RESEARCH

Effect of Albumed milk on albumin serum levels in septic patients

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ABSTRACT

Background: Septic, an infection-induced condition, triggers an inflammatory response leading to life-threatening organ dysfunction and hypoalbuminemia. Albumed milk, containing extracts from egg whites and sprouts, has been considered a potential intervention to prevent hypoalbuminemia.
Objective: This study aimed to evaluate the impact of albumed milk on elevating serum albumin levels in septic patients in the intensive care unit (ICU).
Methods: An experimental study involved two groups totaling 40 patients. The control group received a standard ICU diet, while the treatment group received half of the regular ICU diet supplemented with 30 grams of albumed milk every 8 hours. Albumin levels were measured on days 0 and 3.
Results: A significant reduction in average albumin levels occurred in the control group at 0.605 units (p-value = 0.006). Conversely, the treatment group showed a non-significant decrease, with an average reduction in albumin level of 0.03 units (p = 0.839).
Conclusion: Albumed milk administration preserves albumin levels in septic patients compared to control patients without albumed, who show albumin level reduction. This highlights the potential utility of albumed milk as a supplementary measure in mitigating septic-related hypoalbuminemia.

Keywords: albumed milk; critical care; intensive care; intensive care nursing; nutrition in intensive care

INTRODUCTION

Albumin is the most abundant plasma protein, accounting for a substantial portion of the total plasma protein content in the human body. Albumin, primarily synthesized in the liver, undergoes intravascular secretion, traversing from the intravascular space to the interstitial compartment, and is eventually re-entered into the intravascular milieu via the lymphatic system.[1,2] In humans and most mammals, albumin is synthesized almost exclusively in the liver. Albumin synthesis initiates in the gastrointestinal tract. Upon ingestion of protein-rich foods, proteins are digested in the digestive tract, forming polypeptides, peptides, and amino acids. Subsequently, amino acids are conveyed into the bloodstream via the portal vessels, reaching the liver. Within the hepatic environment, amino acids undergo further degradation, giving rise to pro-albumin, which serves as the principal intracellular precursor of albumin. Albumin synthesis is a continuous but relatively slow process that begins in hepatocytes with transcription of the albumin gene and translation on rough endoplasmic reticulum–bound ribosomes, producing preproalbumin. The signal peptide is rapidly cleaved within minutes to form pro-albumin, which is then transported to the Golgi apparatus. Within approximately 1-2 hours, further post-translational processing occurs in the Golgi, including removal of the N-terminal propeptide, resulting in mature albumin. The mature protein is not stored but is secreted constitutively into the circulation within several hours of synthesis. Once released into the bloodstream, albumin distributes between the intravascular and interstitial compartments and exhibits a long plasma half-life of about 19-21 days. Consequently, serum albumin concentrations reflect cumulative hepatic synthesis over days to weeks rather than acute changes, which explains why albumin is a late marker of alterations in nutritional status, hepatic function, or systemic inflammation.[3,4,5] Serum concentrations of pro-albumin and albumin serve as valuable indicators for identifying physiological stress. Moreover, serum albumin levels can serve as significant indices for assessing morbidity, prognosis, and mortality in critically ill patients admitted to the intensive care unit (ICU).[6,7]

The standard range for serum albumin levels in adults typically falls within 3.5−4.5 g/dL. A reduction in serum albumin levels below 3.5 g/dL is characterized as hypoalbuminemia. This condition may arise from inadequate protein intake, diminished albumin synthesis, and excessive albumin excretion.[7] Hypoalbuminemia can be attributed to a diverse array of conditions, encompassing nephrotic syndrome, cirrhosis hepatis, malnutrition, and septic. In the context of septic, hypoalbuminemia arises from diminished protein synthesis and fluid extravasation resulting from capillary dysfunction.[8] Notably, this hypoalbuminemia state constitutes a notable risk factor contributing to heightened mortality and morbidity in cases of septic.[9,10]

Septic represents a life-threatening condition characterized by the dysregulation of the organ systems, stemming from the body's aberrant response to infection.[11] Septic fundamentally manifests as an inflammatory disorder instigated by the dysregulation of the patient's immune system, leading to an imbalance between pro-inflammatory cytokines and anti-inflammatory cytokines.[12,13] Specific pro-inflammatory cytokines, including interleukin-6 (IL-6), interleukin-1 (IL-1), and tumor necrosis factor-α (TNF-α), contribute to a diminished rate of albumin synthesis.[14,15] This phenomenon ensues as proinflammatory cytokines induce a decrease in the concentrations of messenger ribonucleic acid (mRNA) coding for albumin within the liver.[15,16] Within systemic inflammatory response syndrome (SIRS), there is a consequential reduction in levels of albumin mRNA as a response to infection.[16] The inflammatory response mechanism additionally triggers the augmentation of cell proliferation and cell-matrix deposition, facilitated by growth factors induced by vascular endothelial growth factor (VEGF). VEGF can enhance vascular and capillary permeability, leading to increased leakage of serum albumin into the interstitial space and, consequently, inducing hypoalbuminemia.[14]

The management of hypoalbuminemia is directed at achieving normal serum albumin levels, which involves implementing external nutrition/albumin therapy (administered exogenously) and addressing the underlying disease.[17] External albumin therapy may be administered either intravenously or orally. Intravenous administration of albumin containing human albumin is associated with a relatively high cost. Additionally, some literature suggests that intravenous albumin may inhibit hepatic albumin synthesis.[18,19,20] As an alternative and commonly adopted approach, oral administration of albumin and the consumption of high-protein foods can serve as viable strategies, facilitating increased albumin synthesis.[19]

Albumin synthesis is primarily facilitated by consuming protein-rich foods.[18,21,22] Protein sources in food are categorized into two main groups: animal protein and vegetable protein. Animal protein is derived from meat, fish, milk, and egg whites. On the other hand, vegetable protein is obtained from plant-based sources such as beans and green bean sprouts.[23] Egg white is a protein of high biological value, as nearly all the proteins present in egg whites can be effectively absorbed by the body. The notable advantage of egg whites is their ease of intestinal absorption, which promotes increased liver albumin production.[3] Green bean sprouts boast elevated levels of essential amino acids, which are pivotal for protein production in the human body. Consuming green bean sprouts can help increase albumin levels, as albumin, a protein, is composed of amino acids. The body gains a surplus of raw materials in the form of amino acids through an increased intake of protein in the diet, thereby enhancing its capacity for albumin synthesis.[23,24] Egg whites and green bean sprouts are purported to exhibit anti-inflammatory effects as part of their biological properties.[25,26] Tagashira et al. reported that egg whites contain lysozyme, which suppresses TNF-α and IL-6 production[27], while green bean sprouts contain nutrients such as flavonoids, vitamin E, phenols, calcium, and magnesium. Flavonoids contained in green bean sprouts have an anti-inflammatory effect. Flavonoids prevent inflammation by inhibiting the release of arachidonic acid and the secretion of lysosomal enzymes from neutrophil cells and endothelial cells. In addition, flavonoids prevent the exudative and proliferative phases of the inflammatory process.[28,29]

Boiled egg white preparations or blended forms are cost-effective options. Yet, they come with limitations, notably in less palatable taste or odor, especially when consumed in substantial quantities. Additionally, these forms have a limited shelf life and must be consumed immediately. Another alternative is the ready-to-drink (RTD) preparations, which offer convenience in consumption.[30] An example of an RTD product is albumed milk. Albumed is a dairy product incorporating egg white extract, green bean sprouts, and other ingredients. This composition is expected to inhibit the albumin reduction in septic patients. Therefore, this study was established to evaluate the impact of albumed milk on serum albumin levels in septic patients admitted to the ICU, with the hypothesis that albumed milk supplementation preserves serum albumin levels compared with standard nutritional care. The findings of this study are expected to inform nutritional strategies aimed at improving hypoalbuminemia and supporting clinical management in septic ICU patients.

METHOD

This study has an experimental design with a randomized controlled trial (RCT) design, using double-blinded randomization, incorporating a case-control study within the hospital-based and patient populations treated at the ICU RSUD Dr. Saiful Anwar, Provinsi Jawa Timur. Patients meeting the inclusion criteria underwent measurement of serum albumin levels. Within the control sample group, serum albumin levels were assessed on day 0, followed by the administration of 6x1 skim milk nutrient intake, and then re-examined on the third day. Conversely, the treatment group had serum albumin levels measured on day 0, followed by a nutritional regimen comprising 3x1 skim milk with additional supplementation of albumed milk (3x30 grams). Serum albumin levels in the treatment group were evaluated on the third day.

The study's inclusion criteria encompassed patients treated in the ICU at RSUD Dr. Saiful Anwar Malang, aged between 19 and 64 years, with albumin content greater than 2.5, no history of intravenous albumin transfusion, Nutric Score (with no IL-6) ranging from 0 to 4, and SOFA Score less than 15. Patients receiving Total Parenteral Nutrition, those with chronic renal failure, and individuals with chronic liver disease were excluded from participation. Patients who died during the study period, underwent room assignment changes, or were relocated to different healthcare facilities were excluded from the study.

A total of 40 subjects were recruited, with 20 in the control group and 20 in the treatment group receiving additional intake. Milk was consumed for 3 days of treatment, and 10 patients died during treatment.

The acquired data were analyzed using SPSS 15.0. Initial assessments involved examining homogeneity and sample distribution. Homogeneous data with a normal distribution were analyzed using the T-test, whereas abnormal data were analyzed using the Mann-Whitney Test.

RESULTS

The study included 50 patients; 10 dropped out. In control groups (n=20), patients received a standard diet. The treatment group (n=20) received an additional intake of albumed milk for 3 days of treatment. After receiving these data, an analysis was conducted for each research variable. Then, a correlation test was conducted to examine the relationship between the independent variable, the administration of albumed milk, and the dependent variable, the patient's serum albumin levels. Then, to determine differences across age groups, demographic characteristics, and physical and laboratory examination characteristics, analysis tests were performed, with the results (Table 1).

The sample's demographic characteristics revealed an average age of 48.83 years, ranging from 19 to 69. The male gender accounted for 26 individuals, with 13 in the treatment group and 13 in the control group. A total of 14 female participants, with 7 in each group. Various sources of infection were identified among the subjects, predominantly emanating from the lungs (24 out of 40 cases), with 11 in the treatment group and 13 in the control group. Other infection types included abdominal, open wounds, closed wounds, oral, extensive skin, and brain infections.

There were 10 patients without comorbidities, comprising 8 in the treatment group and 2 in the control group. Meanwhile, patients with comorbidities totaled 30, with 12 in the treatment group and 18 in the control group. The patient cohort was further categorized into septic and septic shock. Among the 30 patients with septic, 16 were in the control group, and 14 were in the treatment group. Additionally, there were 10 patients with septic shock, with 4 in the treatment group and 6 in the control group.

Regarding physical examination characteristics, the average temperature in the treatment group was 36.8 ± 0.41 °C; in the control group, it was 36.89 ± 0.36 °C. The mean pulse rate in the treatment group was 100.4 ± 11.8 times/min, while in the control group, it was 96.50 ± 12.53 times/min. The average respiratory rate for the treatment group was 24.25±2.79 times/min; for the control group, it was 23.40±5.04 times/min. Each physical examination characteristic was analyzed, and the p-value was greater than 0.05, indicating no significant difference between the groups.

Regarding laboratory results, the mean albumin level in the treatment group was 2.85±0.57, and in the control group, 3.30±0.63. The mean level of C-reactive protein examination in the treatment group was 18.03±9.75, while in the control group, it was 16.72±15.56. The average procalcitonin value in the treatment group was 25.78±39.76; in the control group, it was 20.79±35.99. The SOFA Score for the treatment group was 6.25±3.50 units, and for the control group, 7.00±2.53 units. Almost all characteristics of the laboratory results yielded p-values greater than 0.05, indicating no significant difference between the groups. However, the albumin examination yielded a p-value of 0.03, indicating a significant difference between the control and treatment groups (Table 2).

Based on the comparison test, there was an average decrease of -0.605 units in the control group and a p-value of 0.006 ($p < 0.05$). Therefore, it can be concluded that there is a significant difference in the average albumin value in the control group. In contrast, in the treatment group, there was an average decrease of -0.03 units, with a p-value of 0.839 ($p > 0.05$). Consequently, it can be inferred that there was no significant difference in the average decrease in albumin in the treatment group (Table 3).

The comparison of the Albumin difference between the control and treatment groups revealed an average decrease of -0.03 units in the treatment group. In contrast, the control group exhibited an average reduction of -0.61 units. The analysis yielded a p-value of 0.005 ($p < 0.05$), indicating a significant difference in albumin levels between patients in the treatment and control groups (Table 4).

Table 1. Demographic characteristics of research samples

Demographic characteristic	Treatment group (n=20)	Control group (n=20)	p-value
Age (mean)		48.83	
Gender (n)			
Male (26)	13/40	13/40	1.00
Female (14)	7/40	7/40	
Source of infection (n)			
Lungs infection (24)	11/40	13/40	0.904
Abdomen infection (3)	1/40	2/40	
Open wound infection (6)	4/40	2/40	
Closed wound infection (2)	1/40	1/40	
Mouth infection (2)	1/40	1/40	
Skin infection (cellulitis) (2)	1/40	1/40	
Brain infection (1)	1/40	0/40	
Comorbid (n)			
No (10)	8/40	2/40	0.128
Yes (30)	12/40	18/40	
Septic/septic shock			
Septic (30)	16/40	14/40	0.465
Septic shock (10)	4/40	6/40	

^ Chi-Square test

Table 2. Characteristics of physical and laboratory examination results

Parameter	Treatment Mean±Std. dev.	Control Mean±Std. dev.	p-value
Temperature (°C)	36.80±0.41	36.89±0.36	0.492^
Pulse rate (times/min)	100.40±11.98	96.50±12.53	0.321^
Breathing rate (times/min)	24.25±2.79	23.40±5.04	0.149*
Leukocytes Day 0	18351.00±10453.07	16720.25±7819.36	0.758*
Albumin Day 0	2.85±0.57	3.30±0.63	0.023*
CRP Day 0	18.03±9.75	16.72±15.56	0.414*
Procalcitonin Day 0	25.78±39.76	20.79±35.99	0.583*
SOFA Score Day 0	6.25±3.50	7.00±2.53	0.231*

^ Un-paired t-test
* Mann-Whitney test

Table 3. Comparison of H3 and H0 albumin levels in the control and treatment groups

Group	H0	H3	Delta	P-value
	Mean±Std. Dev	Mean±Std. Dev	Mean±Std. Dev	
Control	3.30 ± 0.63	2.70±0.65	-0.605±0.87	0.006^
Traetment	2.85±0.57	2.82±0.44	(-0.03)±0.60	0.839^

Table 4. Comparison of the difference between H3 and H0 albumin in the control group compared to the treatment group

	Treatment Mean±Std . Dev	Control Mean±Std . Dev	P-value
Albumin Day 0	2.85±0.57	3.30±0.63	0.023
Albumin on the 3rd day	2.82±0.44	2.70±0.65	0.491
Albumin difference	(-0.03)±0.60	(-0.61)±0.87	0.005*

DISCUSSION

This study comprised two sample groups: the control and treatment groups. Analysis of the study results revealed that, on day 3, serum albumin levels in the control group averaged 2.70 ± 0.65, whereas on day 0 they averaged 3.30 ± 0.63. The observed average decrease was -0.605 units, with a corresponding p-value of 0.006 ($p < 0.05$), indicating a significant decrease. The notable reduction in albumin levels in the control group on day 3 can be attributed to various mechanisms. Firstly, septic substantially increases systemic inflammatory factors, disrupting vascular endothelium function and elevating capillary permeability. Consequently, albumin leakage occurs outside the vessels, leading to diminished plasma albumin levels and a heightened risk of adverse outcomes.[31] Additionally, elevated cytokine levels can promote albumin catabolism and reduce plasma albumin concentrations.[32] Secondly, physiologically, albumin is synthesized in the liver, and liver function can be impaired in septic states, leading to reduced albumin synthesis.[33] Third, inflammation impairs kidney function, leading to proteinuria by regulating glomerular infiltration and promoting albumin leakage.[34] In addition, in septic conditions, gastrointestinal function disorders occur, which affect nutrient absorption and lead to a malnutrition status. Overall, serum albumin levels in septic patients are indicators of the inflammatory response, capillary leakage, and organ dysfunction associated with prognosis in septic patients.[35]

The albumin comparison test results in the treatment group indicated that serum albumin levels on day 3 averaged 2.82±0.44. In contrast, serum albumin levels on day 0 averaged 2.85±0.57, resulting in an average decrease of -0.03 units. The calculated p-value was 0.839 ($p > 0.05$), signifying no significant difference in the decline. A comparison of albumin differences between the control and treatment groups revealed an average decrease of -0.03 units in the treatment group, compared to an average reduction of -0.61 units in the control group. The analysis yielded a p-value of 0.005 ($p < 0.05$), suggesting that administering albumed milk as a supplement may help maintain serum albumin levels in septic patients. The treatment group consisted of patients receiving additional intake in the form of albumed milk, a dairy product containing egg white extract, mung bean sprouts, and other ingredients, registered with the Ministry of Industry under Number 7487/SJ-IND.8/TKDN/12/2022, with a net weight of 30 grams per sachet.

Chicken egg whites, per 100 grams, contain an average of 10.5 grams of protein, of which 95% is albumin (equivalent to 9.83 grams). Egg whites boast a protein digestibility corrected amino acid score (PDCAAS) of 1.0, the highest achievable score. A PDCAAS score of 1.0 indicates that egg white protein, upon ingestion, provides 100% of essential amino acids. Moreover, Almumed milk also contain 4.5% recommended dietary allowances (RDA) of total energy, 0.50% RDA of lipid, 20% RDA of protein, 3% RDA of carbohydrates, 10.8% RDA of sodium, and other vitamins and minerals. Furthermore, egg whites undergo assessment using the digestible indispensable amino acid score (DIAAS), a measure established by the Food and Agriculture Organization, considering essential amino acid proportions in food protein, alignment of crucial amino acid profiles with human body requirements, and ease of digestion. Egg white protein attains a high DIAAS value due to its essential amino acid content exceeding 40% and because it aligns closely with the essential amino acid profile needed by the human body.[3,22] The role of egg white supplements in elevating albumin levels has been investigated in various clinical cases. Syamsiatun et al.'s study in 2015 involved the intervention of hypoalbuminemia patients with egg white juice at Sardjito Hospital and Bantul Hospital. The subjects who received egg white juice three times a day for seven days, alongside the standard hospital diet, demonstrated a notable average increase in albumin and hemoglobin levels. This improvement was superior to that of the control group, which received only hospital therapy standards without the additional egg white supplementation.[36]

Green bean sprouts contain high enough protein, especially at the beginning of development.[36] In particular, green bean sprouts contain higher levels of essential amino acids, which are involved in protein synthesis in the human body. Consuming green bean sprouts can help increase albumin levels in the body, as albumin is a protein composed of amino acids. The body has more raw materials (amino acids) for albumin synthesis when consuming more protein in the diet. This will increase the body's ability to produce albumin.[23,24] Green bean sprouts are a healthy food that contains high enough protein, especially at the beginning of the development stage.[37] Indeed, green bean sprouts are rich in essential amino acids, crucial for protein synthesis in the human body. The consumption of green bean sprouts contributes to an augmentation in albumin levels, given that albumin is a protein composed of amino acids. By incorporating more protein into the diet, the body gains an increased supply of raw materials, specifically amino acids, enhancing the capacity for albumin synthesis. This dietary practice ultimately bolsters the body's ability to produce albumin.[23,25]

Egg whites and green bean sprouts are also believed to have anti-inflammatory effects.[24] Tagashira revealed that egg whites contain lysozyme, which functions to suppress the production of TNF-α and IL-6.[27] While green bean sprouts contain nutrients such as flavonoids, vitamin E, phenols, calcium, and magnesium. Green bean sprouts, through their content of flavonoids, exhibit anti-inflammatory properties. Flavonoids inhibit inflammation by impeding the release of arachidonic acid and the secretion of lysosomal enzymes from neutrophil cells and endothelial cells. Moreover, these compounds play a role in preventing both the exudation and proliferative phases of the inflammatory process. The anti-inflammatory effects of flavonoids in green bean sprouts contribute to their potential health benefits in mitigating inflammatory responses in the body.[28,29] In adult ICU patients with sepsis who are at risk of hypoalbuminemia, consider adding albumed milk 30 g every 8 hours as a nutritional supplement alongside standard ICU feeding to help preserve serum albumin over the first 3 days. In this study, patients receiving albumed milk had minimal change in albumin compared with controls who experienced a significant albumin decline, suggesting a protective effect against sepsis-related hypoalbuminemia. Use this as an adjunct (not a replacement for sepsis management or adequate protein-calorie delivery) and continue routine monitoring of serum albumin and overall nutritional tolerance.

This study has several limitations. This study has not yet analyzed the correlation between comorbidities and albumin levels. Therefore, future studies can be performed to support this clinical finding.

CONCLUSION

There was a significant decrease in albumin levels of the septic patients without albumed intervention. Conversely, albumed milk administration preserves the albumin level in septic patients. This highlights the potential utility of albumed milk as a supplementary measure in mitigating septic-related hypoalbuminemia.

CONFLICT OF INTEREST

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