The Role of Albumin in Fluid and Electrolyte Balance

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Abstract

Albumin plays an important role in maintaining homeostasis within the body and depends on the cell membrane and the transport mechanism, including diffusion, osmosis, filtration, and active transport. The dissolved proteins, which are the only substances that do not penetrate the pores of the capillary membrane, are responsible for the osmotic pressure of the capillary membrane. Approximately 75% of the total colloid osmotic pressure is related to albumin.

albumin is produced by the liver. Among its many functions are its ability to maintain intravascular oncotic pressure, facilitate transportation of substances, and act as a free-radical scavenger. Levels of albumin depend on wellness or disease state of the body. When levels fall below normal, patient assessment and treatment are necessary. Replacement therapy is controversial, and albumin administration is no longer the immediate answer to fluid and albumin deficits. Generally, available data conclude that the outcomes of colloids and crystalloids are similar in most cases. It is clear that additional research is needed.

Albumin plays an important role in the makeup and function of the body. A general view of the human body and how it functions is helpful in understanding the components and how they mesh to bring balance in the body’s fluids and electrolytes.

The body is made up of approximately 100 trillion cells¹ that do not look alike and do not function in the same way. The cells that make up our bodies are “designer cells,” with each cell created to perform a specific function. Each cell must do its job in order to maintain a complex environment in which it can function—that, in turn, allows the body to function. This balance within our bodies is called homeostasis.

Homeostasis is maintained by fluids, electrolytes, and acid-base balance and is influenced by body water, cap-
illary permeability, and lymphatic drainage. Fluids are made up of water, electrolytes, minerals, and cells and travel throughout the body. They are divided into intracellular and extracellular fluid. The extracellular fluid is further divided into interstitial, transcellular, and intravascular, with blood containing the latter 2 because it contains plasma and cells. The average blood volume is approximately 5 to 6 L, of which 3 L is plasma.

Body fluids move between organs and cells and depend on the ability of the cell membrane and transport mechanism to allow movement of fluid components within the vascular system. These transport processes include diffusion, osmosis, filtration, and active transport.

Osmosis is a process by which a solvent tends to move through a semipermeable membrane from a solution of lower concentration to a solution of higher concentration. The osmotic pressure exerted by particles in a solution is determined by the number of particles per volume of fluid versus the mass/size of the particles.

Capillary pressure tends to force fluid and dissolved substances through the capillary pores into the interstitial spaces. Osmotic pressure, caused by the plasma proteins (called colloid osmotic pressure or oncotic pressure), tends to cause fluid to move via osmosis from the interstitial spaces into the blood, thus preventing a significant loss of fluid volume. However, there are small amounts of protein and fluid that do leak into the interstitial spaces but are returned to circulation by the lymphatic system via the thoracic duct.

The colloid osmotic pressure is influenced by proteins. This is due to the proteins being the only dissolved substance in the plasma and interstitial fluid that do not diffuse readily through the capillary membrane. Therefore, the concentration of protein in plasma is 2 to 3 times greater than proteins found in the interstitial fluid (ie, plasma, 7.3 g/dL; and interstitial fluid, 2 to 3 g/dL).

Only those substances that do not pass through the semipermeable membrane exert osmotic pressure, and proteins are the only substances that do not readily penetrate the pores of the capillary membrane. Thus, the dissolved proteins of the plasma and interstitial fluids are responsible for the osmotic pressure at the capillary membrane.

The osmotic pressure differs at the cell membrane and the capillary membrane. Therefore, the terms are different: at the capillary membrane, the terminology is colloid osmotic pressure, or oncotic pressure, while total osmotic pressure represents the cell membrane osmotic pressure.

• **WHAT IS ALBUMIN?**

Looking at a serum albumin molecule, which resembles a large bunch of grapes, makes it easy to understand the complexity of this substance. Albumin is produced by the liver at 9 to 12 g/day, and approximately 60% of it is located in the extravascular space. It has a single polypeptide chain of 580 amino acids, with 17 intrachain S-S bonds aligned in a multiple-loop structure. Albumin has a strong negative charge of minus 17, allowing it to be very soluble in water. It has no carbohydrate side chains. Total body albumin (in a 70 kg man) is 350 g, with the normal range of adults/elderly people being 3.5 to 5.0 g/dL or 35 to 50 g/L (SI units). Average levels for newborns are 3.5 to 5.4 g/dL; for infants, 4.4 to 5.4 g/dL; and for children, 4 to 4.9 g/dL.

The circulating life span is 12 to 20 days. The turnover rate is around 15 g/day. There is no storage of reserve, and it is not catabolized in starvation.

• **WHAT DOES ALBUMIN DO?**

One of the functions of albumin is to maintain intravascular oncotic (colloid osmotic) pressure. To facilitate movement of fluid throughout the body, the average capillary pressure is 15 to 25 mm Hg greater at the arterial end than at the venous end. Starling’s law describes forces that determine fluid movement across the capillary membrane. Balance between pressures on each side of the capillary membrane is related to hydrostatic pressure pushing fluid out of some capillaries and osmotic pressure pulling fluid back into other capillaries. There is also a small amount of fluid that does not follow this path but leaks through and is returned by way of the lymphatics.

In addition to maintaining colloid oncotic pressure, albumin also facilitates transportation of substances. The presence of many surface-charged groups and many specific binding sites, both ionic and hydrophobic, allow albumin to bind and transport a large number of compounds. These substances include bilirubin, metals, ions, enzymes, amino acids, hormones, free fatty acids, drugs, and phospholipids. Albumin is essential for the metabolism and detoxification of many of these substances. Not only can albumin transport amino acids to tissues but pinocytosed (engulfed liquid) albumin can also serve as a source of amino acids for the tissues.

Albumin functions as a free-radical scavenger. There is 1 free sulphydryl group that reacts with thiol compounds.

• **WHAT IS THE NORMAL LEVEL OF ALBUMIN?**

The plasma protein is made up of a combination of albumin with an average molecular weight of 69,000; globulins, 140,000; and fibrinogen, 400,000. The normal range of albumin in adults/elderly is 3.5 to 5 g/dL and for children, 4 to 5.9 g/dL. The average relative concentrations
of the different types of plasma proteins and their colloid osmotic pressures are as follows: albumin, 4.5 g/dL (21.8 mm Hg); globulins, 2.5 g/dL (6.0 mm Hg); and fibrinogen, 0.3 g/dL (0.2 mm Hg), yielding a total of 7.3 g/dL (28 mm Hg).3

Looking at the components, it can be seen that 75% of the total colloid osmotic pressure is from albumin, 25% from globulins, and a very less percentage from fibrinogen. Even though the colloid osmotic pressure of plasma is weak, it still plays an important role in maintaining normal blood and interstitial fluid volumes.

● WHAT CAUSES THE LEVEL TO CHANGE?

As long as the levels of albumin remain constant, the body runs like a well-tuned car. However, nothing remains constant. Plasma levels of albumin may be increased or decreased depending on the disease state. Elevations of serum albumin concentration occur infrequently. Increases resulting from dehydration can be seen when plasma water decreases. Upon rehydration, the albumin level usually returns to normal.

An example of disruption of these pressures is edema. There are several causes of extracellular edema, such as a decrease in plasma proteins that includes albumin. The cause may be an increased loss of proteins (ie, nephrosis, wounds, etc) or failure to produce proteins (ie, liver disease or malnutrition).

A decrease in the albumin level may be the result of decreased synthesis, increased catabolism (use and loss), or combinations of these. A deficiency known as analbuminemia is possible. There are only approximately 20 families reported to have inherited analbuminemia. However, even with levels of about 1% normal, these patients are reported to be clinically normal except for mild edema and altered lipid metabolism. They have become conditioned to exist with below-normal levels. When albumin infusions are needed in these people, the half-life is 50 to 60 days, which is approximately 3 times the normal life span.3

The most common cause of decreased plasma albumin levels is related to inflammatory processes (ie, acute-phase response and chronic inflammatory disorders). With inflammatory processes, there are 4 potential causative factors, including hemodilution, loss of extravascular space, increased consumption by cells locally, and decreased synthesis.

When it comes to hepatic disease, acute hepatitis, or cirrhosis, albumin levels do not correlate well with the severity, prognosis, or level of total hepatic function.1 The parenchymal damage or loss has to be severe to affect the liver’s ability to synthesize albumin. The mechanisms responsible for the decreased albumin levels seen in most cases of hepatocellular disease include increased immunoglobulin levels; third-space loss (extravasation into the extravascular space); and direct inhibition of synthesis by toxins.

Urinary loss of albumin may lead to decreased levels. As mentioned earlier, albumin is a relatively small and globular molecule. This makeup allows a significant amount to be filtered into the glomerular urine, but most of it is reabsorbed by the proximal tubular cells.

Normal excreted urine contains approximately 20 mg albumin/L urine. Excessive excretion suggests glomerular filtration that exceeds the proximal tubular cell’s ability to reabsorb; proximal tubular damage; hematuria; or combinations of these.3 Except for the analbuminemia, the lowest levels of plasma albumin are seen in patients with active nephrotic syndrome, where small proteins are lost disproportionately. Gastrointestinal loss of albumin does not generally cause concern unless the loss is excessive or long lasting.

● WHAT HAPPENS IF THERE IS A DEFICIT?

In a healthy person with normal nutrition, the liver will produce additional albumin to normalize the level. Very low levels can lead to swelling in the ankles (edema), as well as fluid accumulating in the abdomen (ascites), and in the lungs (pulmonary edema). Edema and ascites are usually secondary to the increased vascular permeability, which permits the loss of albumin into the spaces versus being the direct result of a decreased plasma albumin level. The amount of albumin varies in these fluids as compared with plasma and is usually higher with certain forms of ascites.

Patient assessment is vital in making a medical diagnosis and developing a treatment plan. The assessment should include the patient history (ie, current status, medications), clinical status (ie, body weight; intake/output; urine volume/concentration; vital signs), and laboratory data. There are a variety of methods for testing of protein/albumin, although there are concerns about the accuracy of some of the tests. Today, most albumin levels are determined through the use of an automated chemistry analyzer.

There is some chemical interference when interpreting the tests. There is no naturally occurring hyperalbuminemia, but any condition with decreased plasma water will increase the concentration of all plasma proteins, including albumin. Progesterone may also increase the protein level. In addition to disease processes discussed earlier, including acute and chronic inflammations and decreased liver synthesis, there are some medications that may cause interference, leading to a decrease in protein levels. These medications include allopurinol, asparaginase, azathioprine, chlorpropamide, cisplatin, dapsone, dextran, estrogens, ibuprofen, isoniazid, nitrofurantoin,
oral contraceptives, phenytoin, prednisone (high dose), and valproic acid. Albumin values normally fall in pregnancy, especially in the third trimester, with the increase in plasma volume.

The results of a study indicated that 75% of critically ill children with shock, metabolic acidosis, and hyperlactataemia exhibited hypoalbuminemia. The low albumin level is associated with an artificially low observed anion gap that may fail to detect the presence of lactate and other occult tissue anions. As both have been associated with severity of illness and increased mortality, failure to detect this increase in occult tissue anions might have adverse consequences for the child. The study recommended that the albumin concentration should be measured in all critically ill children with shock and that the corrected anion gap should be calculated to screen for the presence of lactate and other occult tissue anions.

**WHAT CAN BE DONE TO INCREASE THE LEVELS?**

Depression of albumin concentrations occurs frequently in hospitalized patients. Some cases may be due to dilution of body fluids from the administration of intravenous fluids. Once the patient assessment is completed and it is determined that the albumin levels are low and affecting the patient’s recovery, a treatment plan should be developed. This often results in a debate about whether to use a colloid or a crystalloid when replacing albumin.

Colloids include albumin and hetastarch, with dextran sometimes being considered. Crystalloids include lactated Ringer’s and various sodium chloride-containing solutions, with normal saline being the most common. Albumin human is a protein colloid that is a sterile solution of serum albumin prepared by fractionating pooled plasma from healthy human donors. For many years, albumin has been used for plasma volume expansion and maintenance of cardiac output (fluid resuscitation) in the treatment of certain types of shock or impending shock to improve colloid osmotic pressure. Parenteral colloids or crystalloids should not be used as substitutes for blood or blood components when oxygen-carrying capacity is reduced and/or when replenishment of clotting factors or platelets is necessary. According to Blood Weekly, January 15, 2004, research suggests a 3-way interaction among fibrinogen, immunoglobulin, and albumin that synergistically induces red blood cell (RBC) aggregation in plasma.

Because of the risks of blood-derived albumin and the lack of established superiority over alternative products for many indications, as well as cost, healthcare personnel should carefully weigh the potential risks and benefits of albumin therapy. In many areas, a direct causal relationship between hypoalbuminemia and mortality has not been established. One such pooled analysis (by the Cochran Injuries Group) of randomized, controlled clinical studies of albumin human or plasma protein fraction did not show any evidence that albumin reduced mortality compared with control (parenteral crystalloid solutions alone or no albumin) in patients with hypovolemia, burns, or hypoalbuminemia. The analysis further revealed evidence suggesting that mortality risks may not be decreased but actually may be increased by 6% overall when albumin is used. However, others have criticized the study because of its methodological problems.

Most of the information related to albumin versus saline for fluid resuscitation has come from meta-analyses of clinical trials and has provided conflicting results. In 2004, a prospective, multicenter, double-blind controlled trial published in the New England Journal of Medicine looked at albumin versus saline in critically ill patients. The patients were randomly assigned to receive either 4% albumin or normal saline for a period of 28 days. Of the 6997 patients, 3497 received albumin and 3500 received saline, with both groups having similar baseline demographic and clinical characteristics. The findings of SAFE (Saline versus Albumin Fluid Evaluation) clearly showed that the use of albumin or saline yielded similar results in similar clinical outcomes at 28 days.

This study did show that albumin appears to be safe. However, albumin’s lack of incremental efficacy and significantly increased cost negate the routine use of albumin for fluid resuscitation in the most critically ill patients. Additional information is needed to determine the precise role of albumin human in relation to parenteral nonprotein colloids and large-volume crystalloids for plasma volume expansion, maintenance of cardiac output, or the benefit of combination therapy using 25% albumin and diuretics. Specific areas that have been addressed include the guidelines from the University Health System Consortium in the United States, which state that parenteral crystalloid solutions are generally preferred for initial fluid resuscitation in patients with hemorrhagic or nonhemorrhagic shock. In the management of hemorrhagic shock, albumin is generally reserved for patients where there is a contraindication to nonprotein colloids. For shock and trauma patients, there are special considerations related to confined-space rescue. These include the degree of hypovolemia, extent of traumatic crush injury, crush syndrome, and compartment syndrome. The entrapped patient should gain circulatory access as soon as possible. The hemodynamic and clinical status of the individual affects the infusion of choice. An increase in circulating volume will help to increase cardiac output, blood pressure, and end organ perfusion. But there are also some downsides to this fluid resuscitation. The increased volume may counter the protective mechanism of a lowered blood pressure and precipitate rebleeding, dislodge the primary hemostatic thrombus, vasodilation, reduced blood viscosity, and dilution of clotting factors.
While fluid resuscitation may increase the circulating volume, there may not be an increase in the oxygen concentration. To counteract acidosis, pH buffering may be necessary, and that is when albumin may play an important role.11

As for nonhemorrhagic shock, nonprotein colloids and albumin should be used with caution in patients with systemic sepsis. In spite of decades of extensive research, the fundamental principles of resuscitation have changed very little. However, there are some blood substitute products being studied, even though they are not ready for clinical use. These substances have oxygen-carrying capacity and fall into 3 categories: those based on hemoglobin, perfluorocarbons, and liposome-encapsulated hemoglobin.12

Some clinicians recommend the use of albumin in conjunction with diuretics on a short-term basis for nephrotic syndrome when diuretics alone are unsuccessful in treating peripheral and/or pulmonary edema. Albumin may or may not be helpful after renal transplant surgery. It is generally not recommended following hepatic resection unless the resection involves more than 40% of the liver.10 However, the hepatic system has some indications for the use of albumin human. During liver transplantation with excessive blood loss, albumin may be indicated for volume expansion and controlling ascites and severe pulmonary and peripheral edema. It has been used in the acute decompensation of hepatic cirrhosis associated with reduced intravascular volume and encephalopathy, as well as problems related to paracentesis. An article published in *Hepatitis Weekly*, 2004, noted that extracorporeal albumin dialysis improves survival in acute liver failure. Its future may be in the management of moribund hospitalized patients on the transplant list awaiting a donor liver, but further clinical trials are needed to support current findings.13

Albumin has been used as a supplemental caloric protein source, but this is no longer recommended. However, it may be used in patients with diarrhea associated with enteral feeding intolerance. Albumin may be used in the treatment of hypoproteinemia to help relieve edema by increasing the osmotic pressure and facilitating diuresis. Treatment of neonatal hyperbilirubinemia may include albumin to reduce the number of exchange transfusions needed by helping to eliminate more bilirubin with each transfusion. Albumin is being used in nonsurgical patients or with cardiac surgery, though it is not generally recommended. It may be used in conjunction with nonprotein colloids and crystalloids with therapeutic plasmapheresis. To avoid hypoproteinemia, albumin may be used to resuspend large volumes of previously frozen or washed red blood cells prior to administration. If albumin is indicated following careful patient assessment, it is administered by intravascular infusion. Albumin is a blood volume expander that helps to improve cardiac output, prevents marked hemoconcentration, aids in the reduction of edema, and increases serum protein levels. As a result of the way it is processed, albumin has the potential for transmission of human viruses such as hepatitis. No cases of viral diseases have been identified, however, so the risk is considered remote. The low sodium level helps with fluid and electrolyte maintenance. Albumin may be given regardless of the patient’s blood group. The dosage and rate of administration is directly related to the condition of the patient and includes factors such as blood pressure, pulse, presence/degree of shock, hemoglobin/hematocrit values, plasma protein content/oncotic pressure, and degree of venous and pulmonary congestion.10 The amount infused must be titrated according to the individual patient’s needs and responses to treatment. The concentration also depends on the patient’s fluid and protein requirements. A solution containing 5% albumin human is usually indicated in hypovolemic patients, and 25% is more appropriate when fluid and sodium intake should be minimized (eg, hypoproteinemia, cerebral edema, or pediatric patients). A total of 125 g may be administered per 24 hours. No more than 250 g should be administered within 48 hours. A 25-g dose is the osmotic equivalent of 2 U of fresh-frozen plasma and provides as much plasma protein as 500 mL of plasma or 2 U of whole blood. A total of 100 mL of 25% albumin solution draws 350 mL into the intravascular space, increasing plasma volume by 450 mL over 30 to 60 minutes.

Some rate/volume suggestions related to albumin infusion for adults include the following:

- It may be administered rapidly in the initial treatment of hypovolemic shock with 25 g of 5% or 25% solution and repeated in 15 to 30 minutes if needed.10
- As plasma volume returns to normal, the infusion rate should be decreased to lessen the possibility of circulatory overload and pulmonary edema.
- 5% solution should not exceed 2 to 4 mL/minute.
- 25% solution should not exceed 1 mL/minute.10
- With normal blood volumes and low albumin levels, administration rates should be slower.
- 5% solutions should not exceed 5 to 10 mL/minute.
- 20% solutions should not exceed 2 mL/minute.
- 25% solution should not exceed 2 to 3 mL/minute.10

Administration doses/rates for children include

- usual initial dose in emergencies is 25 g
- for nonemergency situations, the dose should be 25 to 50% of the adult dose depending on the age/condition of the child
- premature infants may receive 1 g/kg
- for treatment of hyperbilirubinemia, a dose of 1 g/kg or 120 mL may be administered for 1 to 2 hours
- for hypoproteinemia, a single dose may be administered for 30 to 120 minutes10

Prior to initiating the albumin, IV access should be assessed or initiated to ensure a patent catheter. The solution should be checked for correctness of product, con-
centration, and volume. The solution container should be checked for cracks and intact ports, and the solution checked for turbidity. Aseptic technique should be practiced during site initiation, addition of the set, and connection of the catheter to the venipuncture device. Procedure and albumin information should be properly documented in the patient’s record.

Following initiation, the patient should be monitored. The patient’s blood pressure should be checked. Laboratory values should be monitored, including hemoglobin, hematocrit, electrolytes, and protein elevations, as well as alkaline phosphatase because it may be elevated. Central venous pressure readings are also helpful. The patient should be checked carefully for increased bleeding as the blood pressure begins to return to a normal range. The patient should also be monitored for circulatory overload, pulmonary edema, a lack of diuresis, and allergic reactions (eg, chills, fever, nausea, vomiting, urticaria, and variations of the vital signs). Additional fluids may need to be initiated for dehydrated patients. Elderly patients should be monitored more carefully because they are more susceptible to circulatory overload and pulmonary edema. If side effects occur, the physician should be notified as soon as possible. Resuscitation measures should be initiated if needed.

- Albumin is vital for fluid and electrolyte balance.
- Patient assessment is vital in developing the treatment plan.
- Albumin human administration is no longer the immediate answer to fluid and albumin deficits.
- Colloid versus crystalloid debate

Theoretical advantages of colloids (eg, albumin, heta-starch) include

- greater plasma volume expansion in relation to volume administered
- remains in the intravascular space longer
- causes less interstitial edema
- safety and morbidity rates are controversial

Crystalloids (eg, 0.9% sodium chloride and lactated Ringer’s) are less expensive and require greater volume to achieve equal plasma volume expansion.

- Findings of studies and meta-analyses are controversial.
- Generally, available data conclude that the outcomes are similar in most cases.
- Additional research is needed.

The albumin molecule is complex, and there are many unanswered questions. Infusion nurses can play a vital role in the administration and research related to albumin. A united approach can lead to a safer and more effective use of albumin, which is a win-win situation for patients, staff, and the healthcare system.

**REFERENCES**