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Research Article

Albumin Resuscitation in Patients with Severe Sepsis/Septic Shock: A Multi-Center Study

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Received: January 31, 2020; **Published:** February 25, 2020

Abstract

Objective: Our primary goal was to investigate the effect of albumin infusion with crystalloids compared to crystalloids (normal saline) in adult patients with severe sepsis, suspected severe sepsis and septic shock.

Methods: A retrospective cohort study was conducted. The relevant information of patients with either severe sepsis suspected severe sepsis, and septic shock in ICU of 16 hospitals in West Florida from January 2016 to December 2017 was analyzed. The extracted data were stratified into two groups; patients who received IV albumin and IV crystalloids (group 1) versus patients who received IV crystalloids alone within the first 24 hours of their admission to the ICU (group 2). The length of ICU stay was analyzed by logistic regression, and the Log-rank test was used to evaluate the differences in survival function.

Results: A total of 2,341 patients with severe sepsis were identified [10% (n = 234) vs 90% (n = 2,107); males 55.6% vs. 51.6%, females 44.4% vs. 48.4%; mean age (years) 67.36 ± 14.11 vs 66.8 ± 16.14]. Patients in group 1 had longer length of ICU stay compared to patients in group 2 (days: 5.96 ± 7.28 vs 3.31 ± 3.14, P < 0.01). The Log rank test evaluating differences in survival function revealed no statistical difference between the two study groups (p = 0.13).

Conclusions: Aggressive fluid resuscitation in patients with severe sepsis or suspected severe sepsis or septic shock is a significant predictor of length of ICU stays. Although practice patterns of fluid resuscitation varied amongst the 16 institutions, our results significantly support the administration of IV crystalloids alone for shorter ICU stay.

Keywords: *Albumin; Severe Sepsis; Septic Shock; Normal Saline; Critical Care*

Introduction

According to the third international consensus, sepsis is defined as organ dysfunction due to impaired patient's response to infection [1]. Furthermore, septic shock is classified as patients with sepsis requiring vasopressors despite adequate fluid resuscitation [1]. Table 1 below illustrates defining criteria for the diseased conditions (i.e. sepsis, severe sepsis, septic shock).

Sepsis	Systemic inflammatory response of host due to infection
Severe sepsis	Sepsis with organ dysfunction
Septic shock	Hypotension induced by infection despite appropriate fluid resuscitation

Table 1: *Defining criteria.*

About 1.3% of hospitalization in the United States is due to sepsis and its incidence has increased by 8.7% per year [2]. Mortality of severe sepsis and septic shock is still high at 14.9% and 34.2%, respectively [3]. Early volume resuscitation is a key element in decreasing mortality due to sepsis [4].

The choice of fluid for volume replacement is still ambiguous [5]. Albumin has been used since World War II to save lives [6]. The principle of using colloids such as albumin comprises management of oncotic pressure, binding and transportation of substances (e.g. drugs, hormones), and nitric oxide modulation, which is of particular importance in patients with severe sepsis and septic shock [7]. Clinical evidence suggests increasing mortality and morbidity in this group of patients associated with low albumin [8]. Some of the reported barriers to using albumin over crystalloids include the possibility of infection transmission, bleeding, and anaphylaxis [9,10].

The albumin infusion in this group of patients is still controversial [11,12].

Aim of the Study

Our primary goal was to investigate the effect of albumin infusion with crystalloids compared to crystalloids (normal saline) in adult patients with severe sepsis, suspected severe sepsis and septic shock.

Methods

Study design and setting

A retrospective cohort of adult patients (≥ 18 years) screened for severe sepsis, suspected severe sepsis and septic shock admitted to the hospitals, from January 1, 2016, to December 31, 2017. Data was retrieved by medical record review from 16 urban teaching hospitals in West Florida.

Demographic and clinical factors

We included patients aged 18 years and above; admitted to the hospital intensive care unit (ICU) for severe sepsis or septic shock. For patients with multiple hospital admissions during the study period, only data of their first visit was used. The data was extracted using the institutional enterprise data warehouse (EDW).

Data collection

The medical records of all patients admitted for severe sepsis or septic shock at the 16 afore-mentioned hospitals in West Florida were abstracted. We used ICD-10 codes to extract data from the EDW. The primary outcome was the length of ICU stay.

Statistical analysis

A multivariate logistic regression analysis was performed on the dichotomous groups of resuscitation fluid to compare differences in length of ICU stay and 30-day mortality among the patients with sepsis/septic shock. Group 1 severe sepsis resuscitated with albumin and crystalloids within twenty-four hours of diagnosis and group 2 severe sepsis patients resuscitated with only crystalloids Odds ratio was used as the constant effect for the resuscitation fluids in Group 1 and 2 as predictors of study outcomes. Adjusted Odd ratio accounted for covariates that might have an impact on outcomes. The model included the covariates age, sex, and race with likelihood ratio tests for the comparison between two groups. We performed appropriate diagnostics with the Wald statistic and Hosmer-Lemeshow goodness-of-fit test. A Kaplan-Meier analysis was conducted to evaluate the difference in all-cause mortality between the two groups. The log-rank test (Mantel-Cox) was used to calculate the Chi-Square statistics to test whether the survival functions are equal between the two study groups. Descriptive statistics for demographics and ICU length of stay are provided as a percent. A p-value of 0.05 was considered to be statistically significant. We performed all statistical analyses with Stata (version 10; StataCorp, College Station, TX).

Results

Participants

Baseline characteristics of study patients are denoted in table 2. A total of 2,341 patients with severe sepsis were identified (group 1, n = 234; 10% vs group 2, n = 2,107; 90%). The age (mean ± SD) of study patients was 67.36 ± 14.11 (group 1) vs 66.8 ± 16.14 (group 2. The study included males [55.6% (group 1) vs 51.6% (group 2) and females [44.4% (group 1) vs 48.4% (group 2).

Variables		Albumin + Crystalloids (group 1, n = 234)		Crystalloids (group 2, n = 2,107)	
Age (years; n, mean +SD)		234	67.36 ± 14.11	2,107	66.81 ± 16.14
Sex	Females (%; n, mean ± SD)	113	48 ± 50	940	44 ± 49
	Males (%; n, mean ± SD)	121	52 ± 50	1,167	56 ± 49

Table 2: *Baseline characteristics.*

See figure 1 for graph indicating the gender composition amongst Group 1 resuscitation with albumin and crystalloid (albumin) vs Group 2 resuscitation with crystalloids alone (no albumin).

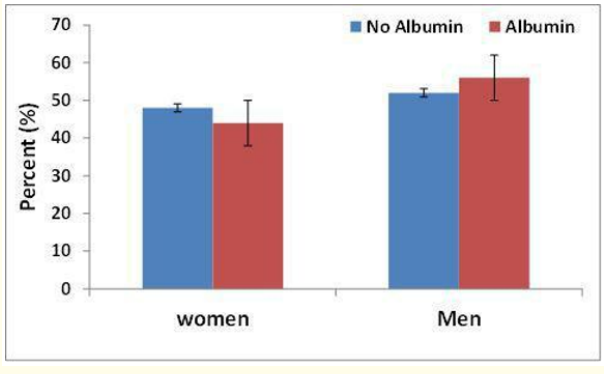

Figure 1: *Graph indicating the gender composition amongst Group 1 resuscitation with albumin and crystalloid (albumin) vs Group 2 resuscitation with crystalloids alone (no albumin).*

See figure 2 for graph indicating the average age between Group 1 resuscitation with albumin and crystalloid (albumin) vs Group 2 resuscitation with crystalloids alone (no albumin).

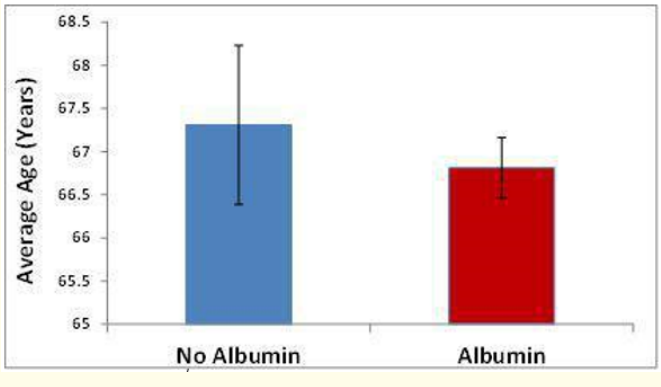

Figure 2: *Graph indicating the average age between Group 1 resuscitation with albumin and crystalloid (albumin) vs Group 2 resuscitation with crystalloids alone (no albumin).*

Length of ICU stay

Patients in group 1 had longer ICU stay (5.96 days ± 7.28) compared to those in group 2 (3.31 days ± 3.14), *P*< 0.01) (See table 3).

	Albumin + Crystalloids (Group 1, n = 234)	Crystalloids (Group 2, n = 2,107)	P-values
ICU LOS (Days)	**Mean ± SD**	**Mean ± SD**	
ICU LOS (Days)	5.96 **±** 7.28	3.30 **±** 3.14	< 0.05 or 0.01
ICU LOS ≥ 15 days	0.08 ± 0.27	0.01 ± 0.11	< 0.05
ICU LOS 10 - 14 days	0.15 ± 0.36	0.04 ± 0.20	< 0.05
ICU LOS 7 - 9 days	0.24 ± 0.43	0.10 ± 0.30	< 0.05
ICU LOS 5 - 6 days	0.37 ± 0.48	0.19 ± 0.39	< 0.05
ICU LOS 3 - 4 days	0.54 ± 0.50	0.38 ± 0.49	< 0.05
ICU LOS = 2 days	0.70 ± 0.46	0.58 ± 0.49	< 0.05
ICU LOS = 1 day	0.90 ± 0.30	0.82 ± 0.39	< 0.05

Table 3: *Length of ICU stay.*

See figure 3 for graph showing the difference of length of ICU stay (mean ± SD) between Group 1 resuscitation with albumin and crystalloid (albumin) vs Group 2 resuscitation with crystalloids alone (no albumin). Patients in group 1 had longer ICU stay (5.96 days ± 7.28) compared to those in group 2 (3.31 days ± 3.14), P < 0.01).

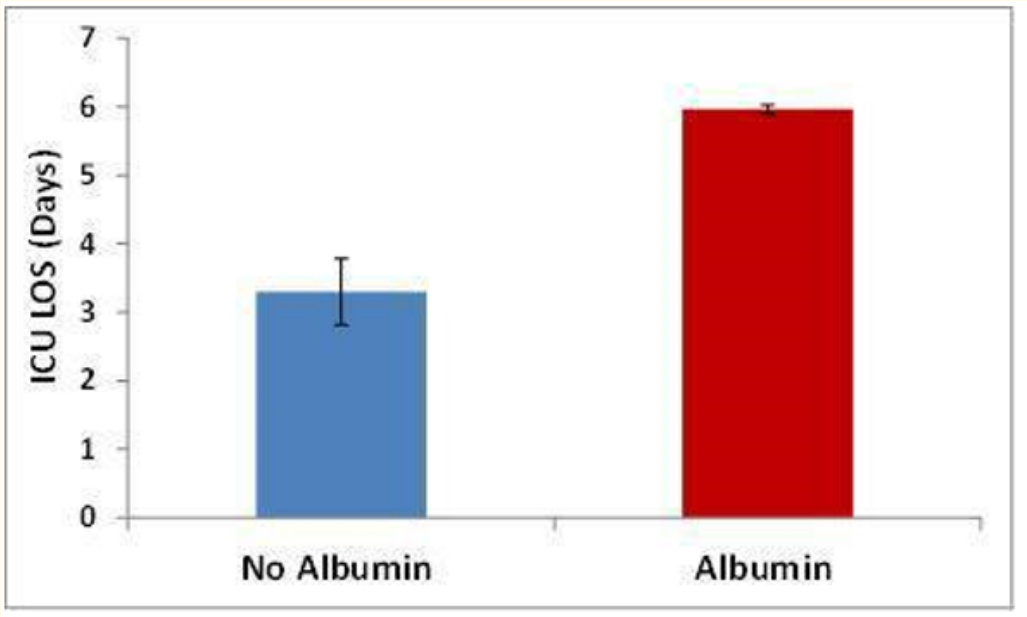

Figure 3: *Graph showing the difference of length of ICU stay (mean ± SD) between Group 1 resuscitation with albumin and crystalloid (albumin) vs Group 2 resuscitation with crystalloids alone (no albumin). Patients in group 1 had longer ICU stay (5.96 days ± 7.28) compared to those in group 2 (3.31 days ± 3.14), P < 0.01).*

Survival function

The Log-rank test evaluating differences in survival function revealed no statistical difference between the two study groups (p = 0.13) (See figure 4).

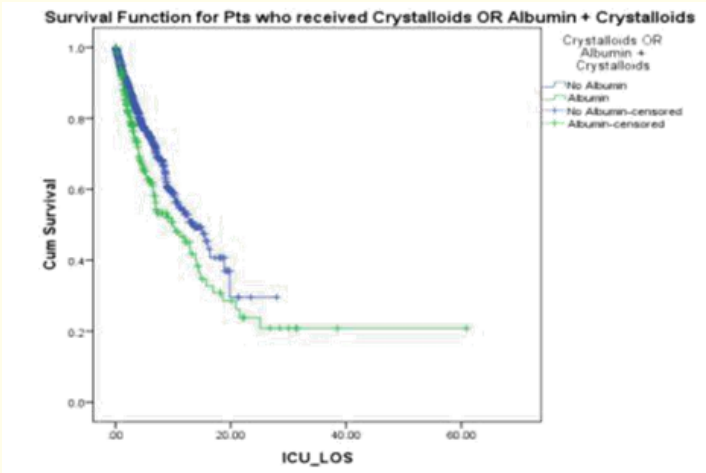

Figure 4: *Survival function for patients who received crystalloids or albumin with crystalloids.*

Discussion

The aim of this retrospective study was to compare the length of ICU stay in patients with severe sepsis/ septic shock who received either IV albumin plus IV crystalloids versus IV crystalloids alone. Comparing both interventions, we found an association with albumin administration and length of ICU stay. There was a statistical difference with longer length of ICU stay in patients who received albumin compared to those who did not. This increase was approximately 2 days. There was no significant survival benefit between patients who received albumin administration verse those that did not receive albumin.

Our results contradict the findings from two prior randomized controlled trials (RCTs) which showed no statistically significant difference between the length of ICU stay and albumin administration [13,14]. In the ALBIOS trial [13], the average ICU length of stay was approximately 9 days in both groups while in the SAFE trial [14] it was 6.2 days and 6.5 days in the crystalloid and albumin group respectively. We observed 3.31 days and 5.96 days in the no albumin and albumin group respectively with statistical difference. In regard to survival benefits, both SAFE and ALBIOS trials showed similar results with no survival benefit which was echoed in our study.

The significance of the length of ICU stay with albumin administration is still unclear. Though current practice guidelines recommend the administration of albumin after patients have received large volumes of fluids, no benefit was reported in a landmark meta-analysis [15,16]. Most recent studies have suggested that increased length of ICU stay may be linked with increased long-term mortality and often can be used as an outcome measure [17,18]. Increased length of ICU stay has also been linked to an increased risk of nosocomial infections which could result in increased mortality [19].

Due to this being a retrospective study, study limitations do exist. Firstly, mortality rates were not recorded as data was restricted. Secondly, the severity of illness between both groups was not calculated. For both reasons, we were unsure if both populations were similar in the risk of mortality and therefore unable to comment if there would be any benefit from albumin based on the severity of the illness. Ultimately, aggressive fluid resuscitation with albumin did not show a significant decrease in ICU days with a survival benefit.

Based on our research, further investigation into the severity of illness should subdivide the patient population to evaluate if a subcategory would truly benefit from albumin in severe sepsis or septic shock. Furthermore, more adequately powered studies or RCTs are needed to validate the results of our study.

Conclusion

Ultimately, aggressive fluid resuscitation with albumin did not show a significant decrease in ICU days with a survival benefit. Based on our research, further investigation into the severity of illness should subdivide the patient population to evaluate if a subcategory would truly benefit from albumin in severe sepsis or septic shock. Furthermore, more adequately powered studies or RCTs are needed to validate the results of our study.

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Volume 9 Issue 3 March 2020