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Clinical Study on the Effects of Different Infusion Solutions on Colloid Osmotic Pressure During Major Abdominal Surgery and Perioperative Albumin in Elderly Patients

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Abstract: ***Objective:*** To explore the effects of different infusion schemes on colloid osmotic pressure during major abdominal surgery and perioperative albumin in elderly patients. ***Methods:*** 140 elderly patients of 65-80 years old undergoing major abdominal surgery were divided into 4 groups according to the method of random number table , and different proportions of crystals and colloids were given to different groups (group A: full crystal, group B: crystal-colloid ratio 1: 1, group C: crystal-colloid ratio 2: 1, Group D: crystal-colloid ratio 1: 2). The plasma colloid osmotic pressure and level of albumin during perioperative period were monitored. Simultaneously observe the arterial blood pH, blood glucose, extubating time of endotracheal tube, postoperative feeding time, *et al*. ***Results:*** The total amount of liquid infusion in the group of whole crystal was 3056ml (3056 ± 253), which was significantly more than other groups (P<0.01). At the same time, the colloid osmotic pressure decreased by 11.9 mmHg (11.9 ± 2.8), which was more obviously decreased than that of the other groups(B group3.9 ± 1.3, C group 1.5 ± 0.3, D group 4.7±2.1). The difference was a statistically significant(P<0.01). On the next day after surgery, the level of albumin decreased by an average of 4.3 g / L (4.5 ± 1.9) compared with that in group B before surgery, and group C decreased by 2.9 g / L (2.9 ± 1.2) in average, which was significantly different (P<0.05) from group A 10.2 g / L (10.2 ± 1.8). There was no statistically significant difference between group A and group D (P>0.05). And the other indexes were not significantly different between the two groups. ***Conclusion:*** This study found that different infusion solutions with different crystal-colloid ratios had an effect on perioperative colloid osmotic pressure and level of albumin.

Keywords: Medical imaging department; Standardized measures; Clinical teaching

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1 Introduction

The aging of the population has become a very serious social problem in our country, which has a critical impact on our country's social and economical development and others. It is predicted that the proportion of the people over 65 years old will reach about 28% of the total population in China in 2040. The situation of aging population is extremely serious[1]. Elderly patients are prone to be lower level of albumin due to liver synthesis, malnutrition and disease.

During perioperative period of major abdominal surgery, it is a major concern to decide amount and type of fluid to infuse due to loss of body fluid , bleeding, albumin loss and other issues caused by fasting, bowl preparation or inability to eat. A good strategy of infusion solutions can improve the prognosis of patients[2].

It is still a controversial issue to choose whether colloidal or crystalloid solution for intraoperative support of plasma volume. The current trend to use a small amount (or not) of colloidal fluids stems from

study on intensive care for severe case, in which the use of hydroxyethyl starch is associated with an increased risk of acute injury of kidney. However, these findings have not been repeated in common surgery[3].

Clinically, there is a normal existence of decline in serum albumin after major abdominal surgery, severe trauma and infection[3]. Hypoproteinemia can reduce colloid osmotic pressure in blood vessels and cause edema in wounds and other organs or tissues. Apart from affecting the healing and recovery of body's wound, it can also increase the possibility of postoperative pulmonary edema, anastomotic leak, wound nonunion, infection and other complications. So the mortality can increase[4-6]. Studies[7] have proposed that major surgical stress leads to inflammatory response of tissue or the whole body and further increases permeability of micrangium as well as causes leakage of albumin, which is the main reason for the early decline in albumin concentration. At present, the main methods of reducing leakage of albumin in micrangium include: use of artificial colloids or hypertonic liquid to increase osmotic pressure in blood vessels, use of inflammatory medium to antagonize and control infection.

Among patients undergoing major abdominal surgery, there is no evidence as a part of the intraoperative object-oriented liquid therapy. After one year of follow-up, there was a statistically significant difference in renal function between hydroxyethyl starch and crystalloid solution. And also the survival without disability in group of colloid was significantly higher than crystal[8].

At the same time, there are several studies suggesting that low colloid osmotic pressure is significantly associated with pulmonary edema and cardiac insufficiency by retention of ejection fraction[9-10]. Therefore, there is an association between colloid osmotic pressure and levels of albumin and the prognosis of elderly patients undergoing major abdominal surgery.

Based on these evidences, we propose the hypothesis: different crystal-colloid ratios will effect colloid osmotic pressure and level of albumin in patients during perioperative period, and thus have effect on the prognosis of patients.

2 content and methods of research

2.1 Inclusion criteria

Selection of major abdominal surgery, age 65-80 years, ASAI-III, BMI 18-25 kg/m^2, and the study obtains the consent of patients and their families and is approved by the clinical research ethics committee of hospital.

2.2 Exclusion criteria

Suffering from a disease of central nervous system and mental disease; taking sedatives or antidepressants for a long time; alcoholic or drug dependent patients; preoperative hypoalbuminemia, severe anemia, infection and coagulation disorders, renal insufficiency, cardiac function of grade III and above; infection and hematoma at the site of puncture; patients who cannot cooperate effectively; those who are allergic to hydroxyethyl starch or anesthetic drugs.

2.3 Rejection criteria

Intraoperative blood loss exceeds 10% of blood volume or those who requires infusion of plasma and albumin.

2.4 Groups of cases

The 140 cases to be included are divided into 4 groups according to the method of random number table , with 35 cases in each group, which are group A (full crystal), group B (crystal-colloid ratio 1: 1), and group C (crystal-colloid ratio 1: 2) and group D (crystal-colloid ratio 2: 1); the crystal is compound sodium chloride injection; the colloid is hydroxyethyl starch 130/0.4 injection.

3 Implementation and monitoring of anesthesia

3.1 reparation of anesthesia

Patients fasted for 8 hours and dehydrated for 4 hours before operation, and the measure value of albumin was recorded before operation. After entering the room and checking the patient correctly, the heart rate, blood pressure, and blood oxygen saturation were monitored. The right internal jugular vein intubation was locally anesthetized. Simultaneously, the central venous pressure was monitored. And artery puncture and continuous invasive blood monitoring were performed. Colloid osmotic pressure, blood gas and urine catheterization were extracted to reserve. Emergency drugs like atropine and adrenaline were also reserved, and dual-channel of peripheral veins was established.

3.2 Induction and maintenance of anesthesia

Methods of anesthesia are all general anesthesia with tracheal intubation. Target concentration of 4ug/ml

and remifentanil of 1.5-2.0 μg/ml were set by target-controlled infusion of propofol. Rocuronium of 0.6-0.8 mg/kg was infused by intravenous bolus. After the breathing was manual-controlled for 3 minutes by giving oxygen and extracting nitrogen gas, with tracheal intubation under video laryngoscope through the mouth. Mechanical ventilation was performed by connecting with an anesthesia machine. Lung protective ventilation strategy was adopted in surgery (tidal volume of 6-8 ml/kg, respiratory rate of 12-16 times/minute, positive end-expiratory pressure of 5mmHg, maintaining the end-expiratory carbon dioxide partial pressure of 35-50 mm Hg). In surgery, propofol and remifentanil were pump casting and BIS of sevoflurane inhalation was maintained at 51-60. And rocuronium was added continuously, while neuromuscular monitoring was conducted to maintain deep neuromuscular effects.

3.3 Liquid infusion

After the venous channel was established and the samples of the first arterial blood gas and colloid osmotic pressure were taken, intravenous fluid infusion was started. Liquid infusion consisted of two parts: preload and continuous infusion. Liquid infusion was given at a ratio of crystal to colloid. The amount of preload was 10 ml/kg, and the time of infusion was 20-30 minutes, with continuous infusion thereafter. The amount of continuous infusion was adjusted according to the central venous pressure and blood pressure.

3.4 Intraoperative monitoring

The central venous pressure was maintained at 8-12 cm H2O, and the blood pressure was maintained at ± 20% of the basal blood pressure before surgery. Under the condition of normal CVP, vasoactive drugs like ephedrine and urapidil were given for expectant treatment; the intraoperative heart rate was maintained at 50-100 times /minute. According to the situation, atropine and esmolol should be given for expectant treatment.

Monitoring of plasma colloid osmotic pressure and blood gas were performed separately after admission, after arterial intubation was established, before liquid infusion, 2 hours after the start of operation, and at the end of the operation.

3.5 Observation indexes

Main indexes: intraoperative colloid osmotic pressure, preoperative and postoperative albumin. Secondary indexes: intraoperative blood pressure, heart rate, fluid volume, bleeding volume, urine volume, blood pH, and blood glucose; postoperative extubation time, time to start eating, total hospitalization time, cardiopulmonary and renal dysfunction events, etc.

3.6 Implementation of blind method, data arrangement and analysis

The anesthesiologist in charge strictly perform according to the operation manual. The data collection, arrangement and analysis were carried out by another specific person who knew nothing about the grouping. The data analysis was carried out by SPSS19.0 statistical software; the qualitative data is tested by chi-square test or Fisher; If measurement data met normality, the independent sample t would be used to test; if not, the rank sum test was used; the data of the two repeated measurement were analyzed by variance; $P<0.05$ was the condition of statistical significance.

4 Results

There were no significant differences in characteristics of demographic and surgical status among groups A, B, C, and D (Table 1). Among these patients, 93.1% of the surgery were performed under laparoscope, and 30% of them were admitted to the intensive care unit after surgery. The operation time in average was 3.02 hours (3.02 ± 0.24), and the extubation was performed in the recovery room 15-45 minutes after surgery. The patients who were admitted to the intensive care unit had an average of 2.1 hours (2.10 ± 0.5) of extubation time. The blood loss during operation was 50-100ml, and the median of urine output was 300 ml (200-500). There were no significant differences between postoperative time of eating and total time of staying in hospital (Table 1).

Table 1. Preoperative demographic characteristics and surgical status of patients in each group

Groups	Group A	Group B	Group C	Group D	ANOVA
Amount of cases	32	35	30	34	
Age(years)	69.8±3.6	68.6±2.1	70.1±3.2	69.2±2.5	NS
BMI(kg/m^2)	20.5±2.3	21.8±2.5	20.9±1.9	21.2±3.1	NS
Male(%)	52.2	68.3	56.5	60.8	

Continued table 1

Groups	Group A	Group B	Group C	Group D	ANOVA
Complications(%)	60.8	56.7	62.5	52.2	
Gastric cancer/Colorectal cancer	8/24	12/23	10/20	9/25	
Abdominal surgery(case)	4	2	2	1	
Duration of anesthesia(min)	232±43	245±62	246±39	242±50	NS
Operation time(min)	199±29	203±35	205±38	189±31	NS
Blood loss(ml)	60	75	80	75	NS
Urine volume(ml)	400	300	275	310	NS
Postoperative time of eating(day)	3.2	2.1	1.9	2.4	NS
Total time in hospital(day)	15.2	13.3	14.0	14.2	NS

The total amount of liquid infusion in the group of whole crystal was 3056 ml (3056 ± 253) in average, which was significantly increased compared with other groups (P<0.01). At the same time, the colloid osmotic pressure decreased by 11.9mmHg (11.9 ± 2.8), which has statistically significant difference (P<0.01), compared with group B of3.9 ± 1.3, group C of 1.5 ± 0.3, group D of 4.7±2.1. On the next day after the surgery, the albumin level decreased by an average of 4.3 g/L (4.5 ± 1.9) in group B compared with that before surgery, and it in average decreased by 2.9 g/L (2.9 ± 1.2) in group C with a statistically significant compared with 10.2 g/L (10.2 ± 1.8) in group A. There was a statistically significant difference (P<0.05), and there was no difference between group A and D (P>0.05). In addition, intraoperative arterial blood pH and blood glucose were not statistically different between the four groups (P>0.05) (Table 2). There were no significant differences in intraoperative blood pressure at any time point (every 30 minutes after admission) in each group and between every group (Figure 1). None of adverse events such as acute pulmonary edema, heart failure, and renal impairment occurred during follow-up until discharge.

Table 2. Total volume of infusions, intraoperative COP, arterial blood gas pH, blood glucose, and perioperative albumin

Group	Group A	Group B	Group C	Group D	ANOVA
Total volume of infusion(ml)	3056±253	1652±235	1538±289	1708±323	P<0.01
Postoperative decrease of albumin(g/L)	10.2±1.8	4.5±1.9	2.9±1.2	7.5±2.2	P<0.05
Postoperative decline of COP(mm Hg)	11.9±2.8	3.9±1.3	1.5±0.3	4.7±2.1	P<0.01
Arterial blood gas(pH)	7.36±0.18	7.32±0.23	7.30±0.32	7.38±0.49	NS
Blood sugar(mmol/L)	6.5±1.7	6.0±1.5	6.8±0.9	6.3±0.7	NS

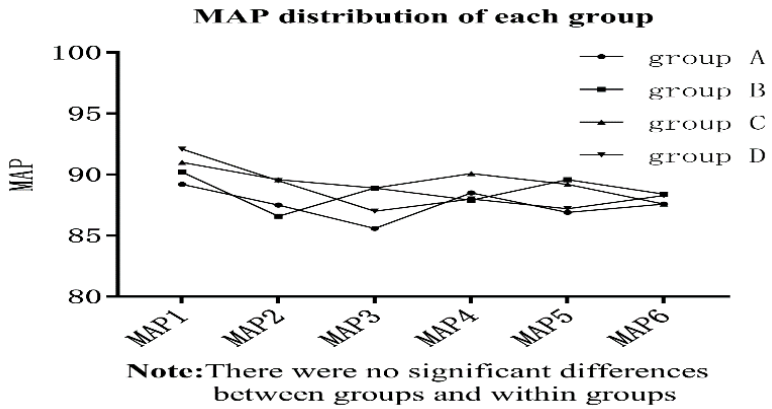

Figure 1. Arterial pressure in average of each group at different time points

5 Discussions

This study found that liquid infusion strategies of different crystal-colloid ratio had a significant effect on perioperative colloid osmotic pressure and level of albumin. Infusion of full crystal would significantly reduce colloid osmotic pressure and perioperative level of albumin. But it didn't have effects on intraoperative hemodynamic parameters such as blood pressure, heart rate, intraoperative blood loss and alkali balance, postoperative time of extubation, food tolerance and the total time in hospital.

The infusion of crystal fluid will significantly reduce the plasma colloid osmotic pressure and level of albumin. When the crystal colloid ratio was 1: 1 or 2: 1, these combinations of liquid species were relatively good for the maintenance of central venous pressure, albumin and plasma colloid osmotic pressure. Although this study did not show any effect on relevant postoperative indexes, Sinclair and others evaluated the effect of intraoperative capacity optimization on the repair of proximal femoral fracture in elderly patients, making a comparison between only receiving lactated Ringer's solution and the combination of lactated Ringer's solution and hydroxyethyl starch[11]. It was pointed out that the length of hospital stay(11 days in average) in the group of combined fluid treatment was significantly shorter than lactated Ringer's solution (20 days), and colloids had clinical significance for fluid management in perioperative period.

In this study, the group of full crystal needed more capacity to maintain hemodynamic stability. The crystal liquid replaced blood loss at a ratio of 3: 1, while the hydroxyethyl starch was 1: 1. That is also why it had to maintain normal blood capacity when using full crystal liquid during the operation. In addition, Boldt *et al*[12] proposed that the inflammation after using crystal fluid, endothelial damage and activated markers in elderly patients were significantly higher than those based on hydroxyethyl starch of 130/0.4. Apart from improving hemodynamics, the optimization of the capacity status in vessels of patients may have an important impact on the immune response. Perioperative fluid optimization during major abdominal surgery is a method to limit the incidence and severity of systemic inflammatory reactions. When the stress from major abdominal surgery results in a systemic inflammatory response, Hydroxyethyl starch 130/0.4 can reduce endothelial cell damage and tissue damage caused by neutrophil, and increase intravascular osmotic pressure, thereby improves micro vascularity and lessen leakage because it has a medium-molecular-weight structure. This also partially explains the mechanism behind the lower decrease in serum albumin and colloid osmotic pressure after crystals combined with colloids in this study[13].

Although in our study, there was no significant difference in the time to start eating after surgery. And it was not possible to evaluate the differences in food intolerance between groups because of the lack of attention to postoperative nausea and vomiting. However, some scholars have suggested that 2 L lactated Ringer's liquid, compared with hydroxyethyl starch, can significantly prolong the recovery time of food intolerance in laparoscopic major abdominal surgery, regardless of whether patients have postoperative complications[14]. At the same time, many studies have proposed the negative impact of large crystal fluid volume in abdominal surgery[15-17].

In this study, 60% of elderly patients with diastolic heart dysfunction accompanied by diastolic heart failure preserved by ejection fraction. Although this study did not find perioperative acute heart failure caused by different fluid infusions, previous studies have emphasized that hypoalbuminemia, especially severe hypoalbuminemia, can lower the hemodynamic threshold acute aggravated by diastolic heart failure in elderly patients, especially for patients with paroxysmal elevated left ventricular filling pressure. In addition, serum albumin and colloidal plasma penetration pressure were an important factors in regulating or exacerbating clinical response of acute pulmonary wedge pressure elevation[9, 18, 19]. At the same time, heart failure patients with normal left ventricular ejection fraction are usually the elderly patients with long-term hypertension and concentric hypertrophy. They are usually very sensitive to sodium and volume. Hypoalbuminemia can be the important factor of frequently occurred acute pulmonary edema Among these people[20]. Therefore, for elderly patients with diastolic heart failure, maintaining perioperative levels of albumin and plasma colloid osmotic pressure have an important effect.

Although the use of crystals or colloids in patients with increased capillary permeability and hypovolemia has been controversial, this study found that the application of hydroxyethyl starch had effects on plasma colloid osmotic pressure and serum albumin in

elderly patients undergoing major abdominal surgery. The Starling mechanism is suitable for normal capillary permeability, and it will increase the permeability of the microvascular wall to water and osmotic pressure in the absence of plasma protein or under the condition of very low plasma protein concentration, which will affect the establishment of reverse osmotic pressure and lead to frequent occurrence of interstitial water poisoning. The previous studies found the use of crystal or colloid load on pulmonary permeability, edema, and injury in patients with severe sepsis accompanied with hypovolemia and in severe patients with non-sepsis and concluded that the severity of pulmonary edema and injury is not affected by the type of fluid used to correct blood volume on the premise that the fluid load was situated at the steep part of cardiac function curve[21].

There are still shortcomings in this study. The small sample size of the study may lead to false negatives in some results. In addition, due to the limitations of the conditions of the study, it may have certain limitations of using central venous pressure to guide fluid infusion; Finally, major abdominal surgery is effected by various factors such as preoperative nausea, vomiting, and bowl preparation. For that reason, the preoperative blood volume of patients is disturbed by many confounding factors. This situation is commonly seen and it is just offered as reference.

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