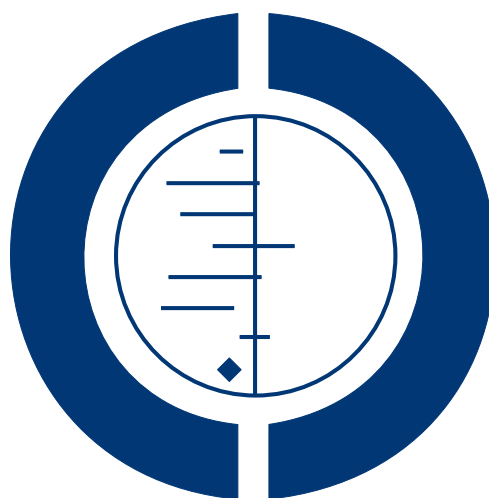


Colloids versus crystalloids for fluid resuscitation in critically ill patients (Review)

Roberts I, Alderson P, Bunn F, Chinnock P, Ker K, Schierhout G



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TABLE OF CONTENTS

HEADER	1
ABSTRACT	1
PLAIN LANGUAGE SUMMARY	2
BACKGROUND	2
OBJECTIVES	2
RESULTS	2
DISCUSSION	3
AUTHORS' CONCLUSIONS	4
ACKNOWLEDGEMENTS	4
REFERENCES	4
SOURCES OF SUPPORT	9
INDEX TERMS	9

[Intervention Review]

Colloids versus crystalloids for fluid resuscitation in critically ill patients

I Roberts, P Alderson, F Bunn, P Chinnock, K Ker, G Schierhout

Contact address: Mr Paul Chinnock, Senior Editor, PLoS Medicine, 7 Portugal Place, Cambridge, CB5 8AF, UK. pchinnock@plos.org.

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ABSTRACT

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.

BACKGROUND

Fluid resuscitation for hypovolaemia is a mainstay of the medical management of critically ill patients, whether as a result of trauma, burns, major surgery or sepsis. Although recent studies (Bickell 1994) have suggested that the timing of volume replacement deserves careful consideration, when it comes to selecting the resuscitation fluid clinicians are faced with a range of options. At one level the choice is between a colloid or crystalloid solution. Colloids are widely used, having been recommended in a number of resuscitation guidelines and intensive care management algorithms (Vermeulen 1995; Armstrong 1994). The US Hospital Consortium Guidelines recommend that colloids are used in haemorrhagic shock prior to the availability of blood products, and in non-haemorrhagic shock following an initial crystalloid infusion. A 1995 survey of US academic health centres, however, found that the use of colloids far exceeded even the Hospital Consortium recommendations (Yim 1995). Surveys of burn care in the US (Fakhry 1995) and in Australia (Victorian DUAC 1991) found that the use of colloids for resuscitation varied without a set pattern. The choice of fluid has considerable cost implications. Volume replacement with colloids is considerably more expensive than with crystalloids. Clinical studies have shown that colloids and crystalloids have different effects on a range of important phys-

iological parameters. Because of these differences, all-cause mortality is arguably the most clinically relevant outcome measure in randomised trials comparing the two fluid types. Although there have been previous meta-analyses of mortality in randomised trials comparing colloids and crystalloids (Velanovich 1989, Bissonni 1991), neither of these satisfy the criteria that have been proposed for scientific overviews (Oxman 1994), and they predate most of the trials that have been conducted using synthetic colloids, and hypertonic crystalloid solutions. The purpose of this review is to identify and synthesise all available unconfounded evidence of the effect on mortality in critically ill patients of colloids compared to crystalloids for volume replacement.

OBJECTIVES

To determine the effects on mortality of using colloids compared to crystalloids, during fluid resuscitation in critically ill patients.

RESULTS

Colloids compared to crystalloids

Albumin or plasma protein fraction

Twenty trials reported data on mortality, including a total of 7576 patients. The pooled RR from these trials was 1.02 (95% CI 0.93 to 1.11). When the one trial with poor quality allocation concealment (Lucas 1978) was excluded, the pooled RR was 1.01 (95% CI 0.92 to 1.01).

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 RR was 1.24 (95% CI 0.94 to 1.65).

Colloids in hypertonic crystalloid compared to isotonic crystalloid

One trial compared albumin and hypertonic saline with isotonic crystalloid. Its relative risk of death was 0.50 (0.06 to 4.33).

Eight trials compared dextran in hypertonic crystalloid with isotonic crystalloid, including 1283 randomised participants. The pooled RR was 0.88 (0.74 to 1.05).

Colloids in isotonic crystalloid compared to hypertonic crystalloid

Three trials compared colloids in isotonic crystalloid with hypertonic crystalloid. In two of these, where the colloid was either gelatin or starch, there were no deaths in either group. In the remaining trial, with 38 participants, there was a relative risk of death of 7.00 (0.39 to 126.93) for use of colloid, based on three deaths in the treatment group and none in the control group.

DISCUSSION

This systematic review synthesises the evidence from randomised controlled trials comparing colloid and crystalloid fluid resuscitation across a wide variety of clinical conditions. The review has been updated and extensively revised to take into account the comments made since it was first published. In particular, several commentators pointed out that it is inappropriate to combine effect estimates from studies of different colloids. For example, it was argued that large molecular weight colloids such as hydroxyethyl starch may be better retained in the vascular compartment than albumin and gelatins, and would therefore be more likely to show a favourable effect on mortality (Gosling 1998). In response to

these concerns, the review has been stratified by type of colloid. However, the pooled relative risks fail to show a mortality benefit for resuscitation with any type of colloid.

There was a trend towards a favourable effect on mortality for colloids in hypertonic crystalloid, compared to isotonic crystalloids. Nevertheless, the results are compatible with the play of chance.

Common to all meta-analyses, this systematic review may have included studies whose interventions and patient characteristics are sufficiently incomparable that the calculation of a summary effect measure may be questioned. The resuscitation regimen differed between trials. Some trials randomised participants to an initial quantity of colloid or crystalloid, and then proceeded with some form of standard resuscitation for all participants. Other trials resuscitated with the allocated fluid to pre-determined end-points, either resuscitation end-points, or in the case of trauma, until corrective surgery. In addition, the type of colloid or crystalloid, the concentration, and the protocol to determine the quantity of fluid varied. Despite these differences, all participants were in need of volume replacement, and we believe that this variation in the intervention would have an impact on the size of the effect, rather than on its direction.

As regards the effects of albumin versus crystalloid, most of the information (as indicated by the weighting in the meta-analysis) was provided by the SAFE trial. The SAFE trial used central randomisation with a minimisation algorithm to ensure balance on known potential confounders. Blinding was assured through the use of specially designed masking cartons and specially designed and manufactured administration sets. The authors report that the effectiveness of the blinding was confirmed in a formal study before the trial was initiated. In brief, this was a well-conducted, high-quality trial. There were 726 deaths (20.9%) in the albumin-treated group and 729 deaths (21.1%) in the saline-treated group (RR of death 0.99; 95% CI 0.91 to 1.09). Although even this large trial was unable to confirm or refute the possibility of a modest benefit or harm from albumin, it has provided some reassurance that any hazard from albumin, if indeed there is any, is unlikely to be as extreme as was suggested by the results from the previously published (now here updated) meta-analysis of much smaller trials. The pooled relative risk for death with albumin in this updated meta-analysis is now 1.02 (0.93 to 1.11). It is important to note that the effect estimate from the SAFE trial is entirely consistent with the results of previous trials of albumin in hypovolaemia and there is no significant heterogeneity ($I^2 = 0\%$, $p = 0.46$).

The results of this updated meta-analysis have important policy implications. There is still no evidence that colloids are superior to crystalloids as a treatment for intravascular volume resuscitation in critically ill patients. Importantly, the SAFE trial also provided no evidence of any other clinical advantages from using albumin. It also debunked the belief, from pathophysiological inference, that very large volumes of crystalloid must be administered to reach

the same resuscitation end-points as can be achieved using much smaller volumes of colloid. In the SAFE trial, the ratio of albumin administered to saline administered was approximately 1:1.4. Colloids, in particular albumin, are considerably more expensive than crystalloids, and albumin is a blood product and so carries at least a theoretical infectious disease risk. The economic opportunity cost of on-going colloid use, particularly albumin use, is likely to be considerable and for this reason its on-going use in this context is unjustified.

AUTHORS' CONCLUSIONS

Implications for practice

There is no evidence from randomised controlled trials that resuscitation with colloids, instead of crystalloids, reduces the risk of death in patients with trauma, burns or following surgery. As

colloids are not associated with an improvement in survival, and further, colloids are considerably more expensive than crystalloids, it is hard to see how their continued use outside the context of randomised controlled trials in subsets of patients of particular concern, can be justified.

Implications for research

Future trials may need to concentrate on specific sub-groups of patients to identify people who may benefit from colloids rather than crystalloids.

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* *Indicates the major publication for the study*

SOURCES OF SUPPORT

External sources of support

- NHS R&D Programme: Mother and Child Health UK

Internal sources of support

- Institute of Child Health, University of London UK
- UK Cochrane Centre, NHS R&D Programme UK

INDEX TERMS

Medical Subject Headings (MeSH)

Colloids [*therapeutic use]; Critical Illness [*therapy]; Fluid Therapy [*methods]; Plasma Substitutes [*therapeutic use]; Randomized Controlled Trials; *Rehydration Solutions; Resuscitation [methods]

MeSH check words

Humans