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# Colloid solutions for fluid resuscitation (Review)

Bunn F, Alderson P, Hawkins V



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[Intervention Review]

# Colloid solutions for fluid resuscitation

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## ABSTRACT

### 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.

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**Colloid solutions for fluid resuscitation (Review)**

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## 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

## BACKGROUND

Colloids are used as plasma substitutes for short-term replacement of fluid volume, while the cause of the problem is being addressed (e.g. stopping bleeding). These solutions can be blood products (human albumin solution, plasma protein fraction [PPF]) or synthetic (modified gelatins, dextrans, etherified starches). Colloid solutions are widely used in fluid resuscitation (Yim 1995) and they have been recommended in a number of resuscitation guidelines and intensive care management algorithms (Armstrong 1994; Vermeulen 1995). Previous systematic reviews have suggested that colloids are no more effective than crystalloids in reducing mortality (Schierhout 2000), and that albumin administration may increase mortality compared to crystalloids or no fluid in a range of uses (CIGAR 2000). Despite this, colloid solutions are still widely used as they are thought to remain in the intravascular space for longer than crystalloids and, therefore, be more effective in maintaining osmotic pressure.

It is plausible that colloids may vary in their safety and effectiveness. Different colloids vary in the length of time they remain in the circulatory system. It may be that some low to medium molecular weight colloids (e.g. gelatins and albumin) are more likely to leak into the interstitial space (Traylor 1996), whereas some larger molecular weight hydroxyethyl starches are retained for longer (Boldt 1996). In addition it is thought that some colloids may effect coagulation or cause other adverse effects.

The previous review of colloids against crystalloids only allows indirect comparison of the different colloids. This review examines direct comparisons of the different colloid solutions in randomised trials to complement the earlier reviews on colloids compared

to crystalloids (Schierhout 2000) and human albumin (CIGAR 2000).

## OBJECTIVES

To quantify the relative effects on mortality of different colloid solutions in critically ill and surgical patients requiring volume replacement, by examining direct comparisons of colloid solutions.

## RESULTS

Of the 57 trials identified 24 reported mortality data. Information on death was obtained from a further 12 trials by contact with the authors. We therefore had data on death from 36 trials.

Albumin or PPF vs starch:

Twenty trials (1029 participants) reported mortality data. The pooled relative risk was 1.17 (95% CI 0.91-1.50).

Albumin or PPF vs gelatin:

Four trials (542 participants) reported mortality but only one of those trials had any deaths. The relative risk was 0.99 (95% CI 0.69-1.42).

Albumin or PPF vs dextran:

Three trials reported mortality and were included in the meta-analysis. There were no deaths so relative risk was not estimable.

Gelatin vs starch:

Eleven trials (945 participants) reported mortality and the pooled relative risk was 1.00 (95% CI 0.78-1.28).

Gelatin vs dextran 70

There were two trials which reported mortality. There were no deaths so the relative risk was not estimable.

Hydroxyethyl starch vs dextran 70:

No trials reported mortality.

Thirty-five trials recorded the amount of blood transfused. As the data was reported in various ways, often lacking a measure of variation, and was also skewed we did not attempt a quantitative synthesis. This data can be seen in the "other data" table. Fifteen trials reported the incidence of adverse or allergic reactions or anaphylactic shock: all reported that there were no such incidents.

The effect of excluding trials judged to have inadequate (scoring C) allocation concealment was examined in a sub-group analysis. This made no significant difference to the results.

## DISCUSSION

Despite finding 57 trials we cannot make any conclusions about the relative effectiveness of different colloid solutions. A previous review suggested that albumin may increase mortality in critically ill patients (CIGAR 2000), but there are too few data available to show in direct comparisons whether the synthetic alternatives are safer. The confidence intervals are wide and do not exclude clinically significant differences between colloids.

Mortality was selected as the main outcome measure in this systematic review for several reasons. In the context of critical illness, death or survival is a clinically relevant outcome that is of immediate importance to patients, and data on death are reported in many of the studies. Furthermore, one might expect that mortality data would be less prone to measurement error or biased reporting than would data on pathophysiological outcomes. The use of a pathophysiological end point as a surrogate for an adverse outcome assumes a direct relationship between the two, an assumption that may sometimes be inappropriate. Finally, when trials collect data on a number of physiological end-points, there is the potential for bias due to the selective publication of end-points showing striking treatment effects.

There was wide variation in the participants, intervention regimens, and the length of follow-up. The length of follow-up is not

reported in many of the studies. Where it is reported it ranges from a matter of hours to months, which may explain a lot of the heterogeneity in overall event rates. The effect of these factors was not examined in a sensitivity analysis, as there was felt to be insufficient data to justify examining subgroups.

Many of the trials were small, and some had been done some time ago. Although older trials will not necessarily be of poorer quality, it may be that treatment protocols have subsequently altered making these trials less relevant to current clinical practice.

## AUTHORS' CONCLUSIONS

### Implications for practice

Previous reviews have failed to show any benefit of colloids over crystalloids for volume replacement (Schierhout 2000) and suggested that albumin solution may increase mortality in critically ill patients (CIGAR 2000).

This review does not provide any evidence that one colloid is safer than another, but does not rule out clinically significant differences.

### Implications for research

Trials of fluid therapy need to be larger in order to exclude clinically significant differences between colloids in patient relevant outcomes. However, trials should probably first address the question of whether colloids are any more effective than crystalloid solutions.

Use of surrogate outcomes, such as physiological measurements should be discouraged unless there is a strong relationship with outcomes of interest to patients and relatives.

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\* Indicates the major publication for the study

## **F E E D B A C K**

### **Colloid solutions for fluid resuscitation**

#### **Summary**

1. Please explain, in the 'what's new' section, in what respects this update differs from the previous version.
2. The drug companies listed in the acknowledgments are not in alphabetic order: please do so or explain the reason for the order shown (e.g. in order of helpfulness).
3. Fresenius is misspelt
4. In the references to included trials, please use an asterisk to identify those trials which are the main publication where there are more than one article referring to a trial.

#### **Author's reply**

1. The review has been marked as an update by mistake. As of September 1999 no substantial updates have been made.
2. The drug companies have been re-ordered alphabetically.
3. The spelling of Fresenius is corrected.
4. The primary reference has been marked with an asterisk.

#### **Contributors**

Comment by Andrew Herxheimer

Response by Frances Bunn

## **SOURCES OF SUPPORT**

### **External sources of support**

- NHS Research and Development Programme UK

### **Internal sources of support**

- University of Hertfordshire UK

## **INDEX TERMS**

### **Medical Subject Headings (MeSH)**

Blood Proteins [\*therapeutic use]; Colloids [therapeutic use]; Dextrans [\*therapeutic use]; \*Fluid Therapy; Plasma Substitutes [\*therapeutic use]; Randomized Controlled Trials; Rehydration Solutions [\*therapeutic use]

### **MeSH check words**

Humans