

Albumin infusion for low serum albumin in preterm newborn infants (Review)

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ABSTRACT

Background

Intravenous albumin infusion is used to treat hypoalbuminaemia in critically ill infants. Hypoalbuminaemia occurs in a number of clinical situations including prematurity, the acutely sick infant, respiratory distress syndrome (RDS), chronic lung disease (CLD), necrotising enterocolitis (NEC), intracranial haemorrhage, hydrops fetalis and oedema. Fluid overload is a potential side effect of albumin administration. Albumin is a blood product and therefore carries the potential risk of infection and adverse reactions. Albumin is also a scarce and expensive resource.

Objectives

The primary objective was to assess the effect of albumin infusions on morbidity and mortality in preterm neonates with low serum albumin. A secondary objective was to assess whether albumin infusion is associated with significant side effects.

Search strategy

Searches were made of MEDLINE from 1966 to December 2006, CINAHL from 1982 to December 2006 and the current Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library, Issue 4, 2006). Previous reviews (including cross references) and abstracts were also searched.

Selection criteria

All randomised and quasi randomised controlled trials in which individual patients were allocated to albumin infusion versus control were included. Cross-over studies were excluded. Participants were preterm infants who had hypoalbuminaemia. Types of interventions included albumin infusion versus placebo (e.g. crystalloid) or no treatment.

Data collection and analysis

The reviewers worked independently to search for trials for inclusion and to assess methodological quality. Studies were assessed using the following key criteria: blinding of randomisation, blinding of intervention, completeness of follow up and blinding of outcome measurement.

Main results

Only two small studies were found for inclusion in this review and only one reported clinically relevant outcomes. This study found no significant differences for the primary outcome measure of death (RR 1.5 [95% confidence interval 0.3 - 7.43]) or secondary outcome measures of intraventricular haemorrhage, patent ductus arteriosus, necrotising enterocolitis, bronchopulmonary dysplasia, duration of mechanical ventilation and duration of oxygen therapy.

Authors' conclusions

There is a lack of evidence from randomised trials to determine whether the routine use of albumin infusion, in preterm neonates with low serum albumin, reduces mortality or morbidity, and no evidence to assess whether albumin infusion is associated with significant side effects. There is a need for good quality, double-blind randomised controlled trials to assess the safety and efficacy of albumin infusions in preterm neonates with low serum albumin.

PLAIN LANGUAGE SUMMARY

There is a lack of evidence from randomised trials to either support or refute the routine use of albumin infusion for premature babies with a low albumin level.

Albumin is a protein that is normally present in the blood. In premature infants, the albumin level in the blood can be low. Albumin is often given to premature babies with a low albumin level. Only two small randomised controlled trials have studied the use of albumin in sick premature babies, and the trials are not big enough or good enough to decide whether giving albumin helps babies in the short or long term. Therefore, the question of whether giving albumin does any good and is safe cannot be answered.

BACKGROUND

This review updates the existing review of "Albumin infusion for low serum albumin in newborn preterm infants" which was published in the Cochrane library, issue 3, 2004 (Jardine 2004).

Serum albumin levels are routinely measured and reported in intensive care nurseries and hypoalbuminaemia is a common finding in preterm (<37 weeks) neonates (<28 days). An older child or adult with a serum albumin level below 30 g/litre is classified as having hypoalbuminaemia (Greenough 1998). Normal albumin levels in preterm infants have been difficult to define. Serum albumin levels in preterm infants are significantly lower than those in term infants (Bergstrand 1972; Carlidge 1986; Zlotkin 1987; Reading 1990). Carlidge and Rutter (Carlidge 1986) demonstrated that serum albumin levels in the early neonatal period increased significantly with gestational age from a mean of 19 g/litre (90% confidence interval -12 to -28 g/litre) below 30 weeks to a mean of 31 g/litre (90% confidence interval -22 to -39 g/litre) at term.

Albumin accounts for approximately 50% of the serum proteins and is the major protein produced by hepatocytes in the liver (Vanek 1998). Albumin is not stored in the liver and is immediately excreted into the hepatic lymph system or the sinusoids (Uhing 2004). Albumin circulates from the intravascular space across the capillary wall into the interstitium and returns to the intravascular space via the lymphatic system. This circulation half-life is approximately 16 hours (Margaron 1998). The degradation half-life of albumin is 17 to 20 days (Doweiko 1991).

There are several clearly defined physiological functions of serum albumin. These include a binding and transport function, an effect on colloid osmotic pressure (with serum albumin accounting for approximately 60-80% of the colloid osmotic pressure), a role as a free radical scavenger and anticoagulant effects (primarily in inhibiting platelet aggregation and increasing prothrombin and partial prothrombin time) (Margaron 1998).

The causes of hypoalbuminaemia can be grouped into four basic categories: decreased synthesis; increased catabolism; increased loss and altered distribution between intravascular and extravascular body compartments (Uhing 2004). Hypoalbuminaemia occurs in a number of clinical situations including prematurity, the acutely

sick infant, respiratory distress syndrome (RDS), chronic lung disease (CLD), necrotising enterocolitis (NEC), intracranial haemorrhage, hydrops fetalis and oedema (Green 1993; Greenough 1999; Atkinson 1989; Bergstrand 1972; Carlidge 1986; Zlotkin 1987; Reading 1990).

In acute and chronic lung disease of the newborn, alveolar capillary membrane permeability is increased and high albumin levels are present in the alveolar aspirate (Watts 1995). In conjunction with this, pulmonary oedema is often found. Protein leakage into the alveolar space has been shown to occur in adults with respiratory distress syndrome. Leakage of protein into the alveolar space interferes with lung function and inactivates surfactant (Moison 1998). It has been suggested that albumin infusions should increase the capillary colloid pressure, thereby resulting in a decrease in flow of fluid out of the capillaries. This should then lessen fluid accumulation in the lungs, bowel wall and other interstitial spaces that could cause decreased pulmonary oxygen uptake, decreased absorption across the bowel wall or increased bowel wall secretions (Vanek 1998). However, it could also be argued that the underlying capillary leak will not be altered by albumin infusion and that increasing the amount of intravascular albumin will increase the amount that leaks out of the circulation, into the tissues, increasing oedema.

Low albumin levels have been found in infants who develop necrotising enterocolitis (Atkinson 1989). Albumin contributes to the antioxidant capacity of plasma; therefore, low levels of plasma albumin may lessen the total plasma antioxidant capacity. This may be of importance for preterm infants who are at risk of disease processes where reactive oxygen species are believed to play an important role such as respiratory distress syndrome, chronic neonatal lung disease and intracranial haemorrhage (Moison 1998).

Hypoalbuminaemia in adult surgical and medical patients has been associated with an increased incidence of pneumonia, septicaemia, mortality and longer hospital stay (Vanek 1998). Goldwasser and Feldman (Goldwasser 1997) showed that serum albumin concentration is inversely related to the risk of death in adult patients. Conversely a systematic review of albumin administration in critically ill adults found no evidence that albumin administration reduced mortality and suggested that it may increase mortality in selected patients (Cochrane 1998). Studies in adults

have looked at the influence of albumin on duration of intensive care stay and rate of recovery. Stockwell et al (Stockwell 1992) showed no difference between duration of stay, complications or outcomes in two groups of patients who had either albumin or gelatin for fluid replacement.

There are documented cases of the complete absence of albumin, analbuminaemia, as a result of a rare genetic condition (Watkins 1994). These patients suffered only mild abnormalities of lipid metabolism and mild oedema; half of the reported patients were entirely asymptomatic. Several studies have shown that oedema in preterm infants is common but poorly correlated with hypoalbuminaemia (Cartledge 1986; Reading 1990; Kenny 1995) and the routine administration of albumin for oedema is not warranted.

Intravenous albumin infusion to treat hypoalbuminaemia is used in intensive care nurseries. Green and Morgan (Green 1993) suggested giving 20% albumin whenever the serum albumin falls below 25 g/litre. Intravenous albumin has also been administered to high risk infants who are hypotensive and in respiratory distress (Lay 1980). It has been advocated in the past that ill infants with RDS should be given albumin infusions whenever their serum albumin falls below 20 g/litre (Greenough 1992); however, it is now recommended that care should be taken as albumin infusions may be harmful (Greenough 1999).

Using albumin to treat hypoalbuminaemia is different from using albumin for volume expansion, which has been assessed in other Cochrane reviews (Alderson 2004; Bunn 2003; Osborn 2004).

Fluid overload is a potential side effect of albumin administration. Complications of fluid overload include PDA, NEC, and possibly CLD (Greenough 1999). Albumin is a blood product and therefore carries the potential risk of infection and adverse reactions. Although the risks are low, these risks should be considered. Albumin (which comes in a number of commercial preparations with concentrations ranging from 4 - 20%) is also a scarce and expensive resource with hospitals frequently experiencing shortages (Golub 1994).

OBJECTIVES

The primary objective was to determine the effect of albumin infusions on morbidity and mortality in preterm neonates with low serum albumin. A secondary objective was to assess whether albumin infusion is associated with significant side effects.

Data permitting, sub-group analyses were planned to determine whether results differed by:

Population:

- i. gestational age (e.g. extremely premature [less than or equal to 28 weeks] versus premature [29 to 36 weeks]).
- ii. birthweight (e.g. very low birth weight infants, < 1500 grams, versus infants greater than or equal to 1500 grams or extremely

low birth weight infants [< 1000 grams] versus infants greater than or equal to 1000 grams).

iii. infants with particular illnesses or signs (e.g. oedema, RDS, CLD)

iv. hypoalbuminaemia (e.g. less than 30 g/L or less than 25 g/L or less than 20 g/L)

Intervention:

i. dose of albumin infused (e.g. < 1.5 g/kg/dose versus greater than or equal to 1.5 g/kg/dose)

ii. type of treatment used in the control group (placebo [e.g. crystallloid] or no treatment)

iii. whether albumin is a single infusion on one occasion or a policy of repeated infusions to maintain a serum albumin above a certain level

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

All randomised and quasi-randomised controlled trials in which individual patients were allocated to albumin infusion versus control. Cross-over studies were excluded.

Types of participants

Preterm infants who had hypoalbuminaemia. Hypoalbuminaemia defined as < 30 g/L, < 25 g/L and < 20 g/L.

Types of intervention

Albumin infusion versus placebo (i.e. any other non-colloidal fluid that does not contain albumin) or no treatment. Albumin infusion included any regimen from a single infusion on one occasion to a policy of repeated infusions to maintain the serum albumin above a certain level.

Types of outcome measures

Primary outcomes:

Mortality (neonatal [28 days], before discharge)

Neurodevelopmental outcome at 1 year, 18 months, 2 years, 5 years

Secondary outcomes:

Chronic lung disease (requiring oxygen at 28 days or 36 weeks postmenstrual age)

Intraventricular haemorrhage (any, grade 3 - 4)

Duration of mechanical ventilation (IPPV) - hours/days

Duration of respiratory support (IPPV or CPAP) - hours/days

Duration of oxygen therapy - hours/days

Septicaemia

Necrotising enterocolitis

Duration of ICN stay - hours/days

Duration of hospital stay - hours/days

Patent ductus arteriosus requiring therapy (medical or surgical)

Cost

Immediate adverse effects (e.g. hypertension, increased ventilation requirements and increased oxygenation)

SEARCH METHODS FOR IDENTIFICATION OF STUDIES

See: methods used in reviews.

The standard search strategy for the Cochrane Neonatal Review Group was used: Searches were made of MEDLINE from 1966 to December 2006, CINAHL from 1982 to December 2006 and the current Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library, Issue 4, 2006), using the following strategy:

MeSH search terms 'serum albumin', OR 'albumins'; OR the text words 'albumin', OR 'albumen', OR 'hypoalbuminemia', OR 'hypoalbuminaemia', OR 'hypo-albuminemia', OR 'hypo-albuminaemia';

AND

MeSH search term 'infant, newborn'

AND

MeSH terms '*Albumins / ad [Administration & Dosage]', OR 'Albumins / tu [Therapeutic Use]', OR '*Albumins / pd [Pharmacology]', OR the text word phrase "albumin infusion"

Previous reviews (including cross references), and abstracts were also searched. Searches were not restricted to publications in the English language or published data.

METHODS OF THE REVIEW

Criteria and methods used to assess the methodological quality of the trials:

Standard methods of the Cochrane Collaboration (Clarke 2002) and its Neonatal Review Group were used. The reviewers worked independently to search for trials for inclusion and to assess methodological quality. Studies were assessed using the following key criteria: blinding of randomisation, blinding of intervention, completeness of follow up and blinding of outcome measurement. However, quality criteria did not determine whether a study was excluded or included from this review. Data were extracted independently by the reviewers. Differences were resolved by discussion and consensus of the reviewers. Investigators were contacted for additional information and data where necessary.

For individual trials, where possible, mean differences (and 95% confidence intervals) were reported for continuous variables. For categorical outcomes, the relative risk and risk difference (and 95% confidence intervals) were reported.

For the meta-analysis, where possible, weighted mean differences (and 95% confidence intervals) were planned to be reported for

continuous variables, and the relative risk and risk difference (and 95% confidence intervals) for categorical outcomes. A fixed effects model was planned. Number needed to treat was to be calculated where appropriate.

Given sufficient numbers of included studies we planned to test for heterogeneity where appropriate before deciding to pool the results.

DESCRIPTION OF STUDIES

The above search strategy found only three possibly eligible studies of albumin infusions in hypoalbuminaemic preterm infants: two are included in this review. Another study has been identified (Porto 2005) that is currently awaiting translation into English and then eligibility assessment.

Kanarek et al (Kanarek 1992) studied the concurrent administration of albumin versus placebo with total parenteral nutrition (TPN) in 24 premature infants (12 in each group). To be eligible the infants had to

- (1) have respiratory distress requiring assisted ventilation
- (2) have had significant hypotension (2 SD below the mean for gestational age, necessitating the use of a plasma expander and/or inotropic agents)
- (3) have a plasma albumin level below 30 g/L at 48 to 72 hours of life
- (4) require TPN for nutritional support

Therefore, the population studied in this study was a subset of the population of interest for this review. The albumin was added to the TPN in quantities that were calculated to raise the serum albumin above 30 g/L (maximum 1 g/kg/day).

Greenough et al (Greenough 1993) studied the effect of albumin infusion versus placebo on 40 premature infants (28 - 34 weeks gestational age, 20 in each group). Study subjects were newborn infants who were ventilator dependant at less than seven days of age and had a serum albumin level of ≤ 30 g/L. Therefore, the population studied in this study was also a subset of the population of interest for this review. Infants were not eligible if they were receiving peritoneal dialysis, had chest drains in situ or were hypotensive (defined as systolic blood pressure less than 40 mmHg). Infants were randomised (the method of randomisation is unknown) to receive either albumin administered as 5 ml/kg of 20% salt-poor human albumin or placebo (5 ml/kg of the infants maintenance fluids). Attempts were made to contact the primary author and no reply was received (we requested clarification of blinding of randomisation, blinding of intervention, completeness of follow up and blinding of outcome measurement; and whether other data were available for any of our primary and secondary outcomes).

The study by Bland et al (Bland 1973) investigated albumin infusions in low birth weight newborn infants at risk for respiratory

distress who were acidaemic with a low total serum protein level (whether they were hypoalbuminaemic or not is unknown).

METHODOLOGICAL QUALITY

Kanarek et al (Kanarek 1992):

- blinding of randomisation (allocation concealment) - yes
- blinding of intervention - yes
- completeness of follow up - yes
- blinding of outcome measurement - unknown

Greenough et al (Greenough 1993):

- blinding of randomisation (allocation concealment) - unknown
- blinding of intervention - unknown
- completeness of follow up - no (data were analysed and reported for only 15 out of 20 subjects in each group)
- blinding of outcome measurement - unknown

RESULTS

The following is a report of the results of individual studies. Due to the significant heterogeneity in study quality and the lack of pre-specified outcomes in one of the studies, there has been no attempt to pool the results.

The results below are organised using our pre-specified primary and secondary outcomes.

Kanarek et al (Kanarek 1992)

This study found no significant effect of albumin infusion on any of our pre-specified primary and secondary outcomes.

Primary outcome measures:

- Mortality - there were 3/12 deaths in the experimental group and 2/12 deaths in the control group: RR 1.5 (95% confidence interval 0.3 to 7.43). It is not stated whether mortality is 28 day mortality or at discharge
- Neurodevelopmental outcomes were not assessed or reported

Secondary outcomes:

- There were 5/12 intraventricular haemorrhages (not further defined) in the experimental group and 4/12 in the control group: RR 1.25 (95% confidence interval 0.44 to 3.55)
- There was 0/12 infants with necrotising enterocolitis in the experimental group and 1/12 in the control group: RR 0.33 (95% confidence interval 0.01 to 7.45)

- 5/12 patients in the experimental group and 6/12 in the control group had bronchopulmonary dysplasia (not further defined): RR 0.83 (95% confidence interval 0.35 to 2.0)

- 5/12 patients in the experimental group and 7/12 in the control group had a patent ductus arteriosus (not further defined): RR 0.71 (95% confidence interval 0.31 to 1.63)

- The mean duration of assisted ventilation in the experimental group was 36.9 days (SD 22.9), the mean duration in the control group was 30.8 days (SD 15.2). Mean difference 6.1 days (95% confidence interval -9.45 to 21.65)

- The mean duration of oxygen therapy in the experimental group was 45.7 days (SD 19.1), the mean duration in the control group was 40.4 days (SD 12.5). Mean difference 5.3 days (95% confidence interval -7.62 to 18.22)

The mean arterial blood pressures (MABP) were reported for days three and six. There were no significant differences between the two groups in the first few days of life: the mean (SD) MABP was 35.8 (3.8) mmHg in the albumin group and 34.4 (2.4) mmHg in the control group. When TPN was commenced on day three the control group's MABP was unchanged for the rest of the study whereas the albumin group's MABP continued to rise up until day six when the mean (SD) MABP was 38.9 (4.8) mmHg. No data are given for MABP on day six in the control group; however it is stated that the difference in MABP between the two groups was statistically significant ($p < 0.05$). Immediate adverse events of albumin infusion including hypertension was one of our secondary outcome measures: none of these data represent hypertension and this reported difference is unlikely to have any clinical significance.

Other outcomes that were reported in this study that we did not pre-specify include:

- Time taken to tolerate full feeds - albumin group mean (SD) 16.8 (7.6) days, and control group mean (SD) 18.8 (6.9) days
- Time taken to regain birth weight - albumin group mean (SD) 18.9 (5.9) days, and control group (SD) 24.9 (2.1) days

Greenough et al (Greenough 1993)

Primary outcome measures:

- Mortality and neurodevelopmental outcomes were not assessed or reported

Secondary outcomes:

None of our secondary outcomes were reported.

The discussion section of the study report states that there were no adverse effects with albumin in this study (none of the infants required increased oxygen or ventilator support).

Other outcomes (that we did not pre-specify) were reported in this study; these included:

- Fluid input versus output in 12 hour periods preceding infusion, during infusion and post infusion. No significant differences were reported.
- Albumin concentration pre and post infusion. The albumin concentration increased significantly in the albumin group but not in the placebo group.
- Weight pre and post infusion. Weight decreased significantly in the albumin group and increased significantly in the placebo group.
- Peak inspiratory pressures pre and post infusion. There was no significant difference reported.
- Inspired oxygen concentration pre and post infusion. This did fall significantly in the albumin group, and in the placebo group it also fell but not significantly.

DISCUSSION

The studies included in our review investigated a small, specific subset of the total number of premature infants receiving albumin infusions. Only one of the studies reported clinically relevant outcomes (Kanarek 1992) - it found no significant differences for our primary outcome measure of death or secondary outcome measures of IVH, PDA, NEC, bronchopulmonary dysplasia, duration of mechanical ventilation and duration of oxygen therapy. There was a statistically significantly higher mean arterial BP in the albumin group at six days of age; however, this is unlikely to have any clinical relevance. The results of this single small study should be treated with caution - the confidence intervals for reported outcomes are wide and a real difference might be masked by a type 2 error. Conversely, any differences seen could easily be due to chance alone. Our second primary outcome (neurodevelopmental outcome) and some of our secondary outcomes were not assessed in the included studies (i.e. there were insufficient or no data to assess other clinically important outcomes). The study by Greenough et al (Greenough 1993) did not report any of our primary and secondary outcome measures.

In some neonatal intensive care units albumin is used frequently. For example, at the Grantley Stable Neonatal Unit in Brisbane, Australia, 12% of all preterm infants admitted and 38% of babies

<30 weeks GA will get at least one infusion of 20% albumin to increase serum albumin levels or treat oedema [data from the NeoData database, Royal Women's Hospital, Brisbane for years 2000 to 2002 inclusive]. Such an extensive use of this treatment should be based on better evidence than is currently available.

AUTHORS' CONCLUSIONS

Implications for practice

There is a lack of evidence from randomised trials to determine whether the routine use of albumin infusion, in preterm neonates with low serum albumin, reduces mortality or morbidity, or is associated with significant side effects.

Implications for research

If albumin infusion for hypoalbuminaemic pre-term infants is thought to be worthwhile then there is a need for good quality, double-blind randomised controlled trials to assess the safety and efficacy of this practice.

POTENTIAL CONFLICT OF INTEREST

None.

SOURCES OF SUPPORT

External sources of support

- Department of Health and Ageing, Commonwealth Government, Canberra ACT - Supporting the Centre for Clinical Studies, Mater Hospital AUSTRALIA

Internal sources of support

- Grantley Stable Neonatal Unit, Royal Women's Hospital, Brisbane AUSTRALIA
- Royal Children's Hospital, Brisbane AUSTRALIA
- Dept of Paediatrics and Child Health, University of Queensland, Brisbane AUSTRALIA
- Centre for Clinical Studies, Mater Hospital, Brisbane AUSTRALIA

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References to other published versions of this review**Jardine 2004**

Jardine LA, Jenkins-Manning S, Davies MW. Albumin infusion for low serum albumin in preterm newborn infants. *Cochrane Database of Systematic Reviews* 2004, Issue 3. Art. No.: CD004208. DOI: [10.1002/14651858.CD004208.pub2](https://doi.org/10.1002/14651858.CD004208.pub2).

T A B L E S**Characteristics of included studies**

Study	Greenough 1993
Methods	RCT. The method of randomisation is unknown. Whether group allocation was blinded is unknown. Whether the intervention was blinded is unknown. Data is analysed and reported for 30 of the 40 enrolled participants. None of the outcomes reported are said to be blinded.
Participants	Infants between 24 and 34 weeks gestation were eligible for the study if they were ventilator-dependant at less than 7 days of age and had a serum albumin level of less than or equal to 30g/l. They were not eligible if they were receiving peritoneal dialysis, had chest drains in situ or were hypotensive. Hypotension was defined as a systolic blood pressure less than 40 mmHg. 40 infants were entered into the study. Data was incomplete for 5 in each group. The analysis was performed on the remaining 30 participants (15 in each group).
Interventions	40 patients were randomly allocated to receive either albumin (n=20; 5 ml/kg 20% salt-poor human albumin) or placebo (n=20; 5 ml/kg of infant's maintenance fluids). The volume of the trial infusion was subtracted from the total daily fluid requirement and given at the maintenance rate.

Outcomes Primary outcome measures: mortality and neurodevelopmental outcomes were not assessed or reported.

Secondary outcomes: none of our secondary outcomes were reported. The discussion section of the study report states that there were no adverse effects with albumin in this study (none of the infants required increased oxygen or ventilator support).

Other outcomes (that we did not pre-specify) reported:
 Fluid input versus output in 12 hour periods preceding infusion, during infusion and post infusion.
 Albumin concentration pre and post infusion.
 Weight pre and post infusion.
 Peak inspiratory pressures pre and post infusion.
 Inspired oxygen concentration pre and post infusion.

Notes

Allocation concealment B – Unclear

Study Kanarek 1992

Methods RCT. The method of randomisation is unknown. Group allocation was blinded (sealed envelopes). The intervention was blinded. Follow up was complete. It is unknown if outcome measurement was blinded.

Participants To be eligible the infants had to (1) have respiratory distress requiring assisted ventilation; (2) have had significant hypotension (2 SD below the mean for gestational age, necessitating the use of a plasma expander and/or inotropic agents); (3) have a plasma albumin level below 30 g/L at 48 to 72 hours of life and (4) require TPN for nutritional support.

24 premature (not defined) infants were enrolled (12 in each group).

Interventions The albumin was added to the TPN in quantities that were calculated to raise the serum albumin above 30 g/L (maximum 1 g/kg/day). 24 patients were randomised to receive either added albumin to their TPN (n=20) or standard TPN solution (n=20).

Outcomes Primary outcome measures:
 Mortality.

Secondary outcomes:
 intraventricular haemorrhages (not further defined).
 Necrotising enterocolitis.
 Bronchopulmonary dysplasia (not further defined).
 Patent ductus arteriosus (not further defined).
 The duration of assisted ventilation.
 The duration of oxygen therapy.
 The mean arterial blood pressures (MABP) were reported for days 3 and 6.

Other outcomes:
 Time taken to tolerate full feeds.
 Time taken to regain birth weight.

Notes

Allocation concealment A – Adequate

Characteristics of excluded studies

Study Reason for exclusion

Bland 1973 This RCT investigated albumin infusions in low birth weight newborn infants at risk for respiratory distress who were acidaemic with a low total serum protein level (whether they were hypoalbuminaemic or not is unknown).

Characteristics of excluded studies (Continued)

ANALYSES

Comparison 01. Albumin vs placebo in infants with plasma albumin <30g/L and requiring assisted ventilation (not defined)

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Mortality			Relative Risk (Fixed) 95% CI	Subtotals only
02 IVH - any grade			Relative Risk (Fixed) 95% CI	Subtotals only
03 Bronchopulmonary dysplasia (not defined)			Relative Risk (Fixed) 95% CI	Subtotals only
04 Necrotising enterocolitis			Relative Risk (Fixed) 95% CI	Subtotals only
05 Patent ductus arteriosus			Relative Risk (Fixed) 95% CI	Subtotals only
06 Duration of assisted ventilation (days)			Weighted Mean Difference (Fixed) 95% CI	Subtotals only
07 Duration of oxygen therapy (days)			Weighted Mean Difference (Fixed) 95% CI	Subtotals only

INDEX TERMS

Medical Subject Headings (MeSH)

Albumins [*administration & dosage; adverse effects]; Hypoalbuminemia [mortality; *therapy]; Infant, Low Birth Weight [blood]; Infant, Newborn; Infant, Premature [*blood]; Infant Mortality

MeSH check words

Humans

COVER SHEET

Title	Albumin infusion for low serum albumin in preterm newborn infants
Authors	Jardine LA, Jenkins-Manning S, Davies MW
Contribution of author(s)	All three reviewers conducted the search for studies and assessed them for inclusion in this review. LAJ wrote the review. MWD and SJM co-wrote the review.
Issue protocol first published	2003/2
Review first published	2004/3
Date of most recent amendment	15 February 2007
Date of most recent SUBSTANTIVE amendment	03 June 2004
What's New	This review updates the existing review "Albumin infusion for low serum albumin in preterm newborn infants" published in The Cochrane Library, Issue 3, 2004 (Jardine 2004). One new paper was identified. This paper is awaiting translation into English to see if it meets eligibility criteria. Other minor additions to the background have been made to provide more information on the normal physiology of albumin.
Date new studies sought but none found	03 January 2007

Date new studies found but not yet included/excluded Information not supplied by author

Date new studies found and included/excluded Information not supplied by author

Date authors' conclusions section amended Information not supplied by author

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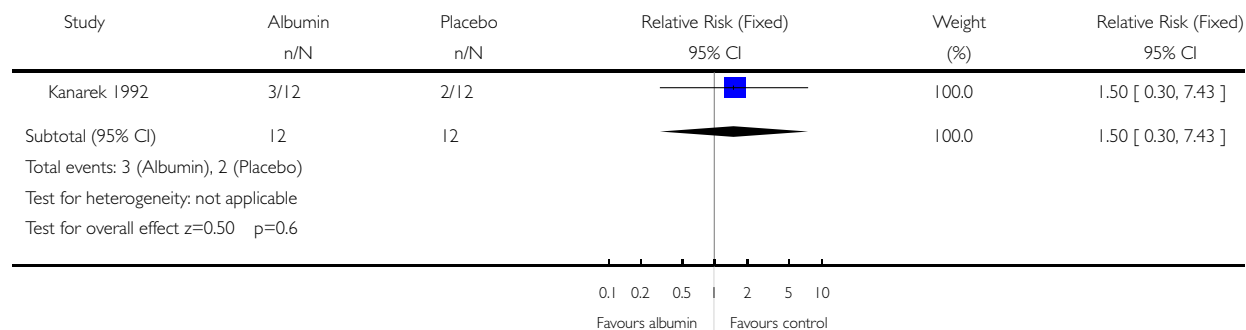
GRAPHS AND OTHER TABLES

Analysis 01.01. Comparison 01 Albumin vs placebo in infants with plasma albumin <30g/L and requiring assisted ventilation (not defined), Outcome 01 Mortality

Review: Albumin infusion for low serum albumin in preterm newborn infants

Comparison: 01 Albumin vs placebo in infants with plasma albumin <30g/L and requiring assisted ventilation (not defined)

Outcome: 01 Mortality

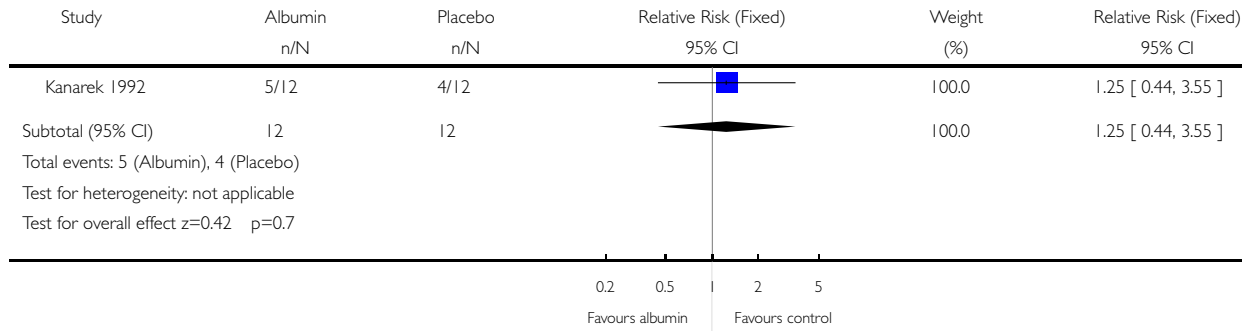


Analysis 01.02. Comparison 01 Albumin vs placebo in infants with plasma albumin <30g/L and requiring assisted ventilation (not defined), Outcome 02 IVH - any grade

Review: Albumin infusion for low serum albumin in preterm newborn infants

Comparison: 01 Albumin vs placebo in infants with plasma albumin <30g/L and requiring assisted ventilation (not defined)

Outcome: 02 IVH - any grade

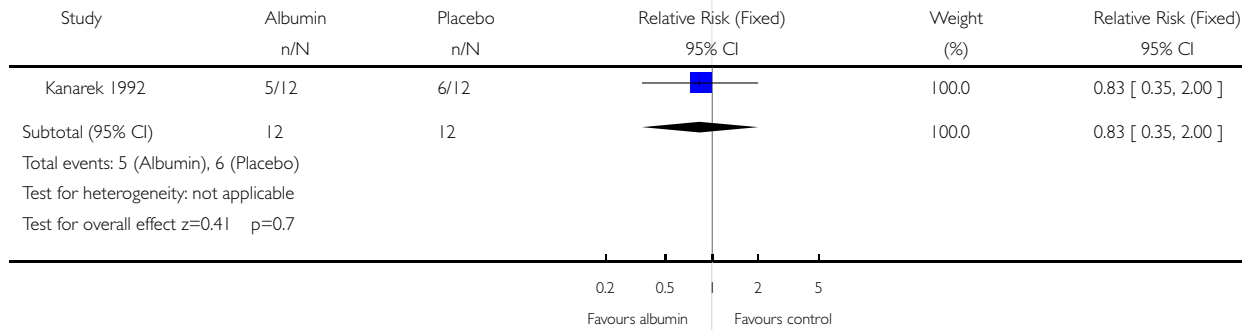


Analysis 01.03. Comparison 01 Albumin vs placebo in infants with plasma albumin <30g/L and requiring assisted ventilation (not defined), Outcome 03 Bronchopulmonary dysplasia (not defined)

Review: Albumin infusion for low serum albumin in preterm newborn infants

Comparison: 01 Albumin vs placebo in infants with plasma albumin <30g/L and requiring assisted ventilation (not defined)

Outcome: 03 Bronchopulmonary dysplasia (not defined)

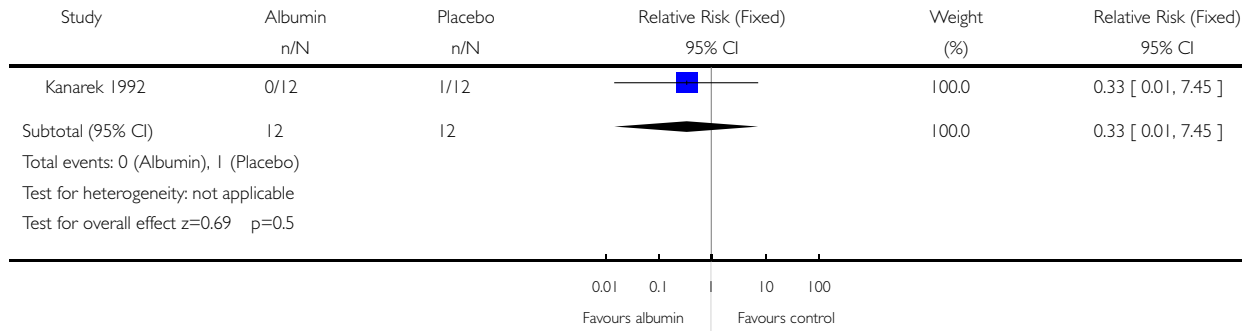


Analysis 01.04. Comparison 01 Albumin vs placebo in infants with plasma albumin <30g/L and requiring assisted ventilation (not defined), Outcome 04 Necrotising enterocolitis

Review: Albumin infusion for low serum albumin in preterm newborn infants

Comparison: 01 Albumin vs placebo in infants with plasma albumin <30g/L and requiring assisted ventilation (not defined)

Outcome: 04 Necrotising enterocolitis

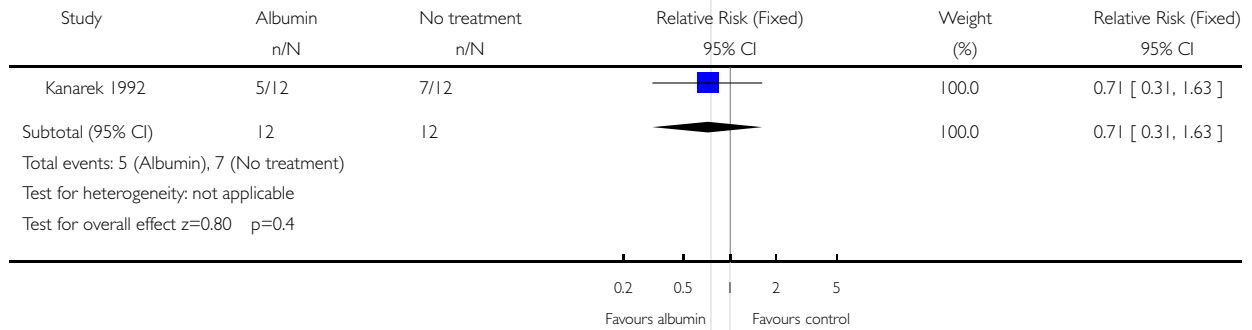


Analysis 01.05. Comparison 01 Albumin vs placebo in infants with plasma albumin <30g/L and requiring assisted ventilation (not defined), Outcome 05 Patent ductus arteriosus

Review: Albumin infusion for low serum albumin in preterm newborn infants

Comparison: 01 Albumin vs placebo in infants with plasma albumin <30g/L and requiring assisted ventilation (not defined)

Outcome: 05 Patent ductus arteriosus

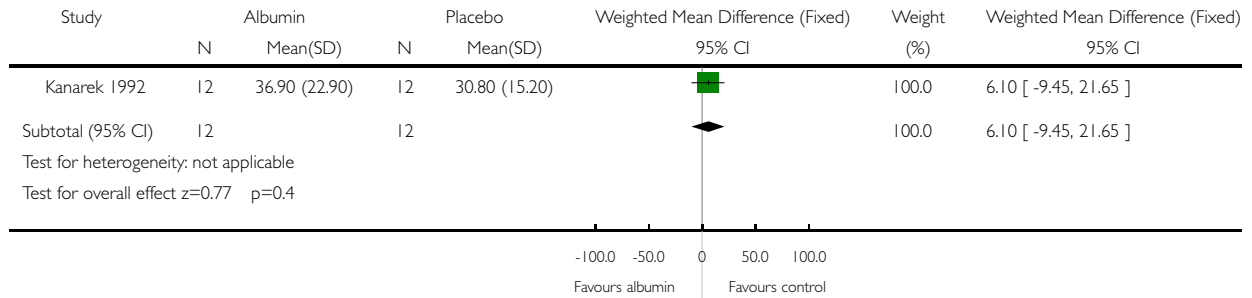


Analysis 01.06. Comparison 01 Albumin vs placebo in infants with plasma albumin <30g/L and requiring assisted ventilation (not defined), Outcome 06 Duration of assisted ventilation (days)

Review: Albumin infusion for low serum albumin in preterm newborn infants

Comparison: 01 Albumin vs placebo in infants with plasma albumin <30g/L and requiring assisted ventilation (not defined)

Outcome: 06 Duration of assisted ventilation (days)



Analysis 01.07. Comparison 01 Albumin vs placebo in infants with plasma albumin <30g/L and requiring assisted ventilation (not defined), Outcome 07 Duration of oxygen therapy (days)

Review: Albumin infusion for low serum albumin in preterm newborn infants

Comparison: 01 Albumin vs placebo in infants with plasma albumin <30g/L and requiring assisted ventilation (not defined)

Outcome: 07 Duration of oxygen therapy (days)

