Colloid solutions for fluid resuscitation (Review)

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[Intervention Review]

Colloid solutions for fluid resuscitation

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Editorial group: Cochrane Injuries Group.
Publication status and date: Commented, published in Issue 4, 2007.
Review content assessed as up-to-date: .

Citation: Bunn F, Alderson P, Hawkins V. Colloid solutions for fluid resuscitation. *Cochrane Database of Systematic Reviews* 2003, Issue 1. Art. No.: CD001319. DOI: 10.1002/14651858.CD001319.

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.

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.

ACKNOWLEDGEMENTS

We wish to acknowledge the help of Ralph Bloch, Olivier Duperrex, Andrew Smith, Peter Smith and Reinhard Wentz, who assisted with translating articles. Also many thanks to the authors who provided us with details of their studies.

We are grateful to the drug companies, Baxter Healthcare Ltd, CIS Ltd, Fresenius, Hoechst, and Pharmalink who responded to our request for information.

REFERENCES

References to studies included in this review

Allison 1999 *{published data only}*
Allison KP, Gosling P, Jones S, Pallister I, Porter K. Randomized trial of hydroxyethyl starch versus gelatine for trauma resuscitation. *Journal of Trauma* 1999;**47**(6): 1114–1121.

Asfar 2000 *{published data only}*
Asfar P, Kereni N, Labadie F, Gouello JP, Brenet O, Alquier P. Assessment of hemodynamic and gastric mucosal acidosis with modified fluid versus 6% hydroxyethyl starch: a prospective, randomized study. *Intensive Care Medicine* 2000;**26**(9):1282–1287.

Beards 1994 *{published and unpublished data}*
Beards SC, Watt T, Edwards JD, Nightingale P, Farragher EB. Comparison of the hemodynamic and oxygen transport responses to modified fluid gelatin and hetastarch in critically ill patients: a prospective, randomized trial. *Critical care medicine* 1994;**22**(4):600–5. [MedLine: 1994192356].

Berard 1995 *{published data only}*
Berard J-P, Curt I, Piech J-J, Ruiz F. Hydroxyethylamidons versus gelatines: impact on the cost of replacement in an emergency (resuscitation) service [Hydroxyethylamidons versus gelatines: Impact sur le cout du rempissage dans un service de reanimation]. *Annales Francaises d'Anaesthesia et de Reanimation* 1995;**14**:R335.

Beyer 1997 *{published and unpublished data}*
Beyer R, Harmening U, Rittmeyer O, Zielmann S, Mielck F, Kazmaier S, Kettler D. Use of modified fluid gelatin and hydroxyethyl starch for colloidal volume replacement in major orthopaedic surgery. *British Journal of Anaesthesia* 1997;**78**(1):44–50. [MedLine: 1997212347].

Boldt 1986 *{published data only}*
Boldt JV, Von Bormann B, Kling D, Borner U, Mulch J, Hempelmann G. Volume replacement with a new hydroxyethyl starch preparation (3% HES 200/0.5) in heart surgery [Volumenersatz mit einem neuen hydroxyathylstarke – praparat (3% HAS 200/0.5) in der herzchirurgie]. *Infusionstherapie und Klinische Ernahrung* 1986;**13**(3):145–151. [MedLine: 1986302988].

Boldt 1993 A *{published and unpublished data}*
Boldt J, Knothe C, Zickmann B, Andres P, Dapper F, Hempelmann G. Influence of different intravascular volume therapies on platelet function in patients undergoing cardiopulmonary bypass. *Anesthesia and Analgesia* 1993;**76** (6):1185–90.

Boldt 1995 *{published data only}*
Boldt J, Heesen M, Welters I, Padberg W, Martin K, Hempelmann G. Does the type of volume therapy influence endothelial-related coagulation in the critically ill?. *British Journal of Anaesthesia* 1995;**75**(6):740–746. [MedLine: 1996246804].

Boldt 1996 A *{published data only}*
Boldt J, Heesen M, Muller M, Pabsdorf M, Hempelmann G. The effects of albumin versus hydroxyethyl starch solution on cardiorespiratory and circulatory variables in critically ill patients. *Anesthesia and Analgesia* 1996;**83**(2): 254–61. [MedLine: 1996302067].

Boldt 1996 B *{published data only}*
Boldt J, Heesen M, Padberg W, Martin K, Hempelmann G. The influence of volume therapy and pentoxifylline infusion on circulating adhesion molecules in trauma patients. *Anaesthesia* 1996;**51**(6):529–535. [MedLine: 1996296856].

Boldt 1996 C *{published data only}*
Boldt J, Mueller M, Menges T, Papsdorf M, Hempelmann G. Influence of different volume therapy regimens on regulators of the circulation in the critically ill. *British Journal of Anaesthesia* 1996;**77**(4):480–487. [MedLine: 1997097789].

Boldt 1998 *{published data only}*
Boldt J, Muller M, Mentges D, Papsdorf M, Hempelmann G. Volume therapy in the critically ill: is there a difference? . *Intensive Care Medicine* 1998;**24**(1):28–36. [MedLine: 1998163949].

Boldt 2000 *{published data only}*
Boldt J, Suttner S, Kumle B, Huttner I. Cost analysis of different volume replacement strategies in anesthesia. *Infusionstherapie und Transfusionsmedizin* 2000;**27**(1): 38–43.

Boldt 2001 *{published data only}*
Boldt J, Suttner S, Huttner I, Kumle B, Piper S, Krumholz W. Are cost of a crystalloid-based volume replacement regimen lower than of a colloid-based volume replacement strategy?. *Infusionstherapie und transfusionsmedizin* 2001;**28** (3):144–149.

Brock 1995 *{published and unpublished data}*
Brock H, Rapf B, Necek S, Gabriel C, Peterlik C, Polz W. Volume replacement after cardiac surgery. A comparison of small-volume resuscitation and two different colloid solutions [Vergleichende untersuchungen zur postoperativen volumentherapie]. *Anaesthesist* 1995;**44**(7):486–492. [MedLine: 1995390424].

Brutocao 1996 *{published and unpublished data}*
Brutocao D, Bratton SL, Thomas JR, Schrader PF, Coles PG, Lynn AM. Comparison of hetastarch with albumin for postoperative volume expansion in children after cardiopulmonary bypass. *Journal of Cardiothoracic and Vascular Anesthesia* 1996;**10**(3):348–351. [MedLine: 1996298754].

Carli 2000 *{published data only}*
Carli P, Goldstein P, Lejay M, Facon A, Orliaguet G, Petit P. Prehospital care of hypovolemic trauma patients: 6% hydroxyethyl starch versus gelatin [Remplissage vasculaire prehospitalier en traumatologie: Hesteril 6% versus

Plasmion]. *Journal Europeen des Urgences* 2000;**13**(1-2): 101–105.

Claes 1992 ***{published data only}***
Claes Y, Van Hemelrijck J, Van Gerven M, Arnout J, Vermylen J, Weidler B, Van Aken H. Influence of hydroxyethyl starch on coagulation in patients during the perioperative period. *Anesthesia and Analgesia* 1992;**75**(1): 24–30. [MedLine: 1992312872].

Diehl 1982 ***{published data only}***
Diehl JT, Lester JL, Cosgrove DM. Clinical comparison of hetastarch and albumin in postoperative cardiac patients. *Annals of Thoracic Surgery* 1982;**34**(6):674–679. [MedLine: 1983073643].

Du Gres 1989 ***{published data only}***
Du Gres B, Gruner MC, Flamens C. A comparison of the hemodynamic effect of Haemaccel and diluted albumin in the immediate postoperative period after heart surgery [Comparaison des effets hemodynamiques de l'Haemaccel et de l'albumine diluee dans la periode postoperatoire immediate apres chirurgie cardiaque]. *Cahiers d'Anesthesiologie* 1989;**37**(5):327–332. [MedLine: 1990029584].

Dytkowska 1998 ***{published data only}***
Dytkowska B, Karwacki Z, Suchorzewska J, Wujtewicz M. Comparative assessment of 200/0.5 HAES 6% and Gelafundin in the treatment of hypovolaemia in post-coronary bypass patients. *Medical Science Monitor* 1998;**4** (6):1000–1003.

Falk 1988 ***{published data only}***
Falk JL, Rackow EC, Astiz ME, Weil MH. Effects of hetastarch and albumin on coagulation in patients with septic shock. *Journal of Clinical Pharmacololgy* 1988;**28**(5): 412–415. [MedLine: 1988273726].

Fulachier 1994 ***{published data only}***
Fulachier V, Sicard MP, Baille Y, Auffray JP. Effects of fluid expansion using albumin or hydroxyethylstarch on oxygen transport after induction of anesthesia for cardiac surgery. *Journal of Cardiothoracic and Vascular anesthesia* 1994;**8** (3Supp2):89.

Gahr 1981 ***{published data only}***
Gahr R, Bock PR. Effect of hydroxyethyl starch HES 450/0.7 and 5% human albumin on the colloid osmotic pressure and hemodynamic parameters in hypovolemic patients after major abdominal procedures [Wirkung von hydroxyathylstarke HAS 450/0.7 und humanalbumin 5% auf den kolloidosmotischen druck und hamodynamische parameter bei hypovolamischen patienten nach grosseren abdominalen eingriffen]. *Infusionstherapie und Transfusionsmedizin* 1981;**8**(3):147–152. [MedLine: 1981262968].

Gallagher 1985 ***{published and unpublished data}***
Gallagher JD, Moore RA, Kerns D, Jose AB, Botros SB, Flicker S, Naidech H, Clark DL. Effects of colloid or crystalloid administration on pulmonary extravascular water in the postoperative period after coronary artery bypass grafting. *Anesthesia and Analgesia* 1985;**64**(8):753–8.

Gold 1990 ***{published and unpublished data}***
Gold MS, Russo J, Tissot M, Weinhouse G, Riles T. Comparison of hetastarch to albumin for perioperative bleeding in patients undergoing abdominal aortic aneurysm surgery. *Annals of Surgery* 1990;**211**(4):482–485. [MedLine: 1990210743].

Haisch 2001a ***{published data only}***
Haisch G, Boldt J, Krebs C, Suttner S, Lehmann A, Isgro F. Influence of a new hydroxyethylstarch preparation (HES 130/0.4) on coagulation in cardiac surgical patients. *Journal of Cardiothoracic and Vascular Anesthesia* 2001;**15** (3):316–321.

Haisch 2001b ***{published data only}***
Haisch G, Boldt J, Krebs C, Kumle B, Suttner S, Schulz A. The influence of intravascular volume therapy with a new hydroxyethyl starch preparation (6% HES 130/0.4) on coagulation in patients undergoing major abdominal surgery. *Anesthesia and Analgesia* 2001;**92**(3):565–71. [MedLine: 21124037].

Hausdorfer 1986 ***{published data only}***
Hausdorfer J, Hagemann H, Heine J. Comparison of volume substitutes human albumin 5% and hydroxyethyl starch 6% in paediatric anaesthesia [Vergleich der volumenersatzmittel humanalbumin 5% und hydroxathylstarke 6% (40.000/ 0.5) in der kinderanasthesie]. *Anasthesie, Intensivtherapie, Notfallmedizin* 1986;**21**(3):137–142. [MedLine: 1986320933].

Hedstrand 1987 ***{published data only}***
Hedstrand U, Hogman C, Zaren B, Lundkvist B. Postoperative complications after blood replacement with or without plasma. *Acta chirurgica Scandinavica* 1987;**153** (9):501–505.

Hiippala 1995 ***{published data only}***
Hiippala S, Linko K, Myllyla G, Lalla M, Hekali R, Makelainen A. Replacement of major surgical blood loss by hypo-oncotic or conventional plasma substitutes. *Acta Anaesthesiologia Scandinavica* 1995;**39**(2):228–235. [MedLine: 1995313480].

Huskisson 1993 ***{published data only}***
Huskisson L, Elliott M, Spitz L. Haemodynamic effects of three colloids following pediatric open heart surgery. *Clinical Intensive Care* 1993;**4**:302.

Huttner 2000 ***{published data only}***
Huttner I, Boldt J, Haisch G, Suttner S, Kumle B, Schulz H. Influence of different colloids on molecular markers of haemostasis and platelet function in patients undergoing major abdominal surgery. *British Journal of Anaesthesia* 2000;**85**(3):417–23.

Karanko 1987 ***{published and unpublished data}***
Karanko MS. Effects of three colloid solutions on plasma volume and hemodynamics after coronary bypass surgery. *Critical Care Medicine* 1987;**15**(11):1015–1021. [MedLine: 1988054051].

Kirklin 1984 ***{published data only}***
Kirklin JK, Lell WA, Kouchoukos NT. Hydroxyethyl starch versus albumin for colloid infusion following

cardiopulmonary bypass in patients undergoing myocardial revascularization. *Annals of Thoracic Surgery* 1984;**37**(1): 40–46. [MedLine: 1984103384].

Lisander 1996 ***{published and unpublished data}***
Lisander B, Jacobsson SA, Ivarsson I, Vegfors M, Engdahl O. Giving both enoxaparin and dextran increases the need for transfusion in revision hip arthroplasty. *European Journal of Surgery* 1996;**162**(11):861–866. [MedLine: 1997115584].

London 1989 ***{published data only}***
London MJ, Ho JS, Triedman JK, Verrier ED, Levin J, Merrick SH, et al.A randomized clinical trial of 10% pentastarch (low molecular weight hydroxyethyl starch) versus 5% albumin for plasma volume expansion after cardiac operations. *Journal of thoracic and cardiovascular surgery* 1989;**97**(5):785–97. [MedLine: 1989218083].

Mastroianni 1994 ***{published data only}***
Mastroianni L, Low HB, Rollman J, Wagle M, Bleske B, Chow MS. A comparison of 10% pentastarch and 5% albumin in patients undergoing open-heart surgery. *Journal of Clinical Pharmacology* 1994;**34**(1):34–40. [MedLine: 1994179580].

Moggio 1983 ***{published data only}***
Moggio RA, Rha CC, Somberg ED, Praeger P, Pooley RW, Reed GE. Hemodynamic comparison of albumin and hydroxyethyl starch in postoperative cardiac surgery patients. *Critical Care Medicine* 1983;**11**(12):943–945. [MedLine: 1984056648].

Munoz 1980 ***{published data only}***
Munoz E, Raciti A, Dove D, Stahl WM, Del Guercio L. Effect of hydroxyethyl starch versus albumin on hemodymanic and respiratory function in patients with shock. *Critical Care Medicine* 1980;**8**(4):255.

Munsch 1988 ***{published data only}***
Munsch CM, MacIntyre E, Machin SJ, Mackie IJ, Treasure T. Hydroxyethyl starch: an alternative to plasma for postoperative volume expansion after cardiac surgery. *British Journal of surgery* 1988;**75**(7):675–678. [MedLine: 1988327292].

Prien 1990 ***{published and unpublished data}***
Prien T, Backhaus N, Pelster F, Pircher W, Bunte H, Lawin P. Effect of intraoperative fluid administration and colloid osmotic pressure on the formation of intestinal edema during gastrointestinal surgery. *Journal of Clinical Anesthesia* 1990;**2**(5):317–23. [MedLine: 1991104037].

Rackow 1983 ***{published data only}***
Rackow EC, Falk JL, Fein IA, Siegel JS, Packman MI, Haupt MT, Kaufman S, Putnam D. Fluid resuscitation in circulatory shock: A comparison of the cardiorespiratory effects of albumin, hetastarch, and saline solutions in patients with hypovolemic and septic shock. *Critical Care Medicine* 1983;**11**(11):839–850. [MedLine: 1984027713].

Rackow 1989 ***{published data only}***
Rackow EC, Mecher C, Astiz ME, Griffel M, Falk JL, Weil MH. Effects of pentastarch and albumin infusion on cardiorespiratory function and coagulation in patients with severe sepsis and systemic hypoperfusion. *Critical Care Medicine* 1989;**17**(5):395–398. [MedLine: 1989209912].

Rosencher 1992 ***{published and unpublished data}***
Rosencher N, Vassilieff N, Guigonis V, Toulin P, Conseiller C. Comparison of effects of Elohes and albumin on haemostasis in orthopedic surgery [Comparaison des effets de l'Elohes et de l'albumine sur l'hemostase en chirurgie orthopedique]. *Annales francaises d'Anesthesie et de Reanimation* 1992;**11**(5):526–530. [MedLine: 1993118965].

Schortgen 2001 ***{published data only}***
Schortgen F, Lacherade J, Bruneel F, Cattaneo I, Hemery F, Lemaire F, Brochard L. Effects of hydroxyethylstarch and gelatin on renal function in severe sepsis: a multicentre randomised study. *Lancet* 2001;**357**(9260):911–916.

Shatney 1983 ***{published data only}***
Shatney CH, Deepika K, Militello PR, Majerus TC, Dawson RB. Efficacy of hetastarch in the resuscitation of patients with multisystem trauma and shock. *Archives of Surgery* 1983;**118**(7):804–809. [MedLine: 1983230251].

Stockwell 1992 ***{published data only}***
Stockwell MA, Scott A, Day A, Riley B, Soni N. Colloid solutions in the critically ill. A randomised comparison of albumin and polygeline: 2. Serum albumin concentration and incidences of pulmonary oedema. *Anesthesia* 1992;**47** (1):7–9.
* Stockwell MA, Soni N, Riley B. Colloid solutions in the critically ill. A randomised comparison of albumin and polygeline: 1. Outcome and duration of stay in the intensive care unit. *Anaesthesia* 1992;**47**(1):3–6. [MedLine: 1992161241].

Stoddart 1996 ***{published data only}***
Stoddart PA, Rich P, Sury MR. A comparison of 4.5% human albumin solution and haemaccel in neonates undergoing major surgery. *Paediatric Anaesthesia* 1996;**6**(2): 103–106. [MedLine: 1996243349].

Tollofsrud 1995 ***{published data only}***
Svennevig JL, Tollofsrud S, Kongsgaard U, Noddeland H, Mohr B, Ozer M, Mollnes TE. Complement activation during and after open-heart surgery is only marginally affected by the choice of fluid for volume replacement. *Perfusion* 1996;**11**(4):326–32.
* Tollofsrud S, Svennevig JL, Breivik H, Kongsgaard U, Ozer M, Hysing E, et al.Fluid balance and pulmonary functions during and after coronary artery bypass surgery: Ringer's acetate compared with dextran, polygeline, or albumin. *Acta anaesthesiologica Scandinavica* 1995;**39**(5): 671–7.

Vogt 1994 ***{published data only}***
Vogt N, Bothner U, Georgieff M. Comparison of 5% human albumin and 6% 200/0.5 HES as exclusive colloid components in large surgical interventions [Vergleich von humanalbumin 5% und 6% HES 200/ 0.5 als ausschliessliche kolloidkomponente bei grossen chirurgischen eingriffen]. *Anasthesiologie, Intensivmedizin, Notfallmedizin, Schmerztherapie* 1994;**29**(3):150–156.

Vogt 1996 *{published data only}*
Vogt NH, Bothner U, Lerch G, Linder KH, Georgieff M. Large-dose administration of 6% hydroxyethyl starch 200/0.5 for total hip arthroplasty: Plasma homeostasis, hemostasis, and renal function compared to use of 5% human albumin. *Anesthesia and Analgesia* 1996;**83**(2): 262–8. [MedLine: 1996302068].

Vogt 1999 *{published data only}*
* Vogt N, Bothner U, Brinkmann A, De Petriconi R, Georgieff M. Peri-operative tolerance to large-dose 6% HES 200/0.5 in major urological procedures compared with 5% human albumin. *Anaesthesia* 1999;**54**(2):121–127.
Vogt N, Bothner U, Lerch G, Georgieff M. [Pharmakokinetik und onkotisches verhalten von hochdosierter hydroxyathylstarke bei operativen eingriffen im vergleich zu humanalbumin 5%]. *Infusion Therapy and Transfusion Medicine* 1998;**25**:212–221.

von Sommoggy 1990 *{published data only}*
Von Sommoggy S, Fraunhofer J, Jelen-Esselborn S, Stemberger A. Coagulation changes during aortofemural bifurcation bypass: is volume and plasma substitution possible with hydroxyethyl starch alone? [Gerinnungsveranderungen bei aortofemoralem bifurkationsbypass: ist eine Volumen –und Plasmasubstitution mit hydroxyathylstarke allein moglich?]. *Anaesthesist* 1990;**39**(7):353–360.

Wahba 1996 *{published and unpublished data}*
Wahba A, Sendtner E, Birnbaum DE. Fluid resuscitation with Haemaccel vs. human albumin following coronary artery bypass grafting. *The Thoracic and Cardiovascular Surgeon* 1996;**44**(4):178–183. [MedLine: 1997051433].

Watkins 1990 *{published data only}*
Watkins J, Wild G, Appleyard TN, Hardy G. Complement activation by polystarch and gelatine volume expanders. *Lancet* 1990;**335**(8683):233.

Woittiez 1997 *{published and unpublished data}*
Hondebrink Y, Jeekel L, Oude Nijhuis J, Woittiez AJJ. Restoration of colloid osmotic pressure in hypoalbuminaemic patients. *Intensive Care Medicine* 1997; **23**(supp 1):S184.
Timmer B, Hondebrink Y, Oude Nijhuis J, Woittiez AJJ. Restoration of colloid osmotic pressure in hypoalbuminaemic patients. *Netherlands Journal of Medicine* 1998;**52**:A42.

References to studies excluded from this review

Boldt 1993
Boldt J, Knothe C, Schindler E, Hammermann H, Dapper F, Hempelmann G. Volume replacement with hydroxyethyl starch solution in children. *British Journal of Anaesthesia* 1993;**70**(6):661–665.

Boldt 2000b
Boldt J, Lehmann A, Rompert R, Haisch G, Isgro F. Volume therapy with a new hydroxyethyl starch solution in cardiac surgical patients before cardiopulmonary bypass. *Journal of Cardiothoracic and Vascular Anaesthesia* 2000;**14**(3):264–8.

Brehme 1993
Brehme S, Keysser G, Turowski A, Schmidt H. Hemorheologic effects of hydroxyethyl starch 200/ 0.5, dextran 40, oxypolygelatine and full electrolyte sodium over 48 hours [Hamorheologische wirkungen von hydroxyathylstarke 200/0.5, dextran 40, oxypolygelatine und vollelekttrolytlosung uber 48 studen]. *Zeitschrift fur die gesamte innerve medizin und ihre grenzgebiete* 1993;**48**(10): 506–510.

Bremerich 2000
Bremerich DH, Lischke V, Asskali F, Forster H, Behne M. Pharmacodynamics and tolerability of acetyl starch as a new plasma volume expander in patients undergoing elective surgery. *International Journal of Clinical Pharmacology and Therapeutics* 2000;**38**(8):408–414.

Charlet 1991
Charlet P, Zerr C, Robert D, Merville C, Renouf P, Khayat MC. Comparative trials of fluid gelatins on hemostasis in heart surgery in adults [Essais comparatifs des gelatines fluides sur l'hemostase dans la chirurgie cardiaque de l'adulte]. *Cahiers d'Anesthesiologie* 1991;**39**(4):233–238.

Christ 1997
Christ F, Niklas M, Kreimeier U, Lauterjung L, Peter K, Messmer K. Hyperosmotic-hyperoncotic solutions during abdominal aortic aneurysm (AAA) resection. *Acta Anaesthesiologica Scandinavica* 1997;**41**(1):62–70.

Emery 1992
Emery EF, Greenough A, Gamsu HR. Randomised controlled trial of colloid infusions in hypotensive preterm infants. *Archives of Disease in Childhood* 1992;**67**(10(S)): 1185–1188.

Gan 1999
Gan TJ, Bennett-Guerrero E, Phillips-Bute B, Wakeling H, Moskowitz DM, Olufolabi Y, et al.Hextend, a physiologically balanced plasma expander for large volume use in major surgery: a randomized phase III clinical trial. *Anesthesia and Analgesia* 1999;**88**(5):992–8.

Hankeln 1990
Hankeln K, Senker R, Beez M. Comparative study of the intraoperative effectiveness of 5% human albumin or 10% hydroxyethyl starch (HAES-steril) on hemodynamics and oxygen transport in 40 patients [Vergleichende Untersuchung zur intraoperativen Wirksamkeit von 5% Humanalbumin oder 10% Hydroxyathylstarke (HAES–steril) auf Hamodynamik und Sauerstofftransport bei 40 Patienten]. *Infusionstherapie* 1990;**17**(3):135–140.

Harke 1976
Harke H, Thoenies R, Margraf I, Momsen W. The influence of different plasma substitutes on blood clotting and platelet function during and after surgery [Der Einfluss verschiedener Plasmaersatzmittel auf Gerinnungssystem und Thrombocytenfunktion wahrend und nach operativen Eingriffen. Vorlaufige Ergebnisse einer klinischen Studie]. *Anaesthesist* 1976;**25**(8):366–373.

Hiippala 1996
Hiippala S, Teppo AM. Perioperative volume effect of HES 120/0.7 compared with dextran 70 and Ringer acetate. *Annales cChirurgiae et Gynaecologiae* 1996;**85**(4):333–339.

Huet 2000
Huet RCGG, Siemons AW, Baus D, van Rooyen-Butijn WT, Haagenaars JAM, van Oeveren W, Bepperling F. A novel hydroxyethyl starch (Voluven(TM)) for effective perioperative plasma volume substitution in cardiac surgery. *Canadian Journal of Anaesthesia* 2000;**47**(12):1207–1215.

Jovanovic 1997
Jovanovic K, Filipovic N, Romic P, Surbatovic M. Hetastarch in replacement of circulation volume compared to haemaccel and dextran 70 in pre-hospital resuscitation of polytraumatised patients. Intensive Care Medicine. 1997; Vol. 23:S184.

Korttila 1984
Korttila K, Grohn P, Gordin A, Sundberg S, Salo H, Nissinen E, et al.Effect of hydroxyethyl starch and dextran on plasma volume and blood hemostasis and coagulation. *Journal of Clinical Pharmacology* 1984;**24**(7):273–282.

Langeron 2001
Langeron ODM, Doelberg M, Ang ET, Bonnet F, Capdevila X, Coriat P. Voluven, a lower substituted novel hydroxyethyl starch (HES 130/0.4) causes fewer effects on coagulation in major orthopedic surgery than HES 200/0.5. *Anesthesia & Analgesia* 2001;**92**(4):855–62.

Puri 1983
Puri VK, Howard M, Paidipaty B, Singh S. Resuscitation in hypovolemia and shock: a prospective study of hydroxyethyl starch and albumin. *Critical Care Medicine* 1983;**11**(7): 518–523).

Rauch 2000
Rauch S, Sefrin P. Comparison of hydroxyethyl starch solutions derived from potato and corn starch [Vergleich von Hydroxyethylstarkelosungen aus Kartoffel– und Maisstarke]. *Anasthesiologie, Intensivmedizin, Notfallmedizin, Schmerztherapie* 2000;**35**(12):750–5.

Rehm 2000
Rehm M, Orth V, Scheingraber S, Kreimeier U, Brechtelsbauer H, Finsterer U. Acid-base changes caused by 5% albumin versus 6% hydroxyethyl starch solution in patients undergoing acute normovolemic hemodilution: a randomized prospective study. *Anesthesiology* 2000;**93**(5): 1174–83.

Strauss 1985
Strauss RG, Stump DC, Henriksen RA, Saunders R. Effects of hydroxyethyl starch and fibrinogen, fibrin clot formation, and fibrinolysis. *Transfusion* 1985;**25**(3):230–234.

Waxman 1989
Waxman K, Holness R, Tominaga G, Chela P, Grimes J. Hemodynamic and oxygen transport effects of pentastarch in burn resuscitation. *Annals of Surgery* 1989;**209**(3): 341–345.

References to studies awaiting assessment

Hopkins 1994
Hopkins PM. 6% hydroxyethylstarch with 4% gelatine as peri-operative intravenous volume replacement in surgical patients. National Research Register Version 1/1998.

Romero 1999
Romero J, Luna P, Fernandez B, Rojas E, Sarrano X, Alvarez H. The use of HAES-Steril 6% as a plasma expander after cardiopulmonary bypass in aortocoronary surgery [Uso de HAES esteril 6% como expansor plasmatico despues de la circulacion extracorporea en revascularizacion coronaria]. *Revista Mexicana de Anestesiologia* 1999;**22**:160–167.

Additional references

Altman 1996
Altman DG, Bland JM. Detecting skewness from summary information. *BMJ* 1996;**313**:1200.

Armstrong 1994
Armstrong RF, Bullen C, Cohen SL, Singer M, Webb AR. *Critical Care Algorithms*. Vol. **Oxford Medical Publications**, Oxford University Press, 1994.

Berlin 1997
Berlin JA. Does blinding of readers affect the results of meta-analyses?. *Lancet* 1997;**350**:185–6.

Boldt 1996
Boldt J, Heesen M, Muller M, pabsdorf M, Hempelmann G. The effects of albumin versus hydroxyethyl starch solution on cardiorespiratory and circulatory variables in critically ill patients. *Anesthesia and Analgesia* 1996;**83**: 254–61.

CIGAR 2000
The Cochrane Injuries Group Albumin Reviewers. Human albumin administration in critically ill patients (Cochrane Review). *The Cochrane Library* 2000, Issue 2.

Clarke 2001
Clarke M, Oxman AD, editors. Optimal search strategy for RCTs. *Cochrane Reviewers Handbook 4.1.5 [updated April 2002] appendix 5c* 2002, Issue 2.

Egger 1997
Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997;**315**:629–34.

Schierhout 2000
Schierhout G, Roberts I, Alderson P. Colloids compared to crystalloids in fluid resuscitation of critically ill patients (Cochrane Review). *The Cochrane Library* 2000, Issue 2.

Schulz 1995
Schulz KF, Chalmers I, Hayes RJ, Altman DG. Empirical Evidence of Bias. Dimensions of methodological quality associated with estimates of treatment effects in controlled trials. *JAMA* 1995;**273**:408–412.

Traylor 1996
Traylor RJ, Pearl RG. Crystalloid versus colloid: All colloids are not created equal. *Anesthesia and Analgesia* 1996;**83**: 209–12.

Vermeulen 1995
Vermeulen LC Jr, Ratko T A, Erstad BL, Brecher ME, Matuszewski K.A. A paradigm for consensus. The University Hospital Consortium guidelines for the use of albumin, nonprotein colloid, and crystalloid solutions. *Archives of Internal Medicine* 1995;**155**(4):373–9.

Yim 1995
Yim JM, Vermeyken LC, Erstad BL, Matuszewski KA, Burnett DA, Vlasses PH. Albumin and nonprotein colloid solution use in US academic health centers. *Archives of Internal Medicine* 1995;**155**(22):2450–5.

* *Indicates the major publication for the study*

FEEDBACK

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