

Comparative study of albumin 5% solution with Ringer's lactate for substitute blood loss of intra-operation on the integrity of the patient's coagulation system, renal function and electrolytes after surgery; a double-blind clinical trial study

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ABSTRACT

Introduction: The type of fluid replace sufficient volume loss during surgery is crucial for normal renal functioning.

Objectives: The aim of this study was to compare the effect of albumin 5% infusion versus Ringer's lactate solution on substitution of intraoperative bleeding on the status of the patient's hemodynamic and coagulation system after surgery.

Patients and Methods: This clinical trial study was performed on 80 patients with non-emergency surgery with the possibility of intraoperative bleeding. Bleeding replacement was performed in the control group with Ringer's lactate serum and in the case group was replaced with 5% albumin. Patients' coagulation status (prothrombin time [PT] and relative thromboplastin time and international normalized ratio; INR), electrolyte concentrations (sodium, potassium, and calcium), renal activity tests (serum urea and creatinine) were performed before and at 6, 12, and 24 hours after anesthesia.

Results: The results of the study showed no significant difference between the two groups regarding renal parameters, electrolytes (sodium, potassium and calcium) in all stages of the study. Additionally, PT and partial thromboplastin time (PPT) at 6, 12, and 24 hours post-operation in albumin receiving group was less than that of the Ringer's lactate group ($P < 0.01$). Additionally, 12 and 24 hours after operation, the INR was significantly less in the albumin group compared to Ringer's lactate serum receiver ($P < 0.05$).

Conclusion: This study showed that the administration of albumin solution in comparison with Ringer's lactate for replacement of intraoperative bleeding reduces the risk of bleeding after surgery due to less coagulation disorder.

Trial registration: The trial protocol was approved by the Iranian registry of clinical trials (identifier: IRCT20191009045037N1; <https://www.irct.ir/trial/42869>, ethical code # IR.SKUMS.REC.1395.211).

Implication for health policy/practice/research/medical education:

To compare the effect of albumin 5% infusion versus Ringer's lactate solution on substitution of intraoperative bleeding on the status of the patient's hemodynamic and coagulation system after surgery, we conducted a clinical trial study on 80 patients with non-emergency surgery. We found that the administration of albumin solution in comparison with Ringer's lactate for replacement of intraoperative bleeding reduces the risk of bleeding after surgery due to less coagulation disorder.

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Introduction

It is important to keep enough blood circulating during surgery and establish a stable hemodynamic status (1).

Failure to provide adequate volume and fluid for the body causes systemic hypoperfusion and tissue hypoxia and acidosis and also renal failure. Hemorrhage during surgery

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causes hypotension reducing blood circulation to the vital organs and, as a result, disrupts tissue oxygenation. Therefore, the correct and accurate replacement of intravascular volume in these patients requires special attention (2).

There are different opinions about determining the type of alternative solution. The amount of bleeding with various compounds including crystalloid and colloidal solutions can be compensated before surgery, based on hemoglobin and hematocrit of patients and whether or not an underlying cardiopulmonary disease is existed.

There are several crystalloid alternative solutions, including normal saline, Ringer's lactate and colloidal serum, such hydroxyethyl starch, gelatin and 5% albumin, which always arise the question of which is the ideal solution (3).

Crystalloids such as Ringer's lactate have a short half-life in the bloodstream and are not a good vascular expander. It is possible that the administration of large amounts of Ringer's lactate can reduce the oxygen transport capacity, and causes peripheral edema in patients with heart disease (4). Additionally, to compensate bleeding with crystalloids, three times as much blood should be given to a patient with crystalloid fluids (5).

Albumin is the most abundant protein in the plasma. The role of albumin is the regulation of blood pressure and blood volume, the transfer of various molecules such as hormones, fatty acids, drugs, bilirubin and vitamins (6).

Additionally, albumin is responsible for maintaining the plasma oncotic pressure. It also binds to drugs and other substances, which eliminates release of radicals from the plasma. In addition, it is used in the treatment of hypovolemia, burn, malnutrition, hypoalbuminemia, diuretic-resistant nephrotic syndrome, pancreatitis and liver disease (7).

An infusion of 5% soluble albumin generates an oncotic pressure equivalent to an equal volume of plasma and increases the volume of blood approximately equal to the size of the infused albumin (8). It is possible that 5% albumin in the short-term had a better resuscitation capacity than Ringer's lactate in liver transplantation surgery (9,10). Some other studies showed the cardiac index was significantly higher in those receiving hydroxyethyl starch 6% than in albumin 5% recipients (11,12). In a previous study, administration of 5% of albumin to patients with cesarean and hypotension improved the Apgar score of the mothers' infants (13). Another study showed that intravenous albumin administration to patients undergoing cardiac surgery did not worsen inflammation or renal function (14).

Objectives

The aim of this study was to compare the effect of albumin 5% infusion with Ringer's lactate solution on substitution of intraoperative bleeding on the status of the patient's

coagulation system after surgery.

Patients and Methods

Study design and participants

The present study was a double-blind clinical trial study. The population of this study was patients who electively needed non-emergency surgery (Figure 1).

Inclusion criteria

Men and women aged 25-75 years. Patients with class ASA (American Society of Anesthesiologist) I and II, BUN less than 18 mg/dL or serum urea less than 38.5 mg/dL, serum creatinine less than 1.3 mg/dL and patient's consent for entering the study.

Exclusion criteria

Patients with the history of liver disease, heart failure or renal insufficiency and preoperative coagulation disorder were excluded from the study. Patients who use anticoagulants, oral contraceptives, vitamin K antagonists, corticosteroids, cyclooxygenase inhibitors or chemotherapy drugs were also excluded from the study.

Data were recorded in a checklist. The checklist contains individual and clinical questions (age, gender, duration of surgery and amount of blood loss). Serum urea, creatinine, partial thromboplastin time (PTT), prothrombin time (PT), international normalized ratio (INR), sodium, potassium and calcium were measured in four steps of before surgery and 6, 12 and 24 hours after operation. Finally, this randomized double-blind clinical trial was performed on 80 patients who needed non-emergency surgery and had an intraoperative bleeding of more than 100 mL. Patients were randomized in two groups of forty patients. The induction of general anesthesia for all subjects was similar and it was conducted by midazolam (1-2 mg/kg) as premedication, fentanyl (2-3 µg/kg) and propofol (2-3 mg/kg), as induction drug and an atracurium as relaxant (0.5 mg/kg), propofol used as an anesthetic preservative (150-100 µg/kg/min). In case of re-requiring relaxant during surgery, atracurium (0.5 mg/kg) was repeated. The fluid therapy was carried out with Ringer's lactate in one group and albumin 5% in another group. In this study, depending on the type of surgery and the amount of bleeding during the operation, the patient's bleeding rate was estimated every 10 minutes based on the suctioning of the bottle and the using of sterile gases.

When the bleeding was above 100 mL, it was replaced with Ringer's lactate or albumin 5% as follows. For each milliliter of bleeding, 1 mL of albumin 5% or 3 mL of Ringer's lactate was replaced. To study the coagulation status of patients, PT, PTT and INR were assessed. The measurements were taken at preoperative time and at the intervals of 6, 12, and 24 hours after surgery. Accordingly, the patients were coded without regarding whether albumin 5% or Ringer's lactate were taken. Besides,

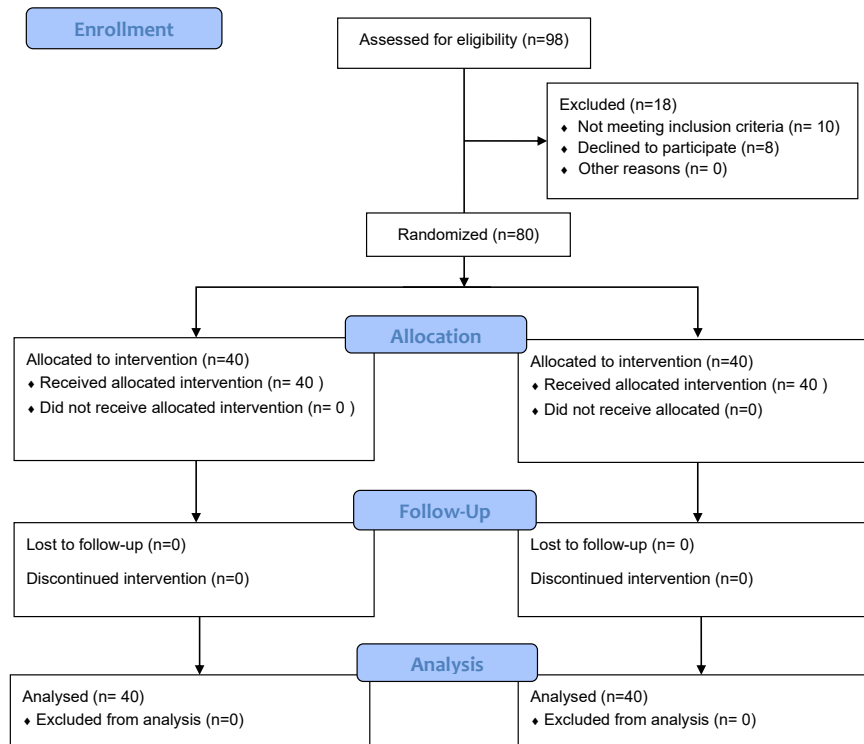


Figure 1. Flow diagram of the study.

each blood sample was taken as a separate code number and was sent to the laboratory. Additionally, electrolyte concentrations (sodium, potassium and calcium), urea and serum creatinine were also measured.

Ethical issues

The research followed the tenets of the Declaration of Helsinki. The study was approved by the ethics committee of the Shahrekord University of Medical Sciences (#IR.SKUMS.REC.1395.211). Prior to participating in the project, the patients were given written consent and informed them about the research objectives. Information from the project was secretly provided only by the project executives. This study was also registered in the Iranian Registry of Clinical Trials (identifier: IRCT20191009045037N1; <https://www.irct.ir/trial/42869>). This study was extracted from the M.D. thesis of Mehdi Hadadzadeh at this university.

Statistical analysis

Data was collected by the SPSS software, and for quantitative variables with normal distribution, the data was described as mean \pm SD. Besides, independent *t* test, analysis of variance of repeated observations for normal observations and Mann-Whitney U tests for abnormal observations were used. Chi-square test was applied for analyzing qualitative variables. The significance level in this study was considered as <0.05 .

Results

A total of 80 patients participated in this clinical trial (40 in each group). The mean age of patients in the Ringer's lactate group was 49.10 ± 9.30 years old in the range of 29 to 73 years and the mean age of the patients in the albumin group was 50.85 ± 9.84 years old in the range of 26 to 75 years. Based on independent *t* test, the two groups did not have any significant difference in age ($P = 0.416$). According to chi-square test, the two groups did not have any significant difference in terms of gender ($P = 0.371$) too. The mean duration of surgery was 1.77 ± 0.87 hours in the Ringer's lactate and 1.36 ± 0.05 hours in the albumin group was 5% ($P = 0.052$). The rate of hemorrhage during surgery was 306.5 ± 125.28 mL in the Ringer's lactate group and 315.50 ± 101.95 mL in the albumin 5% group which was not significantly different between two groups ($P = 0.725$; Table 1). The patient's electrolytes, kidney parameters and blood coagulation indexes in four stages of the study in two groups were presented in Table 2 including stage one (before operation), the second stage (6 hours after operation), the third stage (12 hours after operation), and the fourth stage was 24 hours after operation. According to the Mann-Whitney U test, no statistically significant difference between the two groups in terms of electrolytes including sodium, potassium and calcium in the first to fourth stages of operation was detected ($P > 0.05$).

According to Mann-Whitney test, no significant

Table 1. Mean and standard deviation of age, duration of surgery, and rate of bleeding in patients in the Ringer's lactate and albumin 5%

Variables	Albumin 5% group			Ringer's lactate group			P value
	Max	Min	Mean \pm SD	Max	Min	Mean \pm SD	
Age (y)	75	26	50.85 \pm 9.84	73	29	49.10 \pm 9.30	0.416
Duration of surgery (h)	3	1	1.36 \pm 0.60	4	1	1.77 \pm 0.80	0.052
Bleeding (mL)	500	100	315.50 \pm 101.95	600	150	306.50 \pm 125.28	0.725

difference was observed between two groups in renal index (serum urea and creatinine).

According to Mann-Whitney U and analysis of variance tests, there was a significant difference between the two groups in terms of blood coagulation status (PT and PTT) and INR after surgery in the 5% albumin group, since it was significantly lower in the 5% albumin group.

Discussion

This study was performed to compare the effect of albumin 5% infusion with Ringer's lactate solution on replacement of intraoperative blood loss on renal function, coagulation system and electrolytes after surgery. Patients' electrolytes (Na, K and Ca), blood coagulation indexes (PT, PTT and INR) and renal indices (serum urea and creatinine) in the four stages of the study in the periods of before surgery, 6 hours, 12 hours and 24 hours and post-surgery were evaluated. The electrolytes content including serum sodium, potassium and calcium was not significantly different between the two groups in all four stages.

In the present study, significant differences between both

groups regarding blood coagulation indexes including PT and PTT in the second to fourth stages of the study was seen. PT and PTT at 6, 12 and 24 hours, post-surgery, and also INR 12 and 24 hours after surgery in the albumin 5% group were lower than the Ringer's lactate group.

This coagulation disorder seems to be due to hemodilution due to the amount of solutions infused in the Ringer's lactate group compared to the albumin group 5% (15-17).

Changes in PT, PTT and INR were significantly different in the Ringer's lactate group, the reduction in PT and PTT in the albumin 5% group was higher than the Ringer's lactate group.

Conclusion

The results of this study showed that there was no statistically significant difference in changes of sodium, potassium and calcium electrolytes and renal indices of urea and creatinine between Ringer's lactate and albumin 5%. Changes in PT and PTT tests performed 6, 12 and 24 hours postoperatively were significantly lower in the albumin group by 5% than in the Ringer's lactate group. Significant differences were observed between the two groups regarding the trend of PT and PTT changes. In other words, the probability of postoperative bleeding was 5% lower in the albumin group than in the Ringer's lactate group.

It seems that the coagulopathy in the Ringer's lactate group is more than 5% in the albumin group, so that if the surgery is prolonged, the bleeding rate will be higher than the average in this study.

Postoperative bleeding is also more likely in the Ringer's lactate group.

Limitations of the study

In our investigation, if more samples were studied, we might have had more valuable results.

Authors' contribution

HM and MH as the main investigators, collected the data and wrote the first draft. GRS designed the study, and also read and corrected the draft. All authors read and signed the final manuscript.

Conflicts of interest

The authors declare that they have no conflicting interests.

Table 2. Mean and standard deviation of blood coagulation parameters of patients (PT, PTT, and INR) in both case and control groups

Blood coagulation indexes	Study groups		P value ^a
	Albumin group 5% Mean \pm SD	Ringer's lactate group Mean \pm SD	
PT			
Before surgery	13.08 \pm 1.33	13.26 \pm 0.94	0.101
6 hours after surgery	13.22 \pm 0.99	13.57 \pm 0.69	0.006*
12 hours after surgery	13.25 \pm 0.88	13.74 \pm 0.77	0.001*
24 hours after surgery	13.17 \pm 0.64	13.82 \pm 0.87	0.001*
PTT			
Before surgery	30.03 \pm 2.25	30.57 \pm 2.47	0.051
6 hours after surgery	28.76 \pm 2.67	30.66 \pm 2.98	0.002*
12 hours after surgery	28.82 \pm 2.58	31.32 \pm 3.11	0.001*
24 hours after surgery	28.95 \pm 3.26	31.36 \pm 3.40	0.001*
INR			
Before surgery	1.10 \pm 0.13	1.08 \pm 0.12	0.333
6 hours after surgery	1.14 \pm 0.14	1.17 \pm 0.13	0.052
12 hours after surgery	1.15 \pm 0.08	1.20 \pm 0.09	*0.039
24 hours after surgery	1.14 \pm 0.06	1.19 \pm 0.11	*0.027

Ethical considerations

Ethical issues (including plagiarism, double publication) have been completely considered by the authors.

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