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Commentary

Prime Solution and Administration of Albumin in Pediatric Heart Surgery

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Albumin is the main cause of osmotic pressure of blood. The albumin content of the body is 4-5 grams per kilogram, which is mainly distributed in the extracellular space. 30-40% of the body albumin is found in the intravascular chamber and is responsible for regulating plasma volume and tissue fluid balance [1].

Human albumin as a medicinal product is a sterile water-based solution for intravenous injection. It is a physiological plasma expander and is produced from blood donor plasma.

This product is produced by alcohol fractionation method and is heated at 60 ° C for 10 hours to inactivate infectious agents [1-2].

Human albumin increases plasma volume like crystalloid and colloidal solutions, but has osmotic or oncotic properties, which is the main reason for its clinical use. Hydrostatic pressure across the capillary wall determines the distribution of intravascular fluid and interstitial compartment and is called the balance of capillary gradient so; the two main reasons for the use of human albumin are to compensate for the decrease in plasma volume and the fall in oncotic pressure caused by hypoproteinemia or severe acute hemodilution. Human albumin solution contains 130 to 160 mEq of sodium per liter which help to fluid remain longer time in the vascular space [1-3].

In patients with congenital heart disease; Non-nutritional factors such as hepatic and renal insufficiency, gastrointestinal dysfunction, right heart failure, dilution due to fluid overload and medications can affect serum albumin concentration.

A common mechanism for compensating for hypoalbuminemia is the gradual transfer of extravascular albumin into the circulation [3-4] but, there is no physiological reserve in these patients so, These patients are at higher risk for hypoalbuminemia and decreased plasma oncotic pressure, so the kidneys begin to retain sodium and water to keep plasma volume within the normal range, but sodium and water will be extravasate during the time thus, the plasma volume is kept at the interstitial edema price.

Inflammatory response syndrome because of cardiac surgery insult and using cardiopulmonary bypass pump, leads to endothelial dysfunction so; secondary edema to capillary leakage in the immediate postoperative period occurs. This chain of events and consequences is intensified by the injection of hypotonic fluids and the increase in volume with crystalloids [1-5].

In neonate or pediatric with congenital heart disease who scheduled for heart surgery and cardiopulmonary bypass, we need to establish an artificial circulation by cardiopulmonary bypass pump and due to limited volume

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of circulatory blood; sever hemodilution is a potential risk. Most of the time, this hemodilution compensated by adding packed red blood cell to the prime solution but oncotic deficit resulting from prime solution will be maintain [1-3]. We believe the risk of this iatrogenic hypo albuminemia is considered underestimated and it is not compensated accurately.

Meta-analysis and clinical trials of human albumin administration have been more frequent in critically ill patients in adult with septic shock and have suggested different results regarding albumin administration in critically ill patients. Some have reported that albumin use has been associated with increased mortality among critically ill patients. The power of these studies was limited and patients with different serum albumin level with disease diversity were enrolled in the studies [6-9]. Therefore, the results obtained from these studies can in no way be generalized to patients with underlying heart disease and candidates for heart surgery.

Preliminary clinical observations confirmed severe impairment of plasma oncotic pressure after heart surgery in children with congenital heart disease, and many of these children developed secondary renal impairment, hemodynamic shock, and tissue edema after surgery so; we conducted a small sample study for evaluation our hypothesis.

This prospective observational sample study was conducted in 24 neonates and pediatrics (age between 10 days up to 3 years old) by congenital heart disease was scheduled to undergo intracardiac repair by cardiopulmonary bypass method (on pump method).

Patients were randomly divided into three groups, but subjects were matched in terms of demographic information including age, weight and type of congenital heart disease, coexisting disease, general condition and laboratory date such as arterial blood oxygen saturation and level of blood hemoglobin as much as possible.

The anesthesiologist and surgeon were fixed in all patients and the anesthesia method and prescribed drugs and the method of surgical procedure were the same. A preoperative baseline echocardiography and electrocardiography were performed. Anesthesia was induced with sevoflorane (2– 5%), fentanyl (3–5 mcg/kg), and pancuronium (0.2 mg/kg) to facilitate tracheal intubation. Maintenance of anesthesia was performed with isoflurane (0.4-0.6%) in oxygen-air mixture and fentanyl infusion was continued besides intermittent doses of pancuronium and midazolam were given depending on the patient's condition.

The initial activated clotting time (ACT) before systemic heparinization was reported then 3-4 mg / kg unfractionated heparin was prescribed to achieve the target ACT more than 480 seconds. Monitoring included electrocardiogram, pulse oximeter, arterial line for accurate measurement of blood pressure, cerebral and tissue oximetry, central venous pressure and measurement of urinary output were installed for patients and arterial blood analysis was performed periodically.

Membrane oxygenator with the same brand and characteristics was used for patients during CPB. Conventional CPB circuit was performed which was primed with mannitol (20%) 0.5 g / kg and sodium bicarbonate (7.5%) 1 ml / kg and 100 units / kg unbroken heparin as a fixed component but in first group (traditional prime solution) we used normal saline 20 ml/kg and for secod group (Albumin group) we used Albumin and normal salin in 1 to 4 ratio and total volume considered 20 ml/kg and in the third group (FFP group) we used Fresh Frozen Plasma (FFP) 20 ml/kg.

Packed red blood cells were added to the pump volume before CPB to obtain a primary hematocrit of 20% ±2% for the prim fluid and the target hematocrit was maintained at28% ±5% during the cardiopulmonary bypass pump.

5% human albumin solutions have an osmotic pressure approximately similar to normal plasma. The human Albumin 25% oncotic pressure is four times higher than normal human serum oncotic pressure therefore, in Albumin group after weaning from cardio pulmonary bypass pump, we prescribe all drugs diluted in Albumin and normal saline in 1 to 4 ratios but traditional and FFP groups received drugs diluted by normal saline.

Circulatory arrest and myocardial preservation were achieved by prescribing Custodiol cardioplegia. Arterial blood gas analysis and ACT were performed at 30-45 min intervals and if necessary during surgery. The systemic pump flow was adjusted between 120 and 200 ml / kg / min based on serum lactate levels and tissue and cerebral oximetry numbers. At the end of surgery, systemic heparinization based on total amount of heparin prescription and the half-life of it in one by one ratio, was reversed by protamine. All patients were transferred to the intensive care unit to continue mechanical ventilation and planned extubation in stable conditions.

In patients using traditional prime solution the duration of mechanical ventilation, the duration and dose of prescribed inotropes and the length of stay in the ICU was longer. (p Value; 0.04, 0.027, 0.032 and 0.038 respectively)

Although these times were longer in the FFP group but, they were not statistically significant.

Urine output was better in the albumin group and was similar to the FFP group. Incidence of oliguria was higher in traditional group. We supported many patients after surgery to compensate for decreased renal function with peritoneal dialysis. (18 patients out of 24 patients)

Postoperative bleeding was significantly lower in the FFP group than in the albumin and traditional groups.

Hemodynamic stability after surgery was better in albumin and FFP group. Arterial blood gas parameters in Albumin and FFP group was the same and better than

traditional group. We could not evaluate the risk of infection and adverse effects in our sample study.

Hypoalbuminemia around the time of congenital heart surgery increases the risk [1-2]. Cardiopulmonary bypass pump that used in routine congenital cardiac surgery is an advanced extracorporeal oxygenation system. Extracorporeal oxygenation triggers a systemic inflammatory response that leads to endothelial damage and microcapillary leakage. It is the main mechanism for capillary leakage of plasma, amino acids and protein into the extravascular space, which causes hypoalbuminemia [1-3]. The half life of endogenous albumin is about 3 weeks, while human-derived albumin is only 12-16 hours and is significantly reduced under conditions of increased capillary permeability [2]. During major surgery, more than half of the body's albumin, which is normally in the circulatory system, may be lost [3].

Pediatric or neonate suffering from iatrogenic hypoalbuminemia after cardiac surgery are prone to catabolic stress, decreased amino acid supply, additional impaired protein synthesis, degradation and decomposition of proteins, release of protein into the extra vascular space, and retention of water and salt due to changes in the endothelial permeability. Decreased in serum albumin levels are associated with increased inflammatory and acute reactant proteins, high concentrations of C-reactive protein (CRP), procalcitonin (PCT), interleukin-6 (IL6) and antitrypsin α1 after heart surgery [1-3, 9].

Recent studies have shown that albumin can be used as a postoperative volume enhancer, as a last resort treatment after crystalloids or non-protein colloids, after heart surgery [6,9]. The researchers believe that the first choice for priming the circuit for extracorporeal circulation is a mixture of crystalloids with non-protein colloids that can be preferred to prevent fluid accumulation in the interstitial space of the lung [6,9,11-12].

Some research has shown that adequate blood volume during cardiopulmonary bypass can be maintained with crystalloids as the only priming fluid in the pump, but base on our observation it will be accompany with impaired ABG parameter, hemodynamic instability, and decrease urine output and higher risk of interstitial edema.

A commonly used program is human albumin and crystalloid pump prime, which is adjusted to obtain a hematocrit of 20% and a plasma albumin level of 2.5 g / 100 ml, but the level at which each may be safely reduced has not yet been defined [6-13].

It is not known whether there is a concentration threshold for serum albumin levels below which clinical oncotic function is compromised; however, there is an agreement that oncotic activity remains physiologically acceptable at albumin levels greater than 2 g / dL and total proteins more than 3.5 g / dL. There is evidence that serum oncotic pressure close to 20 mmHg indicates a threshold below which the risk of complications increases [1-3,6,9,11-14]. Based on our clinical observations, the use of human albumin or fresh frozen plasma can be demonstrated in the prime solution.

Compared to our small enrolled patients due to the small study designed, we would like to conclude that human albumin may be necessary to prevent acute complications of hemodilution due to the prime solution but, it need future study for confirmation.

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