Original Article

Investigating the correlation injected albumin based on the patient's weight and APACHE and SOFA score

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ABSTRACT

This retrospective study included data from 39 patients who received albumin in the liver transplantation department of Masih Daneshvari Hospital. The samples of this study were collected from the entire study population in the days before surgery until one week after liver transplantation surgery. SOFA and APACHE scores were used as primary outcomes to find their association with the level of albumin consumption and qualitative parameters including the need for abdominal reoperation, the occurrence of ascites, the occurrence of thrombosis, receiving or non-receiving PC and FFP, the transplant rejection, and the death or survival of the patients one and three months after transplantation as secondary outcomes. The occurrence of pleural effusion, the occurrence of hemodialysis, and the occurrence of CRRT were also collected by extracting data from patients' medical records. Statistical correlation analyses revealed that albumin consumption is significantly associated with the SOFA score (p-value = 0.025 and correlation coefficient = 0.358), but it did not show a significant relationship with the APACHE Score (p-value = 0.097 and correlation coefficient = 0.296). It was found that the level of injected albumin per kilogram of body weight was significantly correlated with the SOFA score on the third day. This means that with the change in the level of injected albumin per kilogram of body weight, the changes in the SOFA score on the third day were also significant.

Keywords: Liver disease, Albumin, Patient weight, APACHE score, SOFA score

Introduction

Liver diseases such as cirrhosis can reduce albumin production, leading to hypoalbuminemia [1]. Malnutrition, particularly protein deficiency, can also reduce albumin levels as the body breaks down muscle tissue to obtain the amino acids essential for protein synthesis[2]. Moreover, kidney disease can increase urinary albumin loss, leading to hypoalbuminemia [3]. Inflammatory disorders, such as sepsis or inflammatory bowel disease, can cause the release of inflammatory cytokines that reduce albumin production and increase capillary permeability, further contributing to hypoalbuminemia [4]. Some medications, such as diuretics and nonsteroidal anti-inflammatory drugs, can also cause hypoalbuminemia through various mechanisms [5]. Albumin is the most abundant protein in human blood plasma. It accounts for about 50% of the total protein content. It is mostly synthesized in the liver and performs many vital functions in the human body, including regulating osmotic pressure, transporting various substances, and maintaining pH balance in the body [6].
Albumin is essential in regulating the osmotic pressure of blood plasma. Albumin helps maintain fluid balance in blood vessels and surrounding tissues thanks to its colloidal properties. This function is vital for the overall distribution and retention of body fluids, preventing edema, and promoting normal tissue hydration [7]. Albumin plays a vital role in maintaining blood pH balance. It acts as a buffer, helping to stabilize the acid-base balance and prevent extreme changes in blood pH. Albumin helps to minimize pH fluctuations, thereby contributing to the overall stability of the internal environment by binding to acidic and basic compounds [8].
Acute transplant rejection is one of the most critical complications after liver transplantation. It occurs when the immune system attacks the donor organ. This can lead to allograft dysfunction and eventual failure. This will require immediate intervention to prevent irreversible damage [9].

Biliary strictures, leaks, and infections are common after transplantation and can lead to major complications. Endoscopic and radiological interventions are often required to manage these complications and preserve the function of the transplanted liver [10]. Hepatic artery thrombosis is a devastating complication that can lead to ischemic cholangiopathy and transplantation loss. Early diagnosis and timely intervention are vital in preventing irreversible damage to the transplanted liver [11]. Many liver transplantation recipients experience impaired renal function due to a combination of pre-existing renal failure and the nephrotoxic effects of immunosuppressive drugs. Chronic kidney disease and end-stage renal disease are frequent long-term complications that affect patient survival [12].

Hypoalbuminemia is one of the important complications. It is a decrease in albumin levels in the blood. This complication is a common postoperative complication in liver transplantation recipients. It is often associated with increased morbidity and mortality. Hypoalbuminemia can be caused by several factors, including surgical trauma, immunosuppressive therapy, reduced hepatic synthesis, and altered vascular permeability. Diagnosis, evaluation, and management of hypoalbuminemia after liver transplantation are critical for successful patient outcomes [13, 14].

Post-liver transplantation hypoalbuminemia is a reduction in albumin levels in the blood after liver transplantation. This condition mostly occurs in the early postoperative period and can cause various complications in the recipient [15]. Live plays a vital role in the synthesis of albumin, a protein that helps maintain oncotic pressure in the blood and regulates fluid balance. Thus, dysfunction or injury to the liver, such as liver transplantation, can reduce albumin production and lead to hypoalbuminemia [16]. An impairment in the regenerative capacity of the transplanted liver is one of the major causes of hypoalbuminemia following liver transplantation. It affects albumin synthesis. Moreover, postoperative complications such as infection, rejection, and transplantation dysfunction can also lead to hypoalbuminemia in liver transplantation recipients. Hypoalbuminemia after liver transplantation is associated with an increased risk of complications and mortality. This can lead to complications such as ascites, peripheral edema, and impaired wound healing, significantly affecting the overall recovery and outcome of the transplantation recipient [17].

Management of hypoalbuminemia after liver transplantation involves nutritional support, including adequate protein intake, and monitoring for potential complications. Moreover, close monitoring of liver function and albumin levels, and timely intervention if complications occur, is crucial in the management of hypoalbuminemia in liver transplantation recipients. Thus, hypoalbuminemia after liver transplantation is common and can lead to several complications in the recipient. Proper management and close monitoring are vital to improve outcomes in liver transplantation recipients. 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 (reduced serum albumin levels) after liver transplantation. Thus, careful monitoring of serum albumin levels and therapeutic measures to correct hypoalbuminemia after liver transplantation can be effective in improving the clinical outcomes of these patients.

Karakala et al. reported a wide range of hypoalbuminemia rates in patients from 20% to 90% before the transplantation and up to 81% in the immediate postoperative period [18, 19]. Feltracco et al. also showed that hypoalbuminemia in liver transplantation patients is associated with an increased risk of postoperative complications, such as wound infection, and prolonged hospital stay. It can also lead to the development of postoperative ascites and renal dysfunction, complicating the recovery process [19]. In another study, Karakala et al. considered exogenous albumin administration as a potential intervention to address hypoalbuminemia and its associated complications in the post-transplantation period. Their studies revealed that albumin administration in the postoperative phase could lead to improved serum albumin levels, reduced incidence of postoperative complications, and shorter hospital stays [18, 19].

Liver transplantation is the definitive treatment for end-stage liver disease. However, the postoperative period is associated with several potential complications affecting the success of the transplantation and the long-term outcome for the recipient. The immediate postoperative period is associated with the risk of surgical complications such as bleeding, bile leakage, and hepatic artery thrombosis. These can occur within the first few days after transplantation and may require immediate intervention to prevent further complications. Infection, rejection of the transplanted liver, and complications related to immunosuppressive drugs can be some of these complications. These can occur in the weeks and months following transplantation and can significantly affect the recipient's recovery and long-term prognosis. Patients undergoing liver transplantation may experience psychosocial complications such as depression, anxiety, and stress related to the life-altering nature of the transplantation. These complications can affect the patient's overall well-being and may require continuous support and intervention [20]. Given what was stated above, the present study investigates the correlation between the level of injected albumin based on the patient's weight and the APACHE and SOFA scores on the third day.

Materials and Methods

This descriptive-analytical and retrospective study analyzed the information on patients hospitalized from January 17, 2010, to March 10, 2022, in Masih Daneshvari Hospital, Tehran. It is one of the teaching, therapeutic, and research hospitals of Shahid Beheshti University of Medical Sciences and Beheshti and Shahid Beheshti Medical Services. The statistical population of this project included 39 patients hospitalized in the liver transplantation department of Masih Daneshvari Hospital who received albumin between September 18, 2010, and May 2022.

The sample studied in this project 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 transplantation patients in the country and the range of patients studied in the articles reviewed due to the small number of liver transplantation patients in all articles was between 15 and 150 patients.

The study inclusion criteria were patients receiving albumin in departments related to liver transplantation patients between September 2010 and March 2012. The exclusion criteria also included patients under 16 years of age, patients undergoing simultaneous organ transplantation from another body, patients with immune system deficiencies, and a history of albumin sensitivity.

A statistician performed statistical analysis after collecting the data and entering them into SPSS software. Statistical analysis was reported in both descriptive and analytical forms. 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 indicated 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 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 examining 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	09.17
Preoperative Diastolic Blood Pressure (mmHg)	41.73	03.9
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	90.58
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	339.56
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	400
Preoperative heart rate	10.85	3913
Day 3 heart rate	18.85	8311
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. Nonparametric correlation between the levels of injected albumin based on patient weight and APACHE score on the third day

Paired data	Sig	Correlation coefficient
Day 3 Apache Score with Albumin per patient weight	0.09	0.296

Table 3. Nonparametric correlation between the levels of injected albumin based on patient weight and the SOFA score on the third day

Paired data	Sig	Correlation coefficient
Day 3 SOFA Score with Albumin per patient weight	0.025	0.358

The SOFA score index included six main modules, each representing the status of one of the vital systems of the human body. The respiratory system is assessed by examining arterial pressure and oxygen saturation. The coagulation system is assessed by determining the status of the platelet count. The liver and glandular system is assessed by calculating bilirubin levels. The cardiovascular system is assessed by calculating blood pressure. The neurological system is assessed by examining the Glasgow Coma Score index. The renal and excretory system is assessed by creatinine clearance. Interestingly, in two studies by Kazumasa Hiroi et al. on 60 patients [21] and a study by Christian Ertmer et al. on 15 patients [22], among the various SOFA score indices, only the cardiovascular system index showed significant improvement, and no significant change was observed between the case and control groups in these two studies in the other SOFA score sub-scores.

The occurrence of hypoalbuminemia is also crucial regarding drug interferences. Tacrolimus is one of the most important drugs used in the drug regimen of transplantation patients. It has about 99% protein binding and is mostly bound to albumin and alpha-acid glycoprotein among blood proteins. In acute conditions after liver transplantation, liver failure and the occurrence of hypoalbuminemia may theoretically expose the patient to tacrolimus toxicity. This will be due to an increase in the unbound fraction of tacrolimus in the blood.

Despite all these conditions, the study by A. Mukhtar et al. did not report a difference between the patients receiving albumin and patients in the control group in the level of tacrolimus [23]. Based on a review of statistics published by the General Administration of Drugs and Substances under the control of the Food and Drug Administration in 2012, more than $15 million was spent on importing albumin from Germany (Biotest Company) and Italy (Kedrion Company). This amount reached more than $21 million in 2013. There may be a significant correlation between the SOFA score and hypoalbuminemia in liver transplantation patients. Several studies have investigated this relationship and highlighted the importance of hypoalbuminemia in predicting transplant rejection after liver transplantation.

Cho Y et al. showed that cumulative postoperative changes in serum albumin levels up to five days after surgery could predict the likelihood of transplant rejection in patients who have undergone liver transplantation. Patients with a small postoperative decrease in cumulative serum albumin levels had a lower SOFA score on the fifth postoperative day compared to patients with a higher reduction in albumin levels [24]. Mukhtar et al. showed that postoperative albumin administration to maintain serum albumin levels of 3 g/dL did not provide additional benefits for the postoperative period in patients undergoing liver transplantation. This study did not specifically examine the relationship between SOFA scores and hypoalbuminemia [23]. Radha et al. compared the performance of various prognostic indices including SOFA scores in predicting mortality in patients with acute versus chronic liver failure. The SOFA score was found to be a significant predictor of mortality, but it did not specifically examine the relationship between SOFA scores and hypoalbuminemia [25].

In short, there is evidence that hypoalbuminemia is associated with higher SOFA scores, but this association is not significant. Further studies are needed to fully understand the relationship between SOFA scores and hypoalbuminemia in liver transplantation patients. Implementing validated guidelines for albumin administration in hospitals will improve the efficiency of albumin administration and its administration based on accurate principles, imposing a lower economic burden on hospitals, patients, and the health system.

Conclusion

Due to the presence of only one patient with an albumin level <2.5 in the study, the development and implementation of an evidence-based guideline for albumin use could significantly reduce the cost and misuse of albumin. The present study revealed that implementing a drug utilization assessment program for albumin could optimize the duration of drug administration and significantly reduce the number of inappropriate doses. One of the limitations of the study was the incompleteness of the patient's medical records or the illegibility of the numbers and results, which inevitably left the relevant section blank. It is recommended to examine the impacts of hypoalbuminemia on the risk of toxicity of transplantation drugs such as tacrolimus.

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