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Original Article

Parenteral Albumin Therapy in Burn Patients: A Randomized Controlled Trial

Ali Akbar Mohammadi[1], Mohammad Jalal Hashemi-Nasab[1], Reza Ershadi[1], Ahmad Reza Tavakkolian[1], Nasir Fakhar[1], Hamid Reza Tolide-ie[1], Mohammad Kazem Mohammadi[2]

Abstract

Background: Administration of albumin for burn patients and its effects on mortality and morbidity has been debated for along time. The aim of this study was to evaluate the effects of albumin administration on wound healing, length of hospital stay, weight change, and mortality of burn patients.

Methods: Two matched groups of patients from Shiraz Burn Care Center were randomly selected. The patients in one group received parenteral albumin in addition to high protein diet and the other group received only high protein diet. The length of hospital stay, healing time, mortality, serum albumin, transferrin levels, and weight loss were compared.

Results: A total of 141 patients were selected; 71 patients in control group and 70 patients in albumin group. There were no significant differences in mortality (P=0.97), length of hospital stay (P=0.45), and healing time (P=0.25) in two groups. The patients who survived had significantly higher serum transferrin level (128 mg/dL versus 102 mg/dL).

Conclusion: Parenteral albumin administration did not have a significant effect on mortality, length of hospital stay, and healing time in burn patients.
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Keywords ● Albumin ● burn ● transferrin ● wound healing

Introduction

The contemporary treatment of burn injury is based on pure volume substitution during the first 24 hours after the trauma. The volume replacement therapy depends on the burn area and the patient's body weight according to the Baxter formula.[1] It is supplemented by electrolytes, proteins, plasma expanders, fresh frozen plasma (FFP), or coagulative factors.[2,3] Proteins are administered without knowledge of the exact quantitative or qualitative need. Albumin has almost no place during the first 24 hours of burn, but beginning from the day 2 after the trauma, it initiates adequate circulatory and microcirculatory response.[4,5] Although there is no evidence that albumin reduces mortality or morbidity in burn patients,[6] the British burn community supports the use of albumin for resuscitation of burn patients.[7] It is common practice in some burn centers to use albumin especially during the post-acute phase.[8] Recommendation for the use of albumin for correcting hypovolemia is somehow surprising, because

[1]Shiraz Burn Research Center, Shiraz University of Medical Sciences, Shiraz, Iran.
[2]Faculty of Science, Islamic Azad University, Ahvaz Branch, Ahvaz, Iran.

Correspondence:
Ali Akbar Mohammadi MD, Department of Surgery, Shiraz Burn Research Center, Shiraz University of Medical Sciences, Shiraz, Iran.
Tel: +98 711 8219640-2
Fax: +98 711 8217090
Email: mohamadiaa@sums.ac.ir
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the administration of albumin has shown no benefit compared with synthetic colloids in other critically ill patients.[9,10]

Burn resuscitation and management is an issue with great controversies. Among others, there is a continuing challenge about albumin administration and its beneficial or detrimental effect on mortality, multiorgan failure, edema, wound healing, and length of hospital stay.[11] Some studies reported adverse effects,[12] and others found no effect.[13] The aim of the present study was to evaluate the effects of albumin administration on wound healing, length of hospital stay, weight change, and mortality of burn patients in an academic medical center.

Patients and Methods

In a double blind randomized controlled clinical trial, from January 2005 to May 2007, 141 women with burn in 20-40% of their total body surface area From Shiraz Ghotbeddin Burn Hospital were randomly divided into two groups by using random allocation software. The protocol of the study was approved by the Ethical Committee of Shiraz University of Medical Sciences. Patients with respiratory burn were excluded. The first group (control group) received high protein diet and the second group (albumin group) received intravenous albumin supplementation (20% albumin solution; 1 gr/kg/day) from a single provider company (CSL Behring GmbH 5041 Marburg, Germany) after the first 24 hours of burn plus high-protein diet. In the control group, each patient who developed severe hypoalbuminemia (serum albumin < 2 gr/dl), was excluded from the study and received intravenous albumin supplement.

On the second day of hospital admission (before starting the intravenous albumin) and then weekly to the end of hospital admission, the patients' weight, serum albumin, serum total protein, and transferrin levels were monitored.

Healing time was considered as the time needed for wound surface to become ready for graft or heal completely.

Continuous variables were compared using independent samples *t* test for normally distributed data, and Mann-Whitney U test for non-normally distributed data. Comparison of dichotomous values was performed using Chi-square test. Normal distribution was tested by Q-Q-Plots using the Kolmogorov-Smirnov test. A two-tailed P<0.05 was considered statistically significant. Statistical analysis was carried out using SPSS software version 11.5 (SPSS Inc., Chicago, IL, USA).

Results

Out of the 71 female patients in the control group, three developed severe hypoalbuminemia. They were excluded from the study and received intravenous albumin. There were 10 deaths in each group during the study. The mean age of the dead patients was 25.8 years. Their mean burned surface area was 36.10%. And their serum albumin and transferrin levels in the second day were 3.53 gr/dL and 151.63 mg/dL respectively, and their length of hospital stay was 19.40 days.

In survivors, the mean age was 25.90 years. Their mean burned surface area was 28.81%. The serum albumin and transferrin levels on the second day were 3.54 gr/dL and 152.16 mg/dL respectively, and the length of hospital stay was 20.76 days. The risk of mortality in the albumin group was not lower than the control group (odds ratio=0.966). The length of hospital stay was longer in the albumin group; however, it was not statistically different from the control group (P=0.45). The wound healing time was longer in the albumin group and the weight change was lesser in this group (table 1). There was a significant positive correlation between serum albumin reduction and mortality (36.37%±11.23 in dead patients versus 22.32%±10.27 in survivors [P<0.001, figure 1]).

There was a statistically significant association between serum transferrin level and mortality (99.16 mg/dl in dead patients versus 131.99 mg/dl in survivors (p value<0.05) (figure 2).

Table 1: Comparison of serum albumin change, length of hospital stay, weight change, mortality, and healing time between the control and albumin groups in burn patients

Variable	Albumin group (Mean±SD)	Control group (Mean±SD)	P value
Percent of serum albumin change	19.02±5.36	29.85±8.14	0.03
Length of hospital stay (day)	20.76±8.63	20.44±9.55	0.45
Percent of weight change	6.78±1.35	7.59±2.25	0.16
Healing time (day)	20.40±5.63	18.76±6.21	0.25
Mortality (percent)	14.28	14.08	0.97

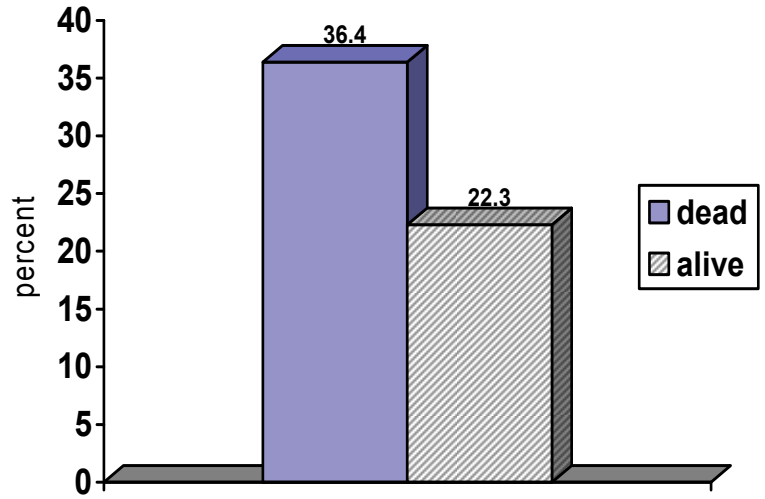

Figure 1: Percent of serum albumin reduction in dead patients and survivors

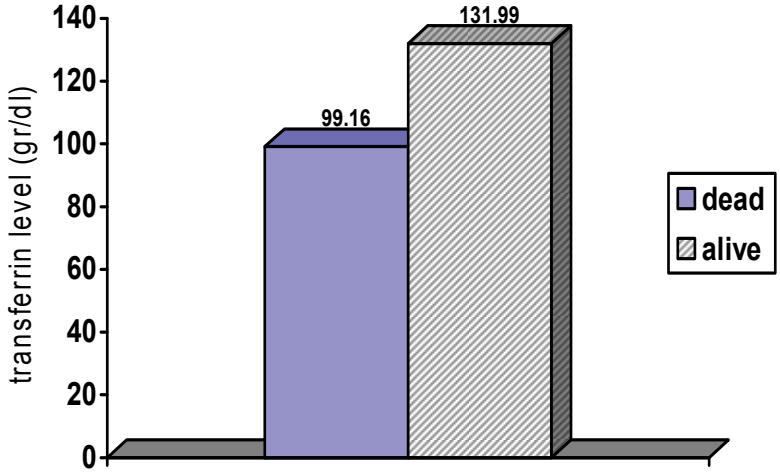

Figure 2: Comparison of serum transferrin level in dead patients and survivors

Discussion

The use of albumin was an important issue in our trial. Although, burn patients tolerate serum albumin level as low as 1-5 g/dL,[14] there is a consensus that oncotic activity remains physiologically adequate at values of albumin ≥2 g/dL.[15] So, we considered the albumin level ≥2 g/dL to exclude the patients from the study.

Up to date, no large study in burn or other critically ill patients could prove the beneficial effects of albumin on patients' morbidity.[1] In a meta-analysis on the benefits of human albumin administration, Wilkes and colleagues included four studies on burn patients.[13] No significant advantage for albumin over non-albumin-based fluid therapy was found. In another systematic review, Haynes and coworkers,[16] included four studies on burn patients. Albumin was compared with Ringer's lactate solution to maintain serum albumin level. No significant benefit for albumin in this situation was shown. A more recent meta-analysis showed a reduction in major morbidity, including mortality, in critically ill patients who received albumin for resuscitation in a variety of settings.[6] A 2001 review of burn units in the U.K. showed that albumin-based protocols persisted in 18 of 22 contacted facilities, and confirmed the absence of consensus about the use of albumin in resuscitation from burn shock.[5] This study adds to the controversy over the role of albumin in burn shock resuscitation with the demonstration of an association between albumin administration and decreased mortality in burn patients.

More than three decades after Baxter and Shires,[2,17] formulated their concepts for fluid therapy, we are still unaware how to guide the volume therapy. Two significant factors in

mortality are presence of inhalational injury and extent of burn[4,5] These factors were excluded from our study. We did not show any significant effect of albumin administration on mortality rate and this is against the results of a meta-analysis in critically ill patients.[6] However, we observed a correlation between the reduction of serum albumin level and mortality.

The acute phase response is a major pathophysiologic phenomenon that accompanies inflammation.[18,19] In inflammatory response, normal homeostatic mechanisms are replaced by new set points that presumably contribute to defensive or adaptive capabilities. Focus on this phenomenon first occurred with the discovery of elevated serum concentrations of C-reactive protein (CRP) during the acute phase of pneumococcal pneumonia.[20] Despite its name, the acute phase response accompanies both acute and chronic inflammatory states. It can occur in association with a wide variety of disorders, including infection, trauma, infarction, inflammatory arthritis, and various neoplasms.

Acute phase proteins are defined as the proteins that their plasma concentrations increase (positive acute phase proteins) or decrease (negative acute phase proteins) by at least 25 percent during inflammatory states.[21] These changes largely reflect their production by hepatocytes. Increases in acute phase proteins may vary from approximately 50% with ceruloplasmin and several complement components to 1000-fold for CRP and serum amyloid A. Other positive acute phase proteins include fibrinogen, alpha-1 antitrypsin, haptoglobin, and ferritin, while negative reactants include albumin, transferrin, and transthyretin (prealbumin). The assumption that the acute phase response is beneficial is based on the known functions of the involved proteins combined with speculation that they may serve useful actions in inflammation, healing, or adaptation to a noxious stimulus. Inflammation is a complex, highly orchestrated process, which involves many cell types and molecules. These cells and proteins may initiate, amplify, sustain, attenuate, or resolve inflammation. A number of participating molecules are also multifunctional, contributing to both the waxing or waning of inflammation at different points in time.[22]

Serum albumin concentration is the most frequently used laboratory marker of nutritional status. A value less than 2.2 g/dL generally reflects severe malnutrition. Despite its popularity as an indicator of nutritional status, the reliability of albumin as a marker of visceral protein status is compromised by its long half life of 14 to 20 days, making it less responsive to acute changes in nutritional status. Furthermore, the serum albumin concentration rises rapidly in response to exogenously administered albumin, and is altered in conditions such as dehydration, sepsis, and trauma.[2] Transferrin has a half-life of 8 days, making it intermediate between prealbumin and albumin in its sensitivity to incipient malnutrition.[23] Plasma protein, hemoglobin, and certain vitamin concentrations during acute illnesses are affected by the acute-phase response as measured by CRP. However, acute-phase response does not seem to have a similar effect on anthropometric nutritional variables. Acute-phase response was associated with deterioration in nutritional status. Recent meta-analyses have reported that aggressive nutritional support in surgical and critically ill patients who are known to have hypermetabolism and increased nutrient requirements does not influence the overall mortality.[24]

Although albumin is the serum protein most commonly measured for assessment of nutritional status, because of its long half-life and reduced degradation during low intake of protein, diagnosis of nutrition depletion can be missed or delayed if it is solely based on serum albumin levels. Moreover, patients frequently and repeatedly receive human albumin during the course of a critical illness. Instead, transferrin and prealbumin have significantly shorter half-lives (8 and 2 to 3 days, respectively), and, presumably, their levels are not directly influenced by human albumin or even fluid status shifts.[25] In recent studies,[26] the most significantly correlated factor to graft healing was found to be serum prealbumin. Serum albumin levels were not in significant correlation with graft healing or prealbumin levels. In addition, serum prealbumin levels were significantly higher in the younger age group and significantly lower in patients with chronic diseases. In the studies, graft healing did not correlate significantly with albumin levels. In addition, albumin levels did not correlate significantly with serum prealbumin levels.

Accordingly, we considered that transferrin and prealbumin would be preferable for nutrition assessment in critically ill patients. Nonetheless, the negative correlation of transferrin to prealbumin was an unexpected finding, possibly related to the significantly different half-lives of these two nutrition markers.

In adult patients after major abdominal trauma, traditional nutrition protein markers (albumin, transferrin, and retinol-binding protein) were restored better in those taking elemental enteral feeding than in those taking

total parenteral nutrition.[25] In this study, the difference of given recommended dietary allowance for protein was significantly correlated to prealbumin levels. A great deal has been made of the relation between albumin abnormalities and morbidity and mortality.[4,5,24,27] However, because this protein has a long half-life (about 18 days), it might not be sensitive enough to capture acute protein energy malnutrition alterations.[28] In addition, albumin has a low specificity, because its levels can be altered in various diseases.[28] These factors suggest that albumin quantification is applicable to population studies but its usefulness as a nutritional parameter in individual subjects may be limited.[28-30] Despite its shorter half-life (about 8 days),[28] transferrin has the same limitations as albumin and is not considered superior to albumin as a nutritional marker.[28,29] In one study, transferrin, but not albumin, was able to predict postoperative complications.[31]

A surprising finding in our study was the association between serum transferrin level and mortality with median of 102 mg/dL and range of 84-110 mg/dL in dead patients and median of 128.5 mg/dl and range of 110-172.9 mg/dL in the survivors. This finding may explain that serum transferrin level maybe a good predictor of mortality at least in burn patients. It seems that high transferrin level, on one hand is an evidence of good nutritional status and on the other hand shows less inflammatory response.

There was a weak positive correlation between the percent of serum albumin reduction and the length of hospital stay and healing time and there was not any significant difference between the two groups in the healing time and the length of hospital stay. These may show that serum albumin level is not a powerful marker for prediction of the healing time and the length of hospital stay and there may be other important factors in determination of healing time and hospital stay period.

Conclusion

Parenteral albumin therapy showed no significant effect on mortality, length of hospital stay, or the healing time. There was not any significant association between serum transferrin level and mortality in burn patients.

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Conflict of Interest: None declared

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