generally requires a systolic blood pressure well above 100 mmHg. Patients without severe brain injury tolerate lower blood pressures (hypotensive resuscitation). Importantly, using systolic blood pressure targets to titrate therapy is not as easy as it seems. Automated (oscillometric) blood pressure measurement devices frequently give erroneously high values. The concept of hypotensive resuscitation has not been validated in the few studies done in humans. Hence, the suggested targeted systolic blood pressures should only provide a mental framework for the decision-making. The ideal pre-hospital fluid regimen may be a combination of an initial hypertonic solution given as a 10-20 minutes infusion, followed by crystalloids and, in some cases, artificial colloids. This review is intended to help the clinician to balance the pros and cons of fluid therapy in the individual patient


Additional references:


OBJECTIVE: To develop a clinical practice guideline that provides recommendations for the fluid, i.e. colloid or crystalloid, used for resuscitation in critically ill neonates and children up to the age of 18 years with hypovolemia. METHODS: The guideline was developed through a comprehensive search and analysis of the pediatric literature. Recommendations were formulated by a national multidisciplinary committee involving all stakeholders in neonatal and pediatric intensive care and were based on research evidence from the literature and, in areas where the evidence was insufficient or lacking, on consensus after discussions in the committee. RESULTS: Because of the lack of evidence in neonates and children, trials conducted in adults were considered. We found several recent meta-analyses that show excess mortality in albumin-treated groups, compared with crystalloid-treated groups, and one recent large randomized controlled trial that found evidence of no mortality difference. We found no evidence that synthetic colloids are superior to crystalloid solutions. CONCLUSIONS: Given the state of the evidence and taking all other considerations into account, the guideline-developing
group and the multidisciplinary committee recommend that in neonates and children with hypovolemia the first-choice fluid for resuscitation should be isotonic saline


Parkhouse D. Sugar solutions used in resuscitation. *J R Army Med Corps* 2005;151(1):5-10. PM:15912678

Although recent studies have shown that the timing of volume replacement deserves careful consideration (56), which fluid to use is less clear, with the perennial debate of crystalloid v colloid and now colloid v colloid still unresolved. This review has examined three sugar solutions, two colloids and one crystalloid. In general, all three agents are unhelpful in the immediate resuscitation of hypovolaemic trauma by virtue of a combination of pathophysiology and side effects. Dextran solutions and mannitol are useful in specific situations.