



HUMAN ALBUMIN INDICATIONS GUIDELINE

Absolute Indications

1. Large Volume Paracentesis in Patients with Cirrhosis

Defined as >4 L removed with documented cirrhosis (or any amount removed if creatinine is \geq 1.5 gm/dL).

Dosing recommendation:

Albumin 20% 6-8 g per liter of ascitic fluid removed.

2. Plasmapheresis

Albumin, in conjunction with large-volume plasma exchange, is appropriate. Large-volume plasma exchange is defined as > 20 mL/kg in one session, or more than 20 mL/kg in repeated sessions.

• Crystalloid solutions and albumin/crystalloid combination should be considered as cost-effective alternatives for smaller volume exchanges.

Dosing recommendation:

Albumin 5% as per plasmapheresis protocol (based on plasma volume and serum fibrinogen level).

3. Spontaneous Bacterial Peritonitis (SBP) and cirrhosis

Defined as patients with ascitic fluid PMN counts ≥250 cells/mm3 plus at least one of the following:

- 1.Serum creatinine >1 mg/dL
- 2. Blood urea nitrogen >30 mg/dL
- 3. Total bilirubin > 4 mg/dL

Dosing recommendation:

Albumin 20% 1.5 g/kg within 6-hours of detection (day 1) and 1 g/kg on day 3

4. Diagnosis of Suspected Hepato-Renal Syndrome (HRS)

Defined as acute renal dysfunction (serum creatinine >1.5 mg/dL) in the presence of cirrhosis.

Dosing recommendation:

Albumin 20% 1 g/kg/day for 2 days (dose up to a maximum of 100 g per day).

5. Hepatorenal Syndrome (HRS), confirmed

Defined as:

- i. Serum creatinine >1.5 mg/dL in the presence of cirrhosis
- ii. Absence of shock, ongoing bacterial infection, and/or current treatment with nephrotoxic drugs
- iii. Absence of sustained improvement in renal function after discontinuation of diuretics and a trial of albumin 1 g/kg
- iv. Absence of proteinuria (<500 mg/day) or hematuria (<50 red cells per high-power field)
- v. Absence of ultrasonographic evidence of obstructive uropathy or parenchymal renal disease

Dosing recommendation:

- 1. Albumin 20% 25-50 g daily for a total of 72 hours (starting 1-2 days after initial diagnostic trial of albumin, if applicable), can last until 14 days and more if necessary.
- 2. Should be used in addition to midodrine and octreotide.

May Be Beneficial

1. Postoperative Volume Resuscitation After Cardiac Surgery

Albumin 5% may only be used if \geq 3 L crystalloid has been administered within a given 24-hour period without an adequate hemodynamic response.

This only includes crystalloids given as a bolus (excludes maintenance fluids, carrier fluids, etc.)

This excludes fluid given intraoperatively

2. Major surgery

The use of albumin may be indicated in subjects undergoing major surgery (> 40% resection of the liver, extensive intestinal resection) when, after normalisation of circulatory volume, the serum albumin is < 2-2.5 g/dL

Dosing recommendation

Albumin 20%, 25 gm/day until albumin is \geq 2.5 gm/dL.If serum albumin remains \leq 2.5, may continue albumin dosing up to 4 days.

3. Refractory edema

For patients with severe hypoalbuminemia (plsma albumin <2~g/dl) and refractory edema infusion of poor salt albumin with furosemide may be helpful. Sodium excretion must be monitored

Dosing recommendation

40-80 mg of furosemide with 200 ml of albumin 20% solution

4. Postoperative Heart Transplant

May be useful to treat anasarca in patients with albumin≤3 gm/dL

Dosing recommendation

- 1. Albumin 20%, 25 gm IV BID x2 doses (or 12.5 gm IV q6h x4 doses) may be used in combination with diuretics.
- 2. Monitor urine output and volume status and assess daily. If successful at achieving diuresis, may reorder albumin until serum albumin is >3 gm/dL but must be renewed each day after daily assessment.

5. Postoperative Lung Transplant

Grade 2 or higher Primary Graf Dysfunction

Dosing recommendation

Albumin 20%, 25 gm IV BID x2 doses (or 12.5 gm IV q6h x4 doses) for up to 48 hours may be used in combination with diuretics to improve oxygenation.

6. Postoperative Liver Transplant

May be useful for the control of ascites and peripheral edema if serum albumin is <2.5 gm/dl

Dosing recommendation

Albumin 20%, 25 gm/day until albumin is ≥ 2.5 gm/dL.

If serum albumin remains <2.5, may continue albumin dosing up to 4 days; consult liver surgeons thereafter for consideration of continued use.

7. Burns/Thermal Injuries

Use only for burns with greater than 50% BSA (body surface area) when unresponsive to crystalloid. After 24 hr: Maintain albumin conc. of $2.5 \pm 0.5 \, \text{g} / 100 \, \text{mL}$ or a total serum protein level of $5.2 \, \text{g} / 100 \, \text{mL}$

Dosing recommendations

All infusion days: Albumin 5% 0.3-0.5 mL/kg/BSA, usually 50-100 mL/hour or 1-2 mL/min

8. Severe Nephrotic Syndrome (e.g. with anasarca or pulmonary edema)

May be used in demonstrated nephrotic syndrome (>3 g/day of urinary protein excretion [or spot protein equivalent] + hypercholesterolemia + hypoalbuminemia) and loop diuretic resistance (defined as an "insufficient response" to an intravenous bolus dose of \geq 160 mg furosemide or 4 mg bumetanide followed by \geq 8-hour infusion of \geq 20 mg/hr furosemide or \geq 0.5 mg/hour bumetanide)

Dosing recommendation

Albumin 20%, 25 gm in combination with diuretics to effect adequate diuresis.

9. Acute Lung Injury/Acute Respiratory Distress Syndrome

It may be considered, but not recommended

Use with Lasix(furosemide). NOT in the same IVF.

Dosing recommendation

Albumin 20% 25 g (100-200 ml) over 30-60 mins to target serum albumin concentrations >25 g/l. it may be Repeated every 8 hours for 3 days

10. Hypotension During Dialysis

These are some other options: saline infusions, adjust antihypertensives,

Caffeine, midodrine, extend dialysis duration.

Dosing recommendation

Albumin 20% 100 mL each episode of dialysis

11. Ovarian Hyperstimulation Syndrome- Treatment

It is not recommended, but it may be used

Dosing recommendation

Albumin 20% - 50 to 100 g over 4 hours and repeated at 4-12 hour intervals as necessary

12. Chronic PICU Patients with Hypoalbuminemia and Edema

May be considered

Dosing recommendation

Albumin 20% 3-4 mL/kg, once or twice a day

13. Hemolytic Disease of the Newborn

An FDA-approved indication for 20% albumin

- According to Micromedex, evidence is inconclusive
- Should not be administered in conjunction with phototherapy, nor should it be used **prior** to exchange transfusion.
- It has been used with mixed results as an adjuvant to exchange transfusions and should be administered **only with concurrent transfusion of blood.**
- Crystalloids & non-protein colloids do not have bilirubin-binding properties and should not be considered as alternatives to albumin

Dosing recommendation

1 g per kilogram body weight prior or during exchange transfusion

14. Cardiac Bypass, Circuit Priming

Possibly, depending on circuits used. Also institution/patient population specific

NOTE: some reports indicate the use of 20% albumin for this purpose. However, it is diluted with non-colloid solutions to approximately 5%

Dosing recommendation

Pediatric: weight dependent Adult: 1200 – 2000 mL

15. Volume Resuscitation for Hypovolemia

It is not routinely used, but albumin 5% may be considered.

NOTE: Albumin resuscitation in traumatic brain injured patients demonstrated a high mortality rate

16. Fluid Resuscitation for Sepsis

5% albumin may be appropriate

17. Nutritional Intervention

Albumin should not be used as a supplemental source of protein calories in patients requiring nutritional intervention.

• However, patients with diarrhea associated with enteral feeding intolerance may benefit from the

administration of albumin if all the following conditions are met:

- i. Significant diarrhea (> 2 liters per day) occurs;
- ii. Serum albumin is < 2.0 g/dl;
- iii. Continued diarrhea occurs despite trial of short-chain peptide and elemental formulas;
- iv. Other causes of diarrhea have been considered and ruled out.

18. Low Serum Albumin in Hemodynamically Unstable Patient in Critical Care (Albumin <2.5 g/dl)

Occasionally HAS 20% may be indicated.

Albumin administration at Low serum albumin in the absence of ascites, SBP or hepatorenal syndrome is not indicated.

Dosing recommendation

(desired albumin-serum albumin) \times patient Wt \times 0.8

19. Subarachnoid Hemorrhage

Cerebral Ischemia or hemorrhage as part of triple H therapy. If Hct is elevated crystalloid should be given as part of hemodilution.

Albumin can be given if: Aneurysmal subarachnoid hemorrhage

Goal CVP 6-8 to decrease risk of vasospasm

If delayed vasospasm occurs, CVP goal of 8-12

Albumin administration may be helpful if serum albumin <3 g/dl

Dosing recommendation

5% albumin 250 ml Q2-4H prn CVP goal; adjust rate of crystalloids by 25% if frequent boluses.

Should Not Be Used

- 1. As A Nutritional Intervention in Serum Albumin ≥2.5 G/Dl
- 2. To Correct Hypoalbuminemia in Serum Albumin ≥2.5 G/Dl (With the Exception of The Particular Cases Listed Above)
- 3. After Abdominal Surgeries (Hepatic and Abdominal Resection) In Serum Albumin ≥2.5 G/Dl or For A Patient Which Have Responded to Fluid Therapy.
- 4. Wound Healing
- 5. Burns in The First 24 Hours
- 6. Acute or Chronic Pancreatitis

Albumin Administration:

20% Albumin is hyperoncotic. The 100ml volume will expand to approximately 400mls within 25 minutes of transfusion. Rapid administration can lead to rapid volume expansion and cardiac failure. There is no UK published data regarding 20% Albumin infusion rates; in clinical practice it is usual to infuse 100mls over 30 minutes (personal communication AL/RS), but infusion rate varies and depends on clinical circumstances.

If 5% albumin bags are not available, may dilute 20% albumin vials with NS or D5W: Albumin 5% - 250ml:

Withdraw 50ml from 250ml NS IV bag and add 50mL 20% albumin (12.5g) albumin.

Albumin 5% - 500ml:

Withdraw 100ml from 500ml NS and add 100mL 20% albumin (25g) albumin.

References:

- 1. Sanyal AJ et al. A Randomized, Prospective, Double-Blind, Placebo-Controlled Trail of Terlipressin for Type 1 Hepatorenal Syndrome. Gastroent 2008;134:1360-1368.
- 2. Uriz J et al. Terlipressin plus albumin infusion: an effective and safe therapy of hepatorenal syndrome. J Hepatol 2000; 33:43-48.
- 3. Martin-Llahi M et al. Terlipressin and Albumin vs Albumin in Patients with Cirrhosis and Hepatorenal Syndrome: A Randomized Study. Gastroent 2008; 134(5):1352-1359.
- 4. Gluud LL et al. Terlipressin for hepatorenal syndrome. Cochr DB of Sys Rev 2006;4: CD005162.
- 5. Sagi SV et al. Terlipressin therapy for reversal of type 1 hepatorenal syndrome: A meta-analysis of randomized controlled trials. JGH 2010;25:880-885.
- 6. Nazar A et al. Effects of albumin administration in patients with cirrhosis and bacterial infections other than spontaneous bacterial peritonitis. A randomized, controlled study. J Hepatol 2009; 50:86.
- 7. Sort P et al. Effect of Intravenous Albumin on Renal Impairment and Mortality in Patients with Cirrhosis and Spontaneous Bacterial Peritonitis. NEJM 1999; 341(6):403-409.
- 8. Sigal SH et al. Restricted use of albumin for spontaneous bacterial peritonitis. Gut 2007; 56(4): 597–599.
- 9. Fernandez J et al. A Randomized Unblinded Pilot Study Comparing Albumin versus Hydroxyethyl Starch in Spontaneous Bacterial Peritonitis. Hepatol 2005;42:627-634.
- 10.Lata J et al. The efficacy of Terlipressin in Comparison with Albumin in the Prevention of Circulatory Changes after the Paracentesis of Tense Ascites: a Randomized Multicentric Study. Hepato-Gastroenterology 2007; 54:1930-1933.
- 11.Bernardi M et al. Albumin infusion in patients undergoing large-volume paracentesis: A meta-analysis of randomized trials. Hepatology 2012 1;55(4):1172-81.
- 12. Alves de Mattos A. Current indications for the use of albumin in the treatment of cirrhosis. Annals of Hepat 2011;10:15-20.
- 13. Singh V et al. Midodrine versus Albumin in the Prevention of Paracentesis-Induced Circulatory Dysfunction in Cirrhotics: A Randomized Pilot Study. Am J of Gastroent 2008; 103:1399-1405.
- 14.Knoll GA et al. A Randomized, Controlled Trial of Albumin vs Saline for the Treatment of Intradialytic Hypotension. J Am Soc Nephrol 2004; 15:487-492.
- 15. Fortin PM et al. Human albumin for Intradialytic hypotension in haemodialysis patients. Cochr DB of Systematic Reviews 2010; 11:CD006758.
- 16. Youssef MAFM et al. Intravenous fluids for the prevention of sever ovarian hyperstimulation syndrome. Cochr BD of Systematic Reviews 2011; 2:1302.
- 17.Jee BC et al. Administration of IV albumin around the time of oocyte retrieval reduces pregnancy rate without preventing OHS: a systematic review and meta-analysis. Gynecol Obstet Invest 2010;70:47-54.

- 18. Venetis CA et al. Intravenous albumin administration for the prevention of severe OHS: a systematic review and metaanalysis. Fertility and Sterility 2011; 95:188-196.
- 19.Tehraninejad ES et al. Comparison of cabergoline and IV albumin in the prevention of OHS: a randomized clinical trial. J Assist Reprod Genet 2012;29:259-264
- 20. Aboulghar M et al. Intravenous albumin for preventing severe OHS: a Cochrane review. Human Reproduction 2002;12:3027-3032.
- 21.Lovgren TR et al. Spontaneous Severe OHS in Successive Pregnancies with Successful Outcomes. Obstet Gynecol 2009;113:493-495.
- 22. Sansone P et al. Intensive care treatment of OHS. Ann NY Acad Sci 2011; 1221:109-118.
- 23.Martin G et al. Albumin and furosemide therapy in hypoproteinemic patients with acute lung injury. Crit Care Med 2002;30:2175-2182
- 24.Martin GS et al. A randomized, controlled trial of furosemide with or without albumin in hypoproteinemic patients with acute lung injury. CCM 2005; 33:1681-1687.
- 25.Cooper A et al. Five percent albumin for adult burn shock resuscitation: lack of effect on daily multiple organ dysfunction score. Transfusion 2006; 46:80-89.
- 26.Fodor L et al. Controversies in fluid resuscitation for burn management: Literature review and our experience. Int J Care Injured 2006;37:374-379.
- 27. Faraklas I et al. Colloid Normalizes Resuscitation Ration in Pediatric Burns. J Burn Care & Research 2011;32:91-97.
- 28.Alderson P et al. Human albumin solution for resuscitation and volume expansion in critically ill patients. Cochr DB Syst Rev 2004;4:CD001208.
- 29. Wilkes MM et al. Albumin Versus Hydroxyethyl Starch (HES) in Cardiopulmonary Bypass Surgery: A Meta-Analysis of Postoperative Bleeding. Ann Thorac Surg 2001;72:527-534.
- 30.Riegger LQ et al. Albumin versus crystalloid prim solution for cardiopulmonary bypass in young children. Crit Care Med 2002;30: 2649-2654.
- 31.Tomi T et al. Gelatin and Hydroxethyl Starch, but Not Albumin, Impair Hemostasis After Cardiac Surgery. Anesth Analg 2006; 102:998-1006.
- 32.Ernest D et al. Distribution of normal saline and 5% albumin infusions in cardiac surgical patients. Crit Care Med 2001; 29:2299-2302.
- 33.Kuitunen A et al. A comparison of the hemodynamic effects of 4% succinylated gelatin, 6% hydroxyethyl starch and 4% human albumin after cardiac surgery. Sc J of Surg 2007; 96:72-78.
- 34.Delaney AP et al. The role of albumin as a resuscitation fluid for patients with sepsis: A systematic review and meta-analysis. Crit Care Med 2011; 39:386-391.
- 35. Vincent JL et al. Is albumin administration in the acutely ill associated with increased mortality? Results of the SOAP (Sepsis Occurrence in Acutely ill Patients) study. Crit Care 2005; 9:745-754.
- 36.Bunn F, Trivedi D, Ashraf S. Colloid solutions for fluid resuscitation. Cochrane Database of Systematic Reviews 2011;3:1319.

- 37. Finfer S et al (SAFE study investigators). A comparison of albumin and saline for fluid resuscitation in the intensive care unit. NEJM 2004;350:2247-2250.
- 38.Cook D. Is albumin safe? NEJM 2004;35:2294-2296.
- 39. The SAFE Study Investigators. Saline or Albumin for Fluid Resuscitation in Patients with Traumatic Brain Injury. New Eng J Med 2007;357:874-884.
- 40.Finfer S et al (SAFE study investigators). Impact of albumin compared to saline on organ function and mortality of patients with severe sepsis. Intensive Care Med 2011; 37:86-96.
- 41.Llufriu S et al. Plasma exchange for acute attacks of CNS demyelination: Predictors of improvement at 6 months. Neurology 2009;73:949-953.
- 42.Balogun R et al. Clinical Applications of Therapeutic Apheresis. J of Clin Aph 2010;25:250-264.
- 43. Polenakovic M et al. Nephrol Dial Transplant 2001;16:99-100.
- 44.Lehmann HC et al. Plasma exchange in neuroimmunological disorders. Arch Neurol 2006;63:930-935. Discusses 3-5 exchanges of a 1 to 1.5 plasma volume exchange; some patients require additional exchanges
- 45. Yuan XY et al. Is albumin administration beneficial in early stage of postoperative hypoalbuminemia following gastrointestinal surgery?: a prospective randomized controlled trial. Amer J of Surgery 2008;196:751-755. No benefits were observed when compared to the saline arm
- 46.The Albumin Reviewers (Alderson P et al). Human albumin solution for resuscitation and volume expansion in critically ill patients. Cochr DB Syst Rev 2004;4:CD001208. "There is no evidence that albumin reduces mortality in critically ill patients with burns and hypoalbuminemia"
- 47.Finfer S et al (SAFE study investigators). Effect of baseline serum albumin concentration on outcome of resuscitation with albumin or saline in patients in intensive care units: analysis of data from the saline versus albumin fluid evaluation (SAFE) study. BMJ 2006;333:1044. "The outcomes of resuscitation with albumin and saline are similar irrespective of patients' baseline serum alb
- 48. Perel P, Roberts I, Ker K. Colloids versus crystalloids for fluid resuscitation in critically ill patients. Cochrane Database Syst Rev 2013;28(2):CD000567
- 49. Dellinger RP, Levy MM, Rhodes A, et al. Surviving sepsis campaign: International guidelines for management of severe sepsis and septic shock: 2012. Crit Care Med 2013;41(2):580-637
- 50. American Thoracic Society Critical Care Assembly. Evidence-based colloid use in the critically ill: American Thoracic Society consensus statement. Am J Crit Care Med 2004;170:1247-1259
- 51. Beekly AC. Damage control resuscitation: A sensible approach to the exsanguinating surgical patient. Crit Care Med 2008;36[Suppl.]:S267-S274
- 52. Finfer S, Bellomo R, Boyce N, et al. A comparison of albumin and saline for fluid resuscitation in the intensive care unit. N Engl J Med 2004;350:2247-2256
- 53. van der Heijden M, Verheij J, van Nieuw Amerongen GP, Groeneveld AB. Crystalloid or colloid fluid loading and pulmonary permeability, edema, and injury in septic and nonseptic critically ill patients with hypovolemia. Crit Care Med 2009;37:1275–1281
- 54. Giancarlo Liumbruno, Francesco Bennardello, Angela Lattanzio, Pierluigi Piccoli,

Gina Rossetti as Italian Society of Transfusion Medicine and Immunohaematology (SIMTI) Working Party; Recommendations for the use of albumin and immunoglobulins

- 55. Johnson PN, Romanelli F, Smith KM, et al. Analysis of the morbidity in liver transplant recipients following human albumin supplementation: A retrospective pilot study. Progress in Transplantation 2006;16:197-205
- 56. Ertmer C, Kampmeier TG, Volkert T, et al. Impact of human albumin infusion on organ function in orthotopic liver transplantation a retrospective matched-pair analysis. Clin Transplant 2015;29(1):67-75
- 57. Runyon, B.A. AASLD Practice Guidelines Committee. Management of adult patients with ascites due to cirrhosis: update 2012. Hepatology. 2013;57:1651–1653
- 58. Duffy M, Jain S, Harrell N, et al. Albumin and furosemide combination for management of edema in nephrotic syndrome: a review of clinical studies. Cells 2015;4(4):622-630
- 58. Frenette AJ, Bouchard J, Bernier P, et al. Albumin administration is associated with acute kidney injury in cardiac surgery: a propensity score analysis. Crit Care 2014;18(16):602
- 59. Lee EH, Kim WJ, Chin JH, et al. Effect of exogenous albumin on the incidence of postoperative acute kidney injury in patients undergoing off-pump coronary artery bypass surgery with a preoperative albumin level of less than 4.0 g/dL. Anesthesiology 2016;124(5):1001-11
- 60. Cribbs SK, Martin GS. Fluid balance and colloid osmotic pressure in acute respiratory failure: Optimizing therapy. Expert Rev Respir Med 2009;3:651-662
- 61. Martin GS, Mangialardi RJ, Wheeler AP, et al. Albumin and furosemide therapy in hypoproteinemic patients with acute lung injury. Crit Care Med 2002;30:2175-2182
- 62. Martin GS, Moss M, Wheeler AP, et al. A randomized, controlled trial of furosemide with or without albumin in hypoproteinemic patients with acute lung injury. Crit Care Med 2005;33:1681-1687
- 63. Uhlig C, Silva PL, Deckert S, et al. Albumin versus crystalloid solutions in patients with the acute respiratory distress syndrome: a systematic review and meta-analysis. Crit Care 2014;18(1):10
- 64. SAFE study investigators. Saline or albumin fluid resuscitation in patients with traumatic brain injury. N Engl J Med
- 65. Knoll GA et al. J Am Soc Nephrol 2004; 15:487-492. Saline just as effective as albumin
- 66. Fortin PM et al. Cochr DB of Systematic Reviews 2010; 11:CD006758. Sparse data. Only one clinical trial
- 67. Aboulghar M et al. (Cochrane review) Human Reproduction 2002;12:3027-3032. Suggestion of prevention benefit as well
- 68. Lovgren TR et al. Obstet Gynecol 2009;113:493-495
- 69. Sansone P et al. Intensive care treatment of OHS. Ann NY Acad Sci 2011; 1221:109-118. Albumin produces a fast collection of extravascular fluid. Also indicates albumin has an important role in prevention

70.globalrph.com

71. A. M. Naidech; Promising Concepts in Subarachnoid Hemorrhage

- 72. Yong Woo Lee, MD·Jung Yong Ahn, MD·In Bo Han, MDYoung Sun Chung, MD·Sang Sup Chung, MD·Nam Keun Kim, MD; The Influence of Hypoalbuminemia on Neurological Outcome in Patients with Subarachnoid Hemorrhage.
- 73. Diego Castanares-Zapatero and Philippe Hantson; Pharmacological treatment of delayed cerebral ischemia and vasospasm in subarachnoid hemorrhage
- 74. Suarez JI, Martin RH. Treatment of subarachnoid hemorrhage with human albumin: ALISAH study. Rationale and design.
- 75. Açıkgöz Ş, Edebali N, Barut F, Can M, Tekin İÖ, Büyükuysal Ç, Açıkgöz B. Ischemia modified albumin increase indicating cardiac damage after experimental subarachnoid hemorrhage.

76.www.uptodate.com

77. Todd Dodick, MD; Steven Greenberg, MD; and Michael O'Connor, MD; New Developments for the Management of Sepsis. The Official Journal of the Anesthesia Patient Safety Foundation

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Pediatrics:

No good published data, but it is common practice throughout Canada with anecdotal positive outcomes