

Determining the pattern of albumin consumption in liver transplant patients hospitalized in Masih Daneshvari Hospital

Amin Yousefi¹, Farzaneh Dastan^{2*}, Alireza Yousefi Mohammadi¹

¹School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran. ²Department of Clinical Pharmacy, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Correspondence: Farzaneh Dastan, Department of Clinical Pharmacy, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran. fzh_dastan@sbm.ac.ir

ABSTRACT

The present study determines the pattern of albumin consumption in liver transplant patients hospitalized in Masih Daneshvari Hospital. This retrospective study examined the data of 39 patients who received albumin in the liver transplant department of Masih Daneshvari Hospital.

SOFA and APACHE scores were used as primary outcomes to examine the relationship with albumin consumption and qualitative parameters including the need for abdominal reoperation, the occurrence of ascites, the occurrence of thrombosis, the receipt of PC and FFP, the rejection of the transplant, and the death or survival of the patients one and three months after transplantation as secondary outcomes. The occurrence of pleural effusion, hemodialysis, and CRRT were also collected by extracting them from the patient's medical records. The mean albumin consumption in g/kg of the patient's body weight was calculated to be 2.43 ± 1.39 g/kg in the patients of this study. This value in vials was also calculated to be 19.02 ± 10.87 vials per patient. The mean albumin level of the patients was also calculated up to one week after transplantation, which was 3.3 ± 1.58 g/dl. In contrast, the mean and standard deviation of the plasma albumin level was 3.05 ± 2.21 g/dl before surgery. Based on the results, albumin consumption cannot have a significant impact on improving the APACHE score index. The present study revealed that implementing a drug consumption assessment program for albumin can optimize the duration of drug administration and significantly reduce the number of inappropriate doses.

Keywords: Albumin, Liver transplant, Hypoalbuminemia, consumption

Introduction

Liver transplantation surgery has a long history with significant advances in surgical techniques, immunosuppressive therapies, and patient care. The first successful liver transplant was performed in 1963 by Dr. Thomas Starzel and his team at the University of Colorado [1]. This surgery has become a vital treatment for patients with end-stage liver disease and various liver-related disorders since that time. More than 8,000 liver transplants were performed in the United States in 2020 Based on the latest data from the United Nations Organization for the Study of Organs (UNOS) [2]. This issue indicates the increasing demand for liver transplantation as a life-saving intervention for patients with liver failure.

Its success depends on the interdisciplinary collaboration of transplant surgeons, hepatologists, anesthesiologists, and immunologists, and ongoing research to improve organ

preservation, donor-recipient matching, and post-transplant care. Moreover, the development of immunosuppressive drugs, such as tacrolimus and mycophenolate mofetil, has significantly increased the long-term survival rate of transplant recipients [3]. Despite significant progress, some challenges remain in this area. They include shortage of donor organs, organ rejection, and the need to achieve better long-term outcomes. Ongoing research in regenerative medicine and bioengineering of donor organs has been promising to address these challenges and improve the accessibility and success of liver transplantation [4]. Generally, liver transplantation remains a progressive and evolving field, giving great hope to the numerous patients with end-stage liver disease.

Hypoalbuminemia is one of the important complications after liver transplantation surgery. It is a reduction in albumin levels in the blood. This complication is a common postoperative complication in liver transplant recipients. It is often associated

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with increased morbidity and mortality. Hypoalbuminemia can be caused by various factors, such as surgical trauma, immunosuppressive therapy, reduced hepatic synthesis, and altered vascular permeability. Diagnosis, evaluation, and management of hypoalbuminemia after liver transplantation are vital for successful patient outcomes [5, 6].

Albumin is a vital protein that is primarily produced in the liver. It plays a vital role in maintaining the osmotic pressure of the blood. It is produced about 15 grams per day on average and has a half-life in the body of about 20 days. This means that about 4% of the albumin in the body is destroyed and replaced every day [2]. As the main plasma protein, it has several functions. Albumin prevents fluid from leaking into the tissues by creating colloid osmotic pressure, thus helping to maintain fluid balance in the body [3]. This protein binds to various substances such as hormones, fatty acids, bilirubin, and mineral ions (calcium, magnesium, and copper) and plays a role in their movement in the blood. A reduction in albumin levels in the blood (hypoalbuminemia) can be a sign of problems such as liver and kidney diseases, malnutrition, and inflammatory conditions. A reduction in albumin can cause problems such as swelling (edema) and metabolic disorders. Additionally, the need for albumin may increase in conditions such as burns or surgery [7]. Finally, albumin is not only essential for maintaining fluid balance in the body. It is also used as an important marker in the diagnosis and monitoring of various diseases [6].

Hypoalbuminemia is a common disorder in liver transplant patients. It is associated with significant postoperative complications. The use of albumin in the postoperative phase has yielded promises in resolving hypoalbuminemia and reducing associated adverse outcomes. However, further studies and consensus among clinical guidelines are needed to optimize the use of albumin in these patients. Hypoalbuminemia, or reduced serum albumin levels after liver transplantation, is a common complication associated with an increased risk of complications and mortality. Investigating liver transplant patients revealed that hypoalbuminemia is associated with increased length of hospital and ICU stay, increased need for mechanical ventilation, and increased rates of surgical complications such as bleeding, infection, stroke, and mortality [8].

Reduced albumin synthesis by the transplanted liver, increased albumin leakage into the extravascular space due to inflammation and increased vascular permeability, and increased albumin excretion due to renal failure are the primary causes of hypoalbuminemia after liver transplantation. Measurement of serum albumin levels after liver transplantation can be used as a simple and accessible method for predicting complications and managing patients [9]. Based on Melendez *et al.*, clinical guidelines and protocols regarding the use of albumin in the postoperative period of liver transplantation vary among medical societies and institutions. Although some support the routine use of albumin to address hypoalbuminemia and its consequences, others question its cost-effectiveness and the lack of conclusive evidence to support its extensive administration in these patients [10, 11].

The study by Ertmer *et al.* indicated an improvement in cardiovascular SOFA score indicators in patients who received continuous albumin infusion [12]. Mukhtar *et al.* did not show a significant difference between patients who received albumin and patients who received a placebo in hemodynamic parameters [13]. Finally, specific guidelines regarding the appropriate albumin concentration in the days after transplantation have not been published so far. Due to the shortage of albumin in the country's pharmaceutical market and the observation of many cases of irrational and unconventional use of albumin in several patients, some other patients might not receive sufficient albumin. Thus, the need for a comprehensive study was strongly felt to determine a specific protocol for administering albumin in the postoperative phase of patients and to determine what dose of albumin should be administered to patients and for how long.

Materials and Methods

This descriptive-analytical and retrospective study was conducted on 39 patients hospitalized from January 17, 2020, to March 10, 2022, in Masih Daneshvari Hospital, Tehran, which is one of the teaching, therapeutic, and research hospitals of Shahid Beheshti University of Medical Sciences and Beheshti and Therapeutic Services. The study population included 39 patients who received albumin and were hospitalized in the liver transplant department of Masih Daneshvari Hospital between September 18, 2020, and May 2022. The sample in this study included all 39 patients receiving albumin between January 2010 and March 2012. The sample size in this project was equal to the study population. This number of patients in this study is appropriate considering the number of liver transplant patients in the country and the range of patients studied in the articles reviewed due to the small number of liver transplant patients in all articles was between 15 and 150 patients. The inclusion criteria for this project included patients receiving albumin in the departments related to liver transplant patients from September 2010 to March 2022. The exclusion criteria were patients under 16 years of age, patients undergoing simultaneous organ transplantation from another body, patients with immune system deficiency, and a history of allergy to albumin.

A statistician performed statistical analysis after collecting the data and entering them into SPSS software. Statistical analysis was reported both descriptively and analytically. P-value <0.05 was considered as a significant level. The Ethics Committee of the Faculty of Pharmacy of Shahid Beheshti University approved this study ethically. This study did not have any costs for the patients. This study was registered in the Faculty's Research System with the code of ethics of "IR.SBMU.PHARMACY.REC.1401.095".

Results and Discussion

The results revealed that 18 male patients were male and 21 patients were female. The patients were at an age range of

49.5±13.53 years. The oldest patient was 71 years old and the youngest one was 19 years old. The results revealed that ascites occurred in 66.7% of the patients and 33.3% of the patients did not have ascites. The results revealed that transplant rejection occurred in 20.5% of the patients and 79.5% of the patients did not have transplant rejection. The results of examining the incidence of transplant rejection at three months revealed that transplant rejection occurred in 20.5% of the patients and 79.5% of the patients did not have transplant rejection. The results of the need for re-intubation revealed that it was needed in 7.7% of the patients and that it was not needed in 92.3% of the patients. The results of the need for re-intubation revealed that it was needed in 7.7% of the patients and that it was not needed in 92.3% of the patients.

The results of abdominal reoperation revealed that it occurred in 28.2% of the patients and that it did not occur in 71.8% of the patients. The results revealed that thrombosis occurred in 10.3% of the patients and that it did not occur in 89.7% of the patients. The results revealed that thrombosis after 3 months occurred in 10.3% of the patients and that it did not occur in 87.2% of the patients. All patients received PC and FFP. The results revealed that pleural effusion occurred in 84.6% of the patients and that it did not occur in 15.4% of the patients. No patient needed hemodialysis. The results of the need for CRRT revealed that it was needed in 5.1% of patients and was not needed in 94.9% of patients. The results of mortality after one month revealed that 5.1% of patients died within one month after transplantation and 94.9% of patients survived. The results of mortality after one month revealed that 5.1% of patients died within one month after transplantation and 92.3% of patients survived. The results revealed that only 2.6% of patients were hypoalbuminemia and 97.4% of patients had albumin values in the normal range after surgery.

Table 1. T-test data including mean and standard deviation

Index	Mean	SD
Day 1 SOFA score	89.4	74.1
Day 3 SOFA score	46.4	77.1
Day 1 systolic blood pressure (mmHg)	41.125	97.11
Day 3 Systolic Blood Pressure (mmHg)	61.126	17.09
Preoperative Diastolic Blood Pressure (mmHg)	73.41	9.03
Day 3 Diastolic Blood Pressure (mmHg)	23.80	71.10
Day 7 systolic blood pressure (mmHg)	41.122	81.10
Day 1 Diastolic Blood Pressure (mmHg)	97.74	01.11
Day 7 Diastolic Blood Pressure (mmHg)	08.77	37.10
Day 1 APACHE score	07.10	98.2
Day 3 APACHE score	35.9	16.3
Day 1 Hemoglobin	88.9	01.2
Day 3 Hemoglobin	83.9	50.1
Day 7 Hemoglobin	97.9	87.1
Day 1 White Blood Cells	91.9	39.5
Day 3 White Blood Cells	77.8	64.5

Day 7 White Blood Cells	89.8	87.1
Day 1 Platelets	20.97	29.60
Day 3 Platelets	02.61	58.90
Day 7 Platelets	07.103	86.85
Day 1 AST enzyme	10.1483	96.1373
Day 3 AST enzyme	78.369	29.373
Day 7 AST enzyme	52.46	38.29
Day 1 ALT enzyme	74,900	01.783
Day 3 ALT enzyme	55.504	56.339
Day 7 ALT enzyme	34.157	36.170
Day 1 Creatinine (mg/dL)	05.1	46.0
Day 3 Creatinine (mg/dL)	11.1	47.0
Day 7 Creatinine (mg/dL)	10.1	40.0
Preoperative heart rate	10.85	39.13
Day 3 heart rate	18.85	83.11
Day 7 heart rate	15.89	84.11
Preoperative respiratory rate	84.18	18.0
Day 3 respiratory rate	46.18	25.0
Day 7 respiratory rate	32.19	28.0

Table 2. Correlation between paired data

Paired data	Sig	Correlation coefficient
Days 1 and 3 SOFA SCORE	0.000	0.866
Days 1 and 3 Systolic Blood Pressure	0.331	0.160
Days 1 and 3 Diastolic Blood Pressure	0.471	0.119
Days 1 and 7 Systolic Blood Pressure	0.994	0.001
Days 1 and 7 Diastolic Blood Pressure	0.517	-1.07
Days 1 and 3 APHACHI SCORE	0.000	0.877
Days 1 and 3 Hemoglobin	0.000	0.615
Days 1 and 7 Hemoglobin	0.033	0.342
Days 1 and 3 WBC	0.169	0.225
Days 1 and 7 WBC	0.804	-0.41
Days 1 and 3 Platelet Count	0.000	0.866
Days 1 and 7 Platelet Count	0.000	0.646
Days 1 and 3 AST	0.000	0.645
Days 1 and 7 AST	0.441	0.129
Days 1 and 3 ALT levels	0.000	0.664
Days 1 and 7 ALT levels	0.53	0.105
Days 1 and 3 Creatinine levels	0.000	0.695
Days 1 and 7 Creatinine levels	0.023	0.362
Heart rate before surgery and Day 3	0.108	0.265
Heart rate before surgery and Day 7	0.005	0.438
Respiratory rate before surgery and Day 3	0.558	0.097
Respiratory rate before surgery and Day 7	0.167	0.232

Table 3. Paired Difference Results

Index	Mean	SD
Injected albumin dose per weight on Day 1 (g/kg body weight)	1.34	0.88
Injected albumin dose per weight on Day 3 (g/kg body weight)	0.25	0.45
Injected albumin dose per weight on	0.08	0.37

Day 7 (g/kg body weight)		
Preoperative Intake level (ml)	83.2150	34.795
Day 3 Intake level (ml)	29.5442	46.1057
Day 7 Intake level (ml)	70.4953	24.1616
Preoperative Output (ml)	64.2415	13.1187
Day 3 Output (ml)	54.7073	52.2012
Day 7 Output (ml)	64.5539	30.2390

Table 4. T-test data including mean and standard deviation					
Paired data	Sig	Mean	SD	Upper bound	Lower bound
Platelet Count					
Day 1 – Day 3 AST Level	000.0	1113.31	1168.64	1497.43	18.729
Day 1 – Day 7 AST Level	000.0	1437.56	1370.49	187.04	10.986
Day 1 – Day 3 ALT Level	000.0	396.19	612.77	597.60	77.194
Day 1 – Day 7 ALT Level	000.0	743.40	783.66	1000.98	81.458
Day 1 - Day 3 Creatinine Level (mg/dL)	336.0	-0.057	0.36	0.061	-0.17
Day 1 – Day 7 Creatinine Level (mg/dL)	604.0	-0.041	0.49	0.11	-0.2
Day 3 and Preoperative Heart Rate	975.0	-0.078	15.34	4.96	-5.12
Day 7 and Preoperative Heart Rate	065.0	-4.05	13.33	0.27	-8.37
Day 3 and Preoperative Respiratory Rate	211.0	0.38	1.88	0.99	-0.22
Day 7 and Preoperative Respiratory Rate	183.0	-0.40	1.81	0.2	-1.01

Table 5. Results related to the correlation of paired data		
Index	Sig	Correlation coefficient
injected albumin per weight on Days 1 and 3		0.407
injected albumin per weight on Days 1 and 7		0.887
Intake before surgery and Day 3		0.026
Intake before surgery and Day 7		0.957
Output before surgery		0.411

Table 4. T-test data including mean and standard deviation					
Paired data	Sig	Mean	SD	Upper bound	Lower bound
Day 1 and Day 3 SOFA Score	0.005	0.43	0.91	0.73	0.14
Day 1 and Day 3 Systolic Blood Pressure (mmHg)	0.698	-1.2	19.24	5.03	-0.744
Preoperative Diastolic pressure – Day 3	0.003	-6.82	13.16	-2.55	-11.08
Diastolic pressure (mmHg)					
Systolic Blood Pressure Day 1 – Day 7 (mmHg)	253.0	3	12.16	8.22	-2.22
Day 1 – Day 7 Diastolic Blood Pressure (mmHg)	415.0	-2.1	92.15	3.05	-7.26
Day 1 – Day 3 APHACHE Score	006.0	0.71	53.1	1.21	0.21
Day 1 – Day 3 Hemoglobin	000.0	1.04	6.1	1.56	0.52
Day 1 – Day 7 Hemoglobin	809.0	-0.08	23.2	0.63	-0.81
Day 1 – Day 3 WBC	31.0	1.13	87.6	3.36	-1.09
Day 1 – Day 7 WBC	362.0	1.01	86.6	3.23	-1.21
Day 1 – Day 3 Platelet Count	000.0	36.17	86.30	46.18	26.17
Day 1 – Day 7	58.0	-5.87	75.65	15.44	-18.27

and Day 3
Output before surgery 0.010 0.481
and Day 7

Table 6. Paired Difference Results

Paired data	Sig	Mean	SD	Upper bound	Lower bound
Injected albumin dose per weight on days 1 and 3 (g/kg body weight)	0.000	1.09	0.93	1.39	0.79
Injected albumin dose per weight on days 1 and 7 (g/kg body weight)	0.000	1.25	0.96	1.57	0.94
Preoperative and Day 3 Intake (ml)	0.000	-3291.45	1083.36	-2910.57	-36.72.33
Preoperative and Day 7 Intake (ml)	0.000	2773.29	1023.51	-2051.93	-3494.65
Preoperative and Day 3 Output (ml)	0.000	-4657.90	2174.33	-3860.35	-5455.45
Preoperative and Day 7 Output (ml)	0.000	-30.8839	2095.58	-2275.85	-3900.97

In 39 patients, the level of injected albumin in grams of albumin per kilogram of the patient's body weight was calculated to be 39.43 ± 1.2 g/kg, with a mean of 2.43 g/kg and a standard deviation of 1.39 g/kg. Statistically, it will be 87.10 ± 19.02 vials per patient.

In the present study, 39 patients were studied. Among them, 11 patients underwent abdominal reoperation after transplantation. This study investigated the impacts of albumin therapy intervention in patients in the postoperative phase. Since the SOFA and APACHE scores were considered as the primary outcomes of the study and due to the small number of patients included, the amount of albumin consumption in g/kg of the patient's body weight was calculated to be 39.43 ± 1.2 g/kg in all patients in this study. Statistical correlation analyses also revealed that the amount of albumin consumption had a significant relationship with the SOFA score, but it did not show a significant relationship with the APACHE score. Additionally, among all patients, only one patient had hypoalbuminemia, and the consumption of this amount of albumin, even in one case in which only one patient suffered from hypoalbuminemia, suggests overuse of this drug. The albumin level on the seventh day after surgery was considered as the basis for measuring the mean albumin level of the patients. It was obtained at 3.3 g/dl.

Based on the guidelines announced by the Stanford University Medical Care Institute, pharmacists working in hospitals should monitor albumin consumption before approving any albumin prescription for patients. In this guideline, the indications in

which albumin has been used experimentally or non-experimentally are classified into 5 categories. The first category includes "likely benefit" (Approved indications), the second category includes "my benefit" (Approved indications), and the third category includes "unclear benefit indications (Approval by nephrology attending required before the use). The fourth category includes "Not indicated" (will NOT be approved). The Postoperative Liver Transplant indication is placed in the second category, indicating that it is approved for the use of injectable exogenous albumin. Regarding the use of albumin in the post-transplant phase, this guideline states that injectable exogenous albumin may be useful for controlling ascites and possible peripheral edema provided that the albumin level is less than 2.5 g/dL. Finally, it is recommended to use 25% albumin, at a dose of 25 g/day, until the albumin level increases to more than 2.5 g/dl [14].

Conclusion

Based on the results, albumin consumption does not significantly improve the APACHE score index. Additionally, due to the small number of patients included in the study, the number of patients is usually small. Additionally, due to the qualitative nature of the data related to secondary outcomes, which practically made statistical analysis impossible, no significant relationship was found between albumin consumption and secondary outcomes. The data revealed a significant reduction in the parameters of liver enzymes ALT and AST on the first and third days, and the first and seventh days after surgery. Regarding other outcomes, platelet count, hemoglobin level, APACHE score, diastolic blood pressure, and SOFA score on the first and third days after surgery. One of the limitations of the study was the presence of only one hypoalbuminemia patient in the study (However, the hypoalbuminemia threshold can be assumed to be less than 3.5, so more patients can be assumed to have hypoalbuminemia). It is recommended to examine the impacts of albumin and determine the intervention impacts in patients with different plasma albumin levels.

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