

Haroldo Falcão^{1,2}, André Miguel Japiassú^{1,3}

Albumin in critically ill patients: controversies and recommendations

Uso de albumina humana em pacientes graves: controvérsias e recomendações

1. Hospital Quinta D'Or, Labs D'Or Network - Rio de Janeiro (RJ), Brazil.
2. Intensive Care Unit of Hospital Central da Polícia Militar do Estado do Rio de Janeiro - Rio de Janeiro (RJ), Brazil.
3. Intensive Care Unit of Instituto de Pesquisa Clínica Evandro Chagas - FIOCRUZ - Rio de Janeiro (RJ), Brazil.

ABSTRACT

Human albumin has been used as a therapeutic agent in intensive care units for more than 50 years. However, clinical studies from the late 1990s described possible harmful effects in critically ill patients. These studies' controversial results followed other randomized controlled studies and meta-analyses that showed no harmful effects of this colloid solution. In Brazil, several public and private hospitals comply with the Agência Nacional de Vigilância Sanitária (the Brazilian Health Surveillance Agency) recommendations for appropriate administration of intravenous albumin. This review

discusses indications for albumin administration in critically ill patients and analyzes the evidence for metabolic and immunomodulatory effects of this colloid solution. We also describe the most significant studies from 1998 to the present time; these reveal an absence of incremental mortality from intravenous albumin administration as compared to crystalloid solutions. The National Health Surveillance Agency indications are discussed relative to the current body of evidence for albumin use in critically ill patients.

Keywords: Albumin; Edema; Sepsis; Hypovolemia; Colloid osmotic pressure; Hypoalbuminemia; Therapeutics; Prognosis

Conflicts of interest: None.

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Corresponding author:

Haroldo Falcão
Av. Almirante Balthazar 435 - São Cristóvão
Zip Code: 20941-150 - Rio de Janeiro (RJ), Brazil.
E-mail: haroldofalcao@gmail.com

INTRODUCTION

Human albumin has been used therapeutically for more than 50 years in several clinical scenarios. This colloid solution is used for volume replacement in critically ill patients, and its use is based on two theoretical arguments. First, it contributes to plasma colloid osmotic pressure recovery by supporting intravascular volume without increasing interstitial edema, a result that is less effectively achieved with crystalloid solutions.⁽¹⁾ Second, serum albumin levels act as a severity indicator for overall clinical status – lower serum albumin levels indicate worse severity.⁽²⁾ However, despite plausible reasons for the use of albumin, trials have failed to show favorable evidence-based data supporting routine use.⁽³⁻⁶⁾

This debate is also galvanized by the concomitant discussion of regulation criteria for albumin use and the effect of such guidelines on daily practice. Restrictive prescribing strategies, which are not exclusive to Brazil, appear to be effective for cost reduction.^(7,8) In Brazil, up to 60% of albumin prescriptions may not comply with the Agência Nacional de Vigilância Sanitária (ANVISA, the Brazilian National Health Surveillance Agency) recommendations.⁽⁹⁾

This paper revisits this topic from the viewpoint of international trials examining the effectiveness of volume replacement using albumin infusions and discusses ANVISA's recommendations.

Study methodology

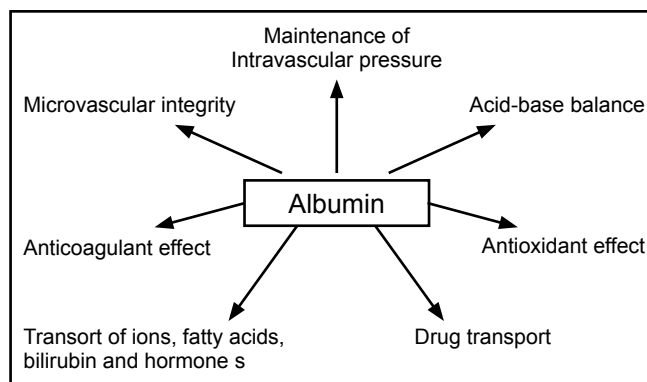
Two of the investigators independently searched the literature and extracted the data from MEDLINE and SciELO databases using the MeSH terms "albumin," "hypoalbuminemia," "critical care," "intensive care," "prognosis" and "treatment." Randomized and controlled clinical trials were selected and reviewed, as were systematic reviews and meta-analyses of human albumin use in critically ill patients and/or those staying in intensive care units. Large-scale observational studies, if published within the last decade, were also considered.

In vitro effects

Albumin is a relatively small molecule (69,000 Da). It is the most abundant plasma protein, and it represents 50% of this compartment's total protein.⁽¹⁾ It is synthesized by the liver at a rate of 250 mg/kg body weight. Its half-life ranges between 18 and 21 days in physiological conditions but can be much shorter in severely ill patients. In normal situations, it is responsible for 80% of colloid osmotic pressure, is part of the acid-base balance, acts as a "buffer" both in metabolic acidosis and alkalosis, and is additionally involved with transport of physiological substances and drugs.⁽¹⁰⁾ After trauma or in sepsis, its serum levels may drop as a result of intravascular space redistribution, reduced synthesis, and increased catabolism despite the molecule's long half-life. This drop may reach levels of 1-1.15 mg/dL within 3 to 7 days.⁽¹¹⁾

Intravenous albumin administration is thought to have multiple effects (Figure 1). It is likely to regulate vascular properties by maintaining osmotic pressure and microvascular integrity; transport hormones (cortisol and thyroxine), fatty acids, biliary salts, bilirubins, and ions (calcium and magnesium); modulate acid-base balance; and exert antioxidant and anti-apoptotic effects.^(1,10-12)

The chemical structure of serum albumin includes a thiol group that contains a sulfhydryl radical (-SH) with antioxidant properties.⁽¹³⁾ It is responsible for 80% of thiol radicals in the circulating blood. Additionally, nitric oxide (NO) may bind to albumin, forming S-nitroso-albumin and regulating its plasma levels.⁽¹⁴⁾



1. Figure 1 – Physiological effects of exogenous albumin.

In pathological conditions there is no evidence for this potential NO regulation mechanism, but it acts as a vasodilator in the genesis of septic shock. Albumin's antioxidant effects have previously been demonstrated in the context of acute lung injury.⁽¹³⁾ Albumin may also act as an antioxidant by binding to bilirubin, a molecule that generates a heme radical when metabolized; heme has proinflammatory effects in conditions such as sepsis.⁽¹⁵⁾ Albumin's antioxidant properties are provided by the cysteine-34 radical that binds to NO, its high affinity and low specificity binding sites for bilirubin and heme, and the N-terminal radical that binds copper, chromium and nickel).

After the first meta-analysis showed harm from albumin administration, several experimental trials were developed. Bar-Or et al. tested the effects of six different commercially available human albumin preparations on cytokine release in mononuclear cell cultures.⁽¹⁶⁾ The authors performed dialysis filtration of each commercial solution and tested the effects of the commercially available albumin solutions and dialyzed albumin in cell cultures. The dialysis treatment removed molecules smaller than 15,000 Daltons. The *in vitro* tumor necrosis factor alpha (TNF-alpha) and interferon production was significantly lower when commercial solutions were used than with dialysis solutions; production of these cytokines dropped about 100% drop from baseline levels. Additionally, lymphocyte T TNF-alpha production stimulated by antigen and autologous antigen presenting cells was reduced with commercial albumin solutions. These data point to possible immunomodulatory effects of exogenous albumin. Albumin oxidation by aspartyl-alanyl-diketopiperazine (DA-DKP) may be responsible for this immunosuppressive effect. The concern regarding possible immunologic effects of albumin

based on amino acid sequence changes in commercial preparations is relatively recent; the authors comment on possible effects for immunologically impaired subjects.⁽¹⁶⁾

Anti-inflammatory effects may alternatively be related to the solute concentration. It is probable that some of these effects are caused by the hyperoncotic presentation. An *in vitro* study with specimens from healthy subjects has shown variable degrees of neutrophil activation in different types of crystalloid solutions. In the presence of hyperoncotic albumin, neutrophil activation was reduced.⁽¹⁷⁾

Hypoalbuminemia and prognosis

The association between hypoalbuminemia and poor prognosis is well recognized. Herrmann et al. performed a retrospective outcome analysis of 15,511 clinical patients above 40 years old within their first 48 hours of admission.⁽²⁾ For each 2.5 mg/L serum albumin drop, the risk of prolonged hospital stay increased by 16%, and risk of increased death by 39%.⁽¹⁸⁾

In outpatients, morbidity and mortality progressively increased with serum albumin reduction from 4.5 to 2.2 mg/dL. This continuous relationship, which lacks distinct levels or thresholds, blurs pre-established replacement boundaries.⁽¹⁹⁾ In these non-critical patients without significant fluid overload or volume replacement needs, nutrition-based therapy may be appropriate for addressing metabolic waste and hypoalbuminemia. In this scenario, there is no favorable evidence for systematic correction of hypoalbuminemia.

Even in critically ill patients, multivariate analysis has shown that serum albumin levels independently predict in-hospital mortality. However, a post-hoc analysis of the SAFE trial data showed no prognostic difference between critically ill patients receiving intravenous saline or albumin, even when the population was categorized by albumin levels above or below a 2.5 mg/L threshold.⁽²⁰⁾

Albumin's prognostic role is more apparent when a patient with significant comorbidity is admitted to the intensive care unit (ICU) with a critical illness. For example, serum albumin is an independent marker of morbidity and mortality in patients with acute acquired immunodeficiency syndrome (AIDS) admitted to the ICU.⁽²¹⁾ In this population, the serum albumin level is a marker for the nutritional deficiency that may influence prognosis. However, the effect of albumin

therapy in certain AIDS-associated conditions, such as acute respiratory failure and sepsis, has not been evaluated.^(22,23)

Main clinical trials and meta-analysis

The four large, landmark trials that have addressed the clinical use of albumin are summarized in Chart 1. In 1998, the Cochrane Collaboration initiated discussions on the use of albumin in critically ill patients.⁽³⁾ Therapeutic albumin use for volume replacement was reassessed in light of the known association between hypoalbuminemia and unfavorable outcomes. The study systematically reviewed the available evidence with all-causes mortality as its primary endpoint. A total of 1,176 patients, 568 in the intervention group and 608 in the control group, were studied to assess the relationship between albumin use and mortality. The patients were additionally categorized in three groups: first, hypovolemic patients, comprised of surgical or trauma patients independent of possible sepsis (only one trial distinguished septic from non-septic patients); second, burn patients who received albumin as directed by a variety of protocols; third, hypoalbuminemic patients. In addition, at least half of these trials included patients who required parenteral nutrition. In addition to the subjects' enrollment criteria, "use of albumin" was not specified, including interventions with isomolar albumin (4 mg.mL) or hyperosmolar (20 mg.mL⁻¹). In all three groups, intervention was associated with higher mortality rates relative to the control group: the relative risk of death for hypovolemic patients was 1.46 (95% confidence interval (95%CI) 0.97 to 2.22), burn patients 2.40 (95%CI 1.11 to 5.19) and hypoalbuminemic patients 1.69 (95%CI 1.07 to 2.67). The total accumulated relative risk of death was 1.68 (95%CI 1.26 to 2.23). No significant heterogeneity was identified for the groups, nor was there a distinction between the time of death and albumin use. Notably, however, mortality was not the primary endpoint of all included trials. Although this trial has received a significant amount of criticism, its publication sparked a high volume of discussion. The Cochrane Library study has offered an indisputable contribution to the field by challenging the wide-spread and indiscriminate use of albumin worldwide.^(5,6,24,25) In a recent update of the meta-analysis originally developed in 2002, the Cochrane Group reviewers included one trial with 100 patients but drew no different conclusions from those in the first review.⁽⁴⁾

Chart 1 – Major characteristics of human albumin therapy trials in critically ill patients

Name	Year	Type	N	Stated aim	Results
Cochrane Injuries Group ⁽³⁾	1998	Meta-analysis	1419		Possible mortality increase among hypovolemia, burn and hypoalbuminemic critically ill patients.
Wilkes et al. ⁽²⁶⁾	2001	Meta-analysis	2958	55 trial review	Lack of effects on mortality; very heterogeneous trials.
SAFE ⁽²⁷⁾	2004	Randomized, controlled trial	6997	Volume resuscitation	Similar 28-day outcomes in patients receiving either 4% albumin or saline for volume replacement; possible subgroups effect (sepsis and trauma).
SOAP ⁽²⁹⁾	2005	Multicenter observational cohort	3147	Not stated	Association with increased 30-day mortality.
Jacob et al. ⁽³⁰⁾	2008	Meta-analysis	1485	Hyperoncotic albumin effectiveness	No differences versus control for the endpoints death, organ dysfunction, time of hospital stay and costs.

SAFE - Saline versus Albumin Fluid Evaluation; SOAP - Sepsis in European Intensive Care Units.

After the publication of the first Cochrane meta-analysis, Wilkes et al. published another meta-analysis that attempted to include a larger number of clinical trials and considered specific groups such as high risk newborns and liver disease patients that were not included in the population originally studied in 1998.⁽²⁶⁾ The authors controlled the trials based on quality and methodology. They selected studies that were blinded, used mortality as an endpoint, implemented a crossover design and had a large enough study size. In those studies with better methodological quality, subgroup analysis showed a relative risk reduction with albumin treatment, but this was not statistically significant (relative risk 0.73 (95%CI 0.48 to 1.12) in better quality studies and 0.94 (95%CI 0.77 to 1.14) in all trials). Again, albumin modalities were not distinguished in this meta-analysis.⁽²⁶⁾

After these two conflicting meta-analyses, the Saline versus Albumin Fluid Evaluation (SAFE) study was published. This was a randomized, controlled, double-blinded, multicenter trial.⁽²⁷⁾ This large clinical trial was designed to identify non-inferiority of albumin versus crystalloids for volume maintenance or expansion in critically ill patients. There were no significant differences between the control and intervention groups when the authors compared the length of ICU stay, length of hospital stay, length of mechanical ventilation or dialysis. The authors concluded that the small amount of albumin used to replenish volume was as effective as saline replacement. This study reintroduced the possibility of a therapeutic use for albumin, and it had a larger international effect than other trials. Because it evaluated a specific population, the SAFE trial prompted the development of new hypotheses for subgroups of critically ill patients, such as trauma patients and septic patients. The Blood Products

Advisory Committee (BPAC) for the U.S. Food And Drug Administration (FDA) stated that “the SAFE trial solved the doubts raised by the Cochrane Injuries Group in 1998, and there is no harm from intravenous albumin in critically ill patients.”⁽²⁸⁾

Following these studies, the Sepsis in European Intensive Care Units (SOAP) multicenter trial was conducted in European ICUs to evaluate the clinical characteristics of patients with sepsis.⁽²⁹⁾ Despite the large variability of albumin use across participant countries, an association between intravenous albumin and clinical severity and mortality was found. Because there is a tendency to give albumin to more severely ill patients, and a false association between albumin and increased mortality rates could exist. The authors conducted statistical analysis to mitigate analysis bias, and the association between albumin use and mortality remained significant. Albumin administration was independently associated with survival shorter than 30 days (relative risk 1.57, 95%CI 1.11 – 2.22). This association was maintained even after evaluation of the trauma and severe sepsis subgroups. Additionally, the 30 days mortality rate, ICU mortality and in-hospital mortality were higher among patients who received albumin (RR 1.57; 95%CI 1.19-2.07). The authors raised new questions that highlighted the complexity of this question. The impact of albumin administration may vary (both in terms of clinical effectiveness and safety) depending on timing of delivery within the scope of the patient's illness. Further criticisms of these conclusions are related to the lack of comments regarding drug indications and therapeutic targets. Because the SOAP was an exclusively observational study, it was not possible to determine whether albumin use was harmful.⁽²⁹⁾

More recently, a meta-analysis specifically addressed hyperoncotic albumin formulations (20-25% solution) for small volume resuscitations.⁽³⁰⁾ The overall analysis showed no association between hyperoncotic albumin administration and increased mortality; it was shown to be safe and effective in subgroups such as liver disease patients and newborn patients. No significant mortality increase was shown in adult critically ill patients. Because only two groups conducted these trials, however, the generalization of these conclusions is limited. In addition, it would be useful to analyze patients receiving a variety of colloids and crystalloids.

We hypothesize that, due to the heterogeneity of available studies and clinical scenarios in addition to the different forms of albumin used clinically, it is difficult to draw unequivocal conclusions regarding the use of albumin for volume replacement. These factors may limit detection of definite effects, particularly in subgroups such as those defined by severe sepsis, trauma or burns. It is therefore still necessary to test experimental models and conduct disease-specific population research. There are currently 17 trials registered on the *clinicaltrials.gov* databank, of which eight address specific albumin replacement effects in sepsis. Some examples include ALBIOS (Volume Replacement With Albumin in Severe Sepsis), CEASE (Comparative Evaluation of Albumin and Starch Effects in Acute Lung Injury) and a study on albumin's antioxidant and hemoglobin-binding effects following extracorporeal circulation in cardiac surgery (Evans TW, personal communication).

Albumin effects in subgroups of severely ill patients

Large cohort studies have failed to detect effects of albumin replacement on mortality; however, a variety of evidence suggests that specific groups studies may reap physiological and biochemical benefits. Additionally, establishing more modest endpoints and focused short-term outcomes, such as hemodynamic stability and improved gas exchange, may provide promising results.

Albumin administration does benefit critically ill patients, most notably by improving respiratory function and gas exchange, cardiovascular stability, neurologic status and fluid balance.^(31,32) Albumin infusion improves organ dysfunction in the first week of stay in ICU in patients with below 3.0 mg/L serum albumin (reduced Sequential Organ Failure Assessment (SOFA) score between the 1st and 3rd days of 3.1 ± 1.0 for the albumin group versus 1.4 ± 1.1 for the Ringer lactate group; $p=0.03$).⁽³¹⁾

Morbidity outcomes in the group of patients with severe hypoalbuminemia are not clear. Product-associ-

ated morbidity was much lower in severely hypoalbuminemic subjects than in patients with albumin levels above 3.0 mg/L, suggesting a dose-dependent relationship.^(33,34) Next, we will briefly analyze three patient categories in which albumin infusion may be more strongly indicated:

a) Sepsis

Exogenous albumin administration was evaluated in a prospective non-randomized trial in 28 acute lung injury patients.⁽³²⁾ Albumin, with or without furosemide, leads to improved oxygenation and hemodynamic function. The partial pressure of oxygen improved 5 minutes after albumin plus furosemide, but this oxygenation gain was not maintained. In another randomized, controlled, double-blind trial of 40 acute respiratory distress syndrome (ARDS) and sepsis patients, the authors attempted to achieve negative fluid balance using albumin plus furosemide infusion.⁽³⁵⁾ Oxygenation benefit was achieved without any negative impact on hemodynamic stability. Hyperoncotic albumin use may also be valuable for septic patients with advanced liver disease or nephrotic syndrome. Albumin administration (dose accumulated) is thought to have renoprotective properties.⁽¹⁾

The SAFE trial has shown a trend toward favorable results after albumin resuscitation relative to saline in septic patients.⁽²⁷⁾ In this subpopulation, albumin therapy in septic patients was associated with an absolute mortality reduction of almost 5% with a relative risk of 0.87 (95%CI 0.74 – 1.02). A repeated analysis performed by the same investigators showed that albumin infusion was an independent contributor to increased 28-day survival and was associated with less progression to liver dysfunction.⁽³⁶⁾

b) Severe liver disease

Exogenous albumin infusion in decompensated cirrhosis is justified in three contexts: prevention of circulatory dysfunction following serial or large-volume paracentesis,⁽³⁰⁾ reduction of renal dysfunction and mortality in spontaneous bacterial peritonitis patients, for whom albumin is superior to synthetic colloids;^(37,38) and, finally, for treatment of hepatorenal syndrome.⁽³⁹⁾

Transient liver dysfunction after liver transplantation appears to be a reasonable indication for prescribing albumin, but studies confirming this suspicion are scarce. At this time, there is no apparent prognostic value in maintaining serum albumin levels above or below 3.0 mg/L.⁽⁴⁰⁾ It is also possible that albumin is as effective for volume resuscitation of this type of patient as HES 130/0.4 modified starch.⁽⁴¹⁾

c) Trauma and postoperative

Although 26% of the albumin given in the United States is targeted to acute volume loss therapy in postoperative, traumatic or hemorrhagic contexts,⁽⁶⁾ it is not superior to crystalloids or other colloids in the context of overall postoperative volume replacement.⁽⁴²⁾ Two conflicting trials address albumin use in trauma patients. Hyperoncotic albumin plus furosemide reduced post-contusion brain edema, and this treatment was associated with significant functional outcome improvement in 18 head trauma patients when compared with conventional normal osmolarity colloid.⁽⁴³⁾ On the other hand, a SAFE trial subgroup analysis revealed increased mortality after isotonic albumin replacement.⁽⁴⁴⁾

The Brazilian Health Surveillance Agency (ANVISA) indications

Guidelines for the use of exogenous human albumin were initiated in 1975 when the National Institute of Health (NIH) issued rules for prescribing albumin in the United States, forming the basis for less liberal albumin use criteria.^(7,45) Prescriptions in situations not recommended are generally accompanied by high costs and are found in countries where 90% of prescriptions may depend on inadequate evidence.^(7,46,47) Development of protocols and compliance with protocols may reduce the use of this drug, leading to cost reductions without influencing outcomes.⁽⁸⁾

In Brazil, albumin prescription is included in the

Ministry of Health special procedures. ANVISA issued its guidelines in 2003, analyzing the available evidence to guide use of albumin.⁽⁴⁸⁾ ANVISA's guidelines form the national reference for albumin use, and they provide the guiding parameter for health insurance prescription criteria.

Matos et al. have shown that in a Brazilian public hospital, 60% of human albumin indications were inappropriate, and that one half of the patients had serum levels above 2.0 mg/L.⁽⁹⁾ This may have corresponded to about 8,000 g human albumin theoretically misused, entailing 16 to 20 thousand dollars of inappropriate expenses.

The main ANVISA indications are⁽⁴⁸⁾ extracorporeal circulation, following paracentesis, therapeutic plasmapheresis, prevention of ovarian hyper-stimulation syndrome, refractory edema of cirrhosis or nephrotic syndrome, major burns, and postoperatively after liver transplant (Chart 2). Treatment of ICU patients is disputable and is not based on adequate evidence. ANVISA's position additionally predicts categories where albumin use is considered as an interim measure until more conclusive evidence is available. The unfounded conditions included those not endorsed by the available literature and those described as contraindications.

Some aspects of ANVISA's rules deserve special consideration. We could not find any specification regarding the critical serum level boundaries for albumin prescription in severe hypoalbuminemia cases

Chart 2 – Brazilian Health Surveillance Agency (ANVISA) indications for human albumin use (2003)

Indisputable indications	<ol style="list-style-type: none"> 1. Extracorporeal circulation pump priming in cardiac surgery; 2. Therapy of large volume ascites with serial paracentesis; 3. Replacement fluid for large volume therapeutic plasmapheresis (removing more than 20 mL/kg plasma per session); 4. Prevention of ovarian hyper-stimulation syndrome on the harvesting day for in vitro fertilization; 5. Immediately life-threatening liver cirrhosis and nephrotic syndrome with edema refractory to diuretics; 6. Major burn patients, after the first 24 hours post-burn; 7. Liver transplant postoperative period, when serum albumin is below 2.5 g%.
Disputable indications	<ol style="list-style-type: none"> 1. Critically ill patients with hypovolemia, hypoalbuminemia, poor fluid distribution; 2. Neonatal hyper-bilirubinemia due to perinatal hemolytic disease.
Indications with inadequate evidence	<ol style="list-style-type: none"> 1. Hypoalbuminemia correction; 2. Acute volume loss correction, including hemorrhagic shock; 3. Chronic liver cirrhosis or nephrotic syndrome therapy; 4. Peri-operative, except for the above mentioned cases.

Continue...

Chart 2 – Continued

<p>Indications not discussed in ANVISA's recommendations but approved for reimbursement by the Sistema Único de Saúde (SUS) [Brazilian public healthcare system]</p>	<ol style="list-style-type: none"> 1. Shock: sepsis; hypovolemia associated with severe hypoalbuminemia; 2. Liver disease: chronic, associated with severe hypoalbuminemia; ascites refractory to classical therapy; acute liver failure; 3. Nephrotic syndrome associated with diuretic-refractory edema and oliguria; associated genital edema unresponsive to classical therapy; 4. Generalized exfoliative dermatitis; 5. Dialysis associated with hypoalbuminemia; 6. Liquor fistulae or external ventricular shunting; 7. Severe hypoalbuminemia; 8. Peritonitis with external drainage; 9. Plasmapheresis and partial exchange blood transfusion; 10. Burns; 11. Liver transplantation; 12. Spontaneous meningeal hemorrhage; 13. Severe pre-eclampsia 14. Enteropathy with protein loss; 15. Volume replacement with colloid; 16. Mediastinitis; 17. Abdominal external surgery; 18. Pulmonary bypass with hemodilution; 19. Heart failure.
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Source: Agência Nacional de Vigilância Sanitária ANVISA, 2003⁽⁴⁸⁾. SUS – Sistema Único de Saúde [the Brazilian public healthcare system].

(lower than 2.0 mg/L). Also, there is no mention of the timing of use, cumulative dose, or the clinical time for its prescription. While new investigations have not provided better specifications for albumin, there is room to prescribe flexibly within existing approved categories.

CONCLUSIONS AND PERSPECTIVES

The experimental and clinical effects of albumin are not completely understood. The ideal dose definitions, time of use and mode of administration (either iso- or hyperoncotic) remain unclear. Furthermore, industrial formulations may be less effective than the endogenous molecule.

The characteristics of large human albumin therapy clinical trials, which generally include widely heterogeneous populations, require more specific subgroup investigations. The recommendations available in Brazil – those used by both public and private payers – fail to offer guidance beyond defining the diagnosis categories that receive more or less benefit; they do not clarify the dose, cumulative dose, timing or even the underlying disease type (they exclude diagnosis categories not discussed by ANVISA). The large trials cur-

rently available illuminate small domains of certainty in a greater context of broad uncertainty.

RESUMO

O uso de albumina humana como terapêutica nas unidades de terapia intensiva é tradicional há mais de 50 anos. No entanto, estudos no final dos anos 90 apontaram um possível malefício em relação ao seu uso em pacientes graves. O efeito da controvérsia causado por esta publicação perdurou mesmo após a publicação de outras meta-análises e estudos randomizados e controlados, que não encontraram relação de prejuízo para o uso desta solução coloidal. No Brasil, vários serviços públicos e privados seguiram recomendações da Agência Nacional de Vigilância Sanitária sobre usos adequados ou não da albumina venosa. Nesta revisão, procuramos abordar as razões da administração de albumina, assim como reunir evidências metabólicas e imunomoduladoras de possíveis efeitos deste colóide no paciente grave. Os estudos de maior impacto desde 1998 até os dias atuais foram pormenorizados, demonstrando que não parece existir aumento de mortalidade com o uso de albumina venosa, em relação às soluções cristalóides. As indicações da Agência Nacional de Vigilância Sanitária foram discutidas diante das evidências atuais sobre o uso de albumina no doente crítico.

Descritores: Albumina sérica; Edema; Sepse; Hipovolemia; Pressão osmótica; Hipalbuminemia; Terapêutica; Prognóstico

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