Albumin in the Critically Ill

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Abstract

Albumin continues to be one of the options for colloid resuscitation in critically ill patients despite limited evidence for its use. It does seem to have an advantage over other colloids with a better side-effect profile. With it's ability to increase intravascular oncotic pressure and other postulated metabolic benefits, albumin is preferred by many practioners worldwide for fluid resuscitation amongst ICU patients. In some studies outcome benefits have been shown, especially in patients with sepsis and post cardiac surgery patients. Limitations of its use are associated with its availability, cost and limited side-effect profile.

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E. Farag et al. (eds.), *Perioperative Fluid Management*,
https://doi.org/10.1007/978-3-030-48374-6_11

Key Points

1. Albumin continues to be one of the main choices for colloid resuscitation amongst critically ill patients.
2. There is paucity of evidence supporting albumin as the mainstay of resuscitation except in sepsis and post-cardiac surgery patients.
3. Albumin use in traumatic brain injury patients has been associated with worse outcomes.
4. Cost and availability of albumin continues to be the predominant limiting factor for its use in critically ill patients.

Introduction

Fluid resuscitation is one of the key aspects of patient care in critically ill patients with absolute or relative hypovolemia. Other than cardiogenic shock, all other forms of shocks require fluid resuscitation or volume expansion. Debate about superiority of one type of fluid over another for resuscitation in this patient population has remained unsettled for most part despite decades of research [1]. Crystalloids still remain the main and initial fluids of choice for volume expansion to counteract hypovolemia. Colloids have been postulated to have significant benefit over crystalloid in resuscitation, as they are more likely to stay intravascular and for a longer period of time.

An international survey of preferred plasma volume expanders for critically ill patients showed significant variability in practice patterns across the world [2]. Except for dehydration and drug overdose, where initial resuscitation was chiefly using crystalloids, the majority (65%) of the survey respondents used a combination of both crystalloids and colloids for initial resuscitation. Colloids were preferred for resuscitation in patients with cirrhosis (42%), coagulation disorders (42%), or adult respiratory distress syndrome (39%). This is despite lack of any evidence for benefit in patients with ARDS along with some deleterious impact of colloid resuscitation amongst patients with coagulation disorders or resuscitation with starches [3]. First-line plasma expanders continue to be isotonic crystalloids (81%), starches (55%), gelatins (35%) whereas albumin (7%) found lower preference. There were regional practice variations also noted with colloids, especially gelatins (68%) alone being preferred more frequently in the United Kingdom (40%) whereas starches more so in Germany (81%) and The Netherlands (66%). The main factors behind preferences for first-line plasma volume expanders were time to volume loss correction, duration of effect, adverse events, and cost [2].

Critical Illness Pathophysiology and Resuscitation

The albumin concentration in plasma in healthy humans' ranges between 33 and 52 g/l. Human serum albumin accounts for about 60% of the total proteins and contributes to almost 80% of the intravascular oncotic pressure [4, 5] and has a

molecular weight of 66,500 Da. The ability of colloids to generate higher oncotic pressure has made them more attractive for resuscitation as they are thought to maintain a higher intravascular oncotic pressure and thus drive more volume intravascular rather than leaking into extravascular space.

Critical illness represents a complex pathophysiologic state with multiple system organ dysfunction, metabolic derangements and a response generated to correct these derangements. In critically ill patients after surgery and patients with sepsis there is altered permeability and increased transcapillary escape resulting in a disruption of this relationship [6] and in loss into spaces that do not contribute to the intravascular volume. Systemic inflammatory response syndrome (SIRS) and MODS (multiorgan dysfunction syndrome) are the hallmarks of this pathophysiologic state. In SIRS one is confronted with vasodilation and capillary leakage of fluid triggered by a cascading reactionary inflammatory response by various of cellular and non-cellular agents in a response to injury. This leads to relative intravascular hypovolemia due to vasodilation creating increasing capacity within the overall vascular space and leakage of fluid into the extravascular space due to capillary leakage. The movement of Human Serum Albumin (HSA) across the capillary wall is defined as the transcapillary escape rate (5% per hour), which indicates the percentage of intravascular HSA leaving the intravascular compartment per hour [7]. MODS also plays an important role in determining fluid balance of the patient as cardiac depression, acute kidney injury and other organ dysfunctions create significant fluid imbalance. Metabolic derangements compound the problem with acidosis, hyperglycemia and associated electrolyte imbalances create a milieu that can further complicate balance between intravascular and extravascular fluid balance.

Fluid resuscitation in these patients has been supported by early goal directed therapy, especially in sepsis, although components of the same has been challenged in the recent times [8, 9]. Restoration of intravascular volume status, improves blood flow and thereby delivery of oxygen to peripheral tissues. Improvement in blood pressure, central venous pressure, decrease in pulse volume variation and lactic acidosis are common measurements for fluid resuscitation in critically ill. Early restoration of fluid status using 30 ml/kg of crystalloid, assessment and follow up of lactate levels and application of vasopressors to restore perfusion to mean arterial pressure to at least 65 mm of Hg, while attaining cultures and appropriate source control including empiric antibiotics has been the main stay of resuscitation of critically ill patients with sepsis [10]. Similar goals with some clinical practice variations have been applied in other vasodilatory shock and hypo perfusion states.

Commercial Preparations of Albumin

Edwin Cohn in the 1940s developed a stable pooled albumin solution during World War II based on a fractionation technique, which was subsequently rapidly adopted by a number of pharmaceutical companies [11, 12]. HSA that is available today is primarily produced by cold ethanol fractionization technique first described by Cohn and then pasteurized for at least 10 h at >60 °C to eliminate the risk of viral

and bacterial infections. Multiple modifications and combinations of this method with chromatography have been described and readers are encouraged to visit the mini review article by Raoufinia et al. [13].

The excessive demand for the HSA solutions has encouraged its production using recombinant DNA technology in both prokaryotic and eukaryotic hosts. Recently, transgenic rice Oryza sativa has been used successfully as a novel bioreactor to produce sufficient quantities of safe rHSA [14].

With the advances made in the extraction and purification processes, the use of albumin is considered safe practice; in a study evaluating adverse event reporting between 1998 and 2000, the incidence of all reported serious nonfatal and fatal adverse events was 5.28 per 10^6 doses. For non-fatal serious adverse events, the observed incidence was 4.65 per 10^6 doses while the observed incidence of fatal serious adverse events possibly related to albumin was 0.185 per 10^6 doses though no patient death was classified as directly related to albumin administration [15].

Currently available human albumin solutions may differ in protein content and composition, binding capacity, metal ion content, antioxidants prosperities, and capacity to bind drugs [6]. Albumin solutions are available in a variety of concentrations as a 3.5–5% or as a hypertonic solution 20–25%. Hypertonic albumin (20–25%) is used in patients with edema as it avoids excessive sodium and chloride loads, and is able to deliver higher oncotic pressure with minimal volume load [16]. Hypotonic albumin preparations should not be used in patients with traumatic brain injury [17].

Albumin Advantages and Disadvantages: Where Is This Evidence?

In patients with acute and chronic illness, serum albumin concentration has been shown to inversely affect the mortality risk [18]. Albumin has also been shown to play an instrumental part in maintaining the integrity of the endothelial barrier [19], as an antioxidant [20, 21], and transporter of nitric oxide [20, 22, 23] and fatty acids and drugs.

(A) Albumin and interaction with other proteins

HSA may protect other proteins including hemoglobin, insulin, and immunoglobin from glycation in the early stages of diabetes due to its long half-life and its high concentrations compared to other proteins [24]. Similarly, patients with Obstructive sleep apnea may demonstrate an increased oxidative stress that can contribute to cardiovascular and metabolic morbidities due to decreased HSA antioxidant properties [25]. The irreversible damages associated with diabetes such as retinopathy, nephropathy, neuropathy, and coronary artery disease could also be attributed to reduced antioxidant properties of glycated HSA.

(B) Albumin and effects of acid-base balance and serum electrolytes

Irrespective of the type of fluid used, administration of large amounts of resuscitation fluids over a short period of time has been associated with the development of acid base imbalances [1–3, 8, 9]. Belloma et al. in 2006 looked at the effects of saline or albumin resuscitation on acid-base status and serum electrolytes [26]. They concluded that the volume of fluid administered is a much stronger predictor than the type of fluid and these were also influenced by illness severity and the passage of time [26].

(C) Albumin and effect on the coagulation system

HSA has anticoagulant and antithrombotic functions [27]. Therefore, the use of HSA might be very beneficial in cases with hypercoagulable conditions such as during the perioperative period.

Bellomo, R., et al. in 2009 looked at the Effects of saline or albumin resuscitation on standard coagulation tests [3] and concluded that administration of albumin or of larger fluid volumes is associated with a prolongation of APTT and in ICU patients, the choice and amount of resuscitation fluid may affect a routinely used coagulation test. A recent article by Rasmussen et al. in 2016 [28] confirmed that finding that administration of HSA does not increase the amount of blood loss, the need for blood transfusion but decreases coagulation competence during major surgery.

Albumin in Critical Care

The crystalloid versus colloid debate in critical care has spanned several decades. Some of the issue seems to stem around safety, efficacy and risk benefit ratio of colloids versus crystalloid use and the expense of albumin compared with the relatively lower cost to crystalloids. More than two decades ago, a postal survey conducted in 451 ICUs in Germany showed that no real protocols or standards existed for volume replacement therapy in these units, with a large variance in the kind of fluid used [29]. Several systematic reviews in the past had led to conflicting evidence as far as the safety and efficacy of albumin was concerned. A lot of these analytics compared colloids and crystalloids and used hydroxyethyl starch and related gelatins in the colloid group, certainly something that has over the years shown clear disadvantage in terms of organ system failure and renal injury. An important specific question is the use or utility of albumin during resuscitation of a septic/critically ill patient. The evidence to support this is minimal and no difference in all-cause mortality has been seen spread over several years of evidence. Despite this, albumin is a safe solution for this practice and no harm has been associated with its use either [30].

In 2004, Finfer and colleagues examined nearly 7000 patients in a multicenter, randomized, double blind trial to compare mortality and safety using saline or 4% albumin in a mixed ICU population. This landmark experiment, named the SAFE trial, still holds as the major weight of evidence when it comes to evaluating the usefulness of albumin resuscitation in the critically ill. The authors saw similar outcomes (death at 28 days, ICU days, hospital days, days on mechanical

ventilation, or days on renal replacement therapy) in both groups [31]. Subgroup analysis of the albumin-treated group revealed a trend towards decreased mortality in patients with septic shock, and a trend towards increased mortality in trauma patients, especially those with traumatic brain injury. This trial also forms the largest weight of evidence for a large Cochrane review that established no mortality benefit to albumin in either patients with hypovolemia or those with burns. The authors used data from 38 trials, and 10,842 patients and recommended further question into whether albumin use maybe indicated in select critically ill patients [18]. Annane and colleagues conducted the CRISTAL trial and used albumin and crystalloids in an open-label randomized manner in several ICUs in Europe, where they saw no significant difference in 28-day mortality. Amongst the nearly 1500 trial participants in either arm, there was a significance signal to improved 90-day mortality, and more days alive without mechanical ventilation, and without vasopressors, though these findings were regarded as exploratory and deserving of the need for further study [32]. Albumin use was associated with a higher chloride concentration during large volume resuscitation. The actual difference seemed minor compared to the volume of fluid, illness severity and duration of illness seemed to be a bigger driver of these outcomes [26]. Similarly, a post-hoc analysis of the SAFE trial showed a prolongation of coagulation time, with albumin resuscitation and larger volumes used for replacement [3]. Both 20% and 4% albumin were shown to be safe in healthy subjects, and was associated with an increase in stroke volume along with a reduction in afterload, compared with crystalloids [33]. Albumin has been previously used in combination with diuretic therapy and the combination seems to improve oxygenation, provide hemodynamic stability and achieve better negative fluid balance in patients with acute lung injury [34]. Although hypoalbuminemia is associated with increased mortality, use of albumin for volume resuscitation of critically ill patients with a serum albumin concentration ≤25 g/l is not associated with reductions in mortality, duration of ICU stay or mechanical ventilation, or in use of renal replacement therapy. Such practices, as 'routine" administration of albumin to 'build up' serum albumin in critically ill surgical patients in the ICU, is without evidence, and may not provide any clinical benefit whatsoever. Similarly, there is no substantive evidence to justify the use of hyperoncotic albumin solutions for resuscitation or supplementation in critically ill patients. An area of promise appears to be in the prevention of development and progression of pressure ulcers in the ICU [35].

Use of albumin for resuscitation has been guided chiefly by the SAFE trial and Cochrane analysis in the recent times [31]. A Cochrane analysis of use of human albumin solution for resuscitation and volume expansion in critically ill demonstrated important outcomes [18]. Importantly, overall estimates were influenced by the results of the SAFE trial, which contributed 75.2% of the information (based on the weights in the meta-analysis). The analysis demonstrated that for burns, the relative risk of death was 2.93 and for hypoalbuminemia the relative risk was 1.26. There was no substantial heterogeneity between trials in the various categories. The pooled relative risk of death with albumin administration was 1.05. Even in patient populations such as those with extensive fluid losses or hypoalbuminemia there has

not been any proven benefit of albumin resuscitation or colloid resuscitation. High cost is a significant issue since albumin is human derived and an expensive solution relative to crystalloids or even most of the colloids.

Albumin in Hypoalbuminemic States

Hypoalbuminemia is a very common finding in hospitalized and critically ill patients. Mechanisms that can contribute to this state can be decreased production (uncommon cause due to liver dysfunction), increased loss of albumin due to third spacing (as seen in sepsis and burns) or hemodilution due to use of large volume of crystalloids, or loss through the kidneys (as seen in chronic kidney disease and nephrotic syndrome), gastrointestinal tract (as seen in crohn's disease or increased lymphatic pressure) [36], loss of blood, or due to increased catabolism of albumin. Vincent et al. [37] in 2003 conducted a meta-analysis of 90 cohort studies with 291,433 patients looking at hypoalbuminemia as an outcome predictor and nine prospective controlled trials with 535 patients on correcting hypoalbuminemia and concluded that for every 10-g/l decline in serum albumin concentration, mortality was increased by 137%, morbidity by 89%, prolonged intensive care unit by 28%, hospital stay and 71%, resource utilization by 66% [37]. They also concluded that association between hypoalbuminemia and poor outcome appeared to be independent of both nutritional status and inflammation and complication rates may be reduced when the serum albumin level attained during albumin administration exceeds 30 g/l [37].

Albumin in Burns

There are multiple strategies that have been proposed for the fluid management in burn patients. Most have advocated different combinations of crystalloids, colloids, or plasma. A survey of the actual clinical practices of volume replacement regimen in burn patients in Europe was conducted in 2008. Sent out a total of 187 questionnaires consisting of 20 multiple-choice questions and the response rate was 43%. The answers came from a total of 20 European countries. They looked at the type of volume resuscitation, monitoring technique (use of CVP)use of PiCCO-system, and mixed-venous saturation datasets.

They concluded that there was no standardized therapy and the protocols differed widely among European burn units. They also found that the widely accepted importance of goal-directed therapy or data concerning use of albumin in the critically ill, have not yet influenced strategies of volume replacement in the burn patient [38].

Navickis, et al. in 2016 [39], conducted a metanalysis looking at recent data from both randomized and nonrandomized studies that evaluated the use of albumin and its effects on mortality and morbidity in adult patients. Randomized and nonrandomized controlled clinical studies were identified by computer database searches

and examination of journal contents and reference lists. The data that was extracted data were quantitatively combined by random-effects meta-analysis. A total of four randomized and four nonrandomized studies with 688 total adult patients were included. They found that the albumin infusion during the first 24 h showed no significant overall effect on mortality. However, when the studies that included high risk patients was excluded, use of albumin was associated with a reduction in mortality. Use of albumin also resulted in a lower incidence of compartment syndrome. They concluded that albumin can improve outcomes of burn shock resuscitation in some patients.

In general, hypertonic solutions, albumin, and plasma have been associated with lower volume requirements for initial resuscitation, lower intra-abdominal pressure, and a lower incidence of compartment syndrome [40].

Eljaiek et al. in 2017 [41] did a review the literature summarizing the effect on mortality of albumin compared to non-albumin solutions during the fluid resuscitation phase of burn injured patients with >20% body surface involvement. Data was collected by searching MEDLINE, EMBASE and CENTRAL and the content of Burns and Journal of Burn Care and Research. A total of 4 trials (out of 164) involving 140 patients met their inclusion criteria. They did not find any significant benefit of albumin solutions as resuscitation fluid on mortality in burn patients. They did find that the total volume of fluid infusion during the phase of resuscitation was lower in patients receiving albumin containing solution. They concluded that there was not enough data to demonstrated benefit on mortality in burn patients resuscitated acutely with albumin solutions.

Albumin After Neurological Insult

Human serum albumin is a unique pleiotropic protein with neuroprotective properties. Intravenous administration of albumin has been reported to ameliorate neuronal damage during the acute phase of stroke, to preserve the blood–brain barrier by abolishing the hyperactivation of metalloproteinases [42], contribute to stroke recovery via neuroprotective properties and improve microvascular hemodynamics and to exert proendothelial effects [43]. Albumin administration has been shown to improve microcirculatory blood flow, increase organ perfusion, decrease leukocyte rolling and adherence, and reduce the inflammatory response [44]. The mechanisms of the neuroprotective effects of albumin could be explained by its ability to serve as an antioxidant by serving as an endogenous NO reservoir [7] and attenuate brain edema and inhibit the endothelia cell apoptosis [45, 46].

Belayev et al. demonstrated this neuroprotective effect of albumin as compared to normal saline infusion in Rats following a 2-h middle cerebral artery occlusion (MCAO). They showed that while albumin therapy does not induce major increases in parenchymal perfusion, it resulted in significant increases in arteriolar diameter, and reversed the stagnation, thrombosis, and corpuscular adherence within cortical venules in the reperfusion phase after focal ischemia by laser-Doppler perfusion imaging (LDPI) [43]. Thus they demonstrated that albumin therapy markedly

improved neurological function, and reduced infarction volume and brain swelling by improved erythrocyte perfusion within the ischemic penumbra [43]. Kim et al. in 2007 looked at the therapeutic efficacy of albumin and its effects on the recovery of stimuli-induced cerebral hemodynamics using functional magnetic resonance imaging (fMRI) in a rat model [47]. They concluded that restoration of fMRI response magnitudes, temporal profiles, and correlations with structure may reveal the extent and specific traits of albumin treatment associated stroke recovery.

There are very few large published trials for the use of albumin after acute ischemic stroke and subarachnoid hemorrhage (SAH). In a randomized, double-blind, parallel-group multicenter trial in patients with acute ischemic stroke with a baseline National Institutes of Health Stroke Scale (NIHSS), 422 patients were randomly assigned to receive 25% albumin (2 g [8 ml] per kg; maximum 750 ml) and 419 to receive an equivalent volume of isotonic saline. The trial was stopped prematurely for futility after 841 participants were randomized. The primary outcome did not differ by treatment assignment (albumin, 44.1%; saline, 44.2%) at the end of the 90 ± 30 days of follow up. Secondary outcomes were also neutral. The main adverse event that occurred within 48 h of initialization of the treatment was mild-to-moderate pulmonary edema, which was more common with albumin (13.1%) than saline (1.2%), a rate consistent with that of albumin-treated subjects in the ALIAS Pilot Trial [48] and the Part 1 Trials [49]. The incidence of symptomatic intracranial hemorrhage within 24 h was also almost 2.4-folds higher with albumin (4.1%) as compared to saline (1.7%) [50] resulting in a higher (2.8-folds) risk of a larger parenchymal hemorrhage in the albumin treated group by CT.

In the ALIAS pilot trial, Albumin in doses ranging up to 1.25 g/kg/day for 7 days was tolerated by patients with subarachnoid hemorrhage without major complications and it was thought to be neuroprotective. They showed that Albumin in the dose of 1.25 g/kg/day for 7 days had lower rates of cerebral vasospasm measured by transcranial Doppler (TCD), delayed cerebral ischemia (DCI), and cerebral infarctions [51].

In the SAFE trial, patients with traumatic brain injury (TBI) treated with albumin had worse outcomes than saline, most probably because the hypo-osmolar (4%) albumin solution with mean measured osmolarity of 266. Van Aken et al. very eloquently showed that osmolality of an infusion solution rather than the colloid osmotic pressure per se represents the key determinant in the pathogenesis of cerebral edema formation [52].

Albumin in the Cardiovascular ICU

Cardio-pulmonary bypass (CPB) that is commonly used in patients undergoing routine and complex cardiovascular surgery triggers a systemic inflammatory response due to a combination of surgical trauma, activation of blood components in the extracorporeal circuit, endotoxin release, ischemia and reperfusion injury [53] resulting in fibrin formation, platelet activation/consumption, and endothelial damage [54]. This ultimately contributes to low grade fever, increased third spacing [55]

due to loss of endothelial integrity, hemodynamic instability, coagulopathy and sometimes leading to multiple organ failure and even death [53, 54]. Multiple attempts to mitigate these by off pump surgery, limiting the extracorporeal circuit, biocompatible coating, steroids etc. have failed to date. The use of 5% albumin in priming the CPB machine has many advantages, such as preservation of oncotic pressure, preventing fibrinogen and platelet adhesion, and endothelial glycocalyx protection. In addition, it maintains the vascular barrier competency, prevents interstitial edema, and keeps the integrity of the microcirculation [56].

Oliver et al. in 2003 compared 5% albumin priming with fresh frozen plasma (FFP)-based priming in pediatric patients [57]. In acyanotic, non-complex pediatric patients, use of 5% albumin in the prime as compared to use of FFP was associated with a significantly lower need of blood products. A post hoc analysis showed that cyanotic patients undergoing complex operations, use of fresh frozen plasma was associated with less blood loss.

The use of albumin in priming the adult CPB may compete with fibrinogen in the formation of the protein layer coating the circuit and the oxygenator, and the preadsorption of albumin prevents fibrinogen adsorption and platelet adhesion. In 2004 Russell et al. [58] conducted a meta-analysis which included 21 controlled studies with a total of 1346 patients and concluded that albumin prime preserves platelet counts and significantly reduced the on bypass drop in platelets count.

Golab et al. in 2011 assigned 70 children with body weight <10 kg into two groups [59]. One group received 0.5 g/kg albumin in the priming solution with the goal of maintaining colloid oncotic pressure (COP) >15 mmHg. The second group received 5% albumin in the priming solution to reach a COP > 18 mmHg. There was a comparable postoperative weight gain in both groups. Patients in the high-COP group had a shorter duration of mechanical ventilation, a higher platelet count, and higher levels of plasma lactate concentration at 24 h postoperatively.

The use of albumin in the postoperative period after cardiac surgery has resulted in the preservation in clot formation time and maximum clot firmness. However, the use of low molar hydroxyethyl starch solutions (HES) (6% 200/0.5 or 130/0.4) resulted in prolongation in clot formation time and reduction in maximum clot firmness [60].

Navickis et al. in 2012 conducted a meta-analysis looking at 18 trials with 970 total patients comparing the use of HES solutions with albumin. They conclude that the hemodynamics were similar in both groups, but the use of HES was associated with increased blood loss (33.3%), the need for packed cells (28.4%), fresh frozen plasma (30.6%), and platelet (29.8%) transfusions [61]. They did not find any differences in fluid balance, ventilator time, intensive care unit stay, or mortality.

An important finding that seemed to affect the postoperative outcome was the presence of hypoalbuminemia (cutoff 18 g/l) after cardiac surgery. Fritz et al. in 2003 found that a postoperative albumin of <18 g/l and a procalcitonin level of >2.5 ng/l are associated with a higher 28-day mortality after cardiac surgery. These were found to be better predictors than the EURO score in these patients [62].

In a recently published prospective, randomized, double-blind, placebo-controlled trial, the preemptive correction of a low preoperative albumin level by administering HSA in patients undergoing off-pump coronary artery bypass

(OPCAB) was associated with a significant reduction in the incidence of AKI, from 26% in the control group to 13.7% in the albumin group. The editorial that accompanied the study has suggested that restoring the target level is associated with reduction in AKI in amplitude greater than that of any known intervention in patients undergoing OPCAB [63, 64].

Efficacy and Safety of 20% Albumin as Compared to 5% Albumin

Recently, buffered salt solutions and 20% albumin (small volume resuscitation) have been advocated as an alternative fluid for intravenous resuscitation. In a randomized, double blind, cross over study of six healthy male subjects Bihari et al. compared the pulmonary and hemodynamic effects following intravenous administration of 30 ml/kg of 0.9% saline, Hartmann's solution and 4% albumin, and 6 ml/kg of 20% albumin (albumin dose equivalent). Pulmonary function tests (spirometry, ultrasound, impulse oscillometry, diffusion capacity, plethysmography), two/three-dimensional Doppler echocardiography, carotid applanation tonometry, blood gases, serum/urine markers of endothelial and kidney injury were measured before and after each fluid bolus. The colloids caused greater left atrial stretch, decrease in lung volumes and increase in diffusion capacity than the crystalloids, but without producing pulmonary edema. Stroke work increased proportionally to increase in preload with all four fluids, but the increase was more after colloid administration, associated with a reduction in afterload. The cardiac performance was increased mediated through a smaller volume of infusion when compared 4% albumin [33]. In addition, there was no evidence of interstitial pulmonary edema with 20% albumin, but there was an increase in Ang-1/Ang-2 ratio, which has been associated with endothelial integrity [33]. Albumin at 20% caused minimal disruption to serum electrolyte concentrations except for a decrease in calcium concentration [65].

A recent SWIPE (Small volume resuscitation With albumin in Intensivecare: Physiological Effects randomized trial compared resuscitation volume requirements, fluid balance, and biochemical and physiological efficacy of 20% albumin vs. 4–5% albumin for fluid resuscitation in ICU patients [16]. They demonstrated that the cumulative volume of resuscitation fluid at 48 h (primary outcome) was lower, peak albumin levels were higher but sodium and chloride levels lower with 20% albumin.

Limitations of Use of Albumin

The cost factors associated with albumin have been examined in great detail and assume even more importance when albumin does not seem to significantly decrease mortality. In a 1400 patient trial in a cardiac intensive care unit, a restrictive albumin use policy saved about $45,000 of wholesale costs savings per month without a change in clinical outcomes [66].

Colloids, including albumin are not without their own set of toxicities. Albumin has been associated in particular with intravascular volume overload and myocardial depression. Other toxic effects may include, but are not limited to dilutional coagulopathy, capillary leak especially in the setting of a systemic inflammatory syndrome, and anaphylactoid reactions [67].

Conclusion

Despite higher cost and limited evidence for use in critically ill patients, albumin continues to remain a colloid of choice for many across the world. Although postulated to reduce overall fluid balance in a patient and keep the fluid intravascular, repeated studies have not demonstrated such efficacy and improved outcomes. In the context of limited availability of other colloid options, chiefly due to their side effect profile, albumin continues to be accepted as one of the key resuscitative fluids currently and in the near future.

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