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## Original Research

# Assessing adherence to current national guidelines for appropriate albumin use at an academic medical center

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### Abstract

**Objective:** To assess adherence to current national guidelines for appropriate albumin use at an academic medical center.

**Methods:** This retrospective chart review of 150 randomly selected patients prescribed and administered at least one dose of albumin was conducted in an urban academic medical center to evaluate the adherence of albumin orders to current national guidelines. Inclusion criteria consisted of discharged patients at least 18-years-old admitted to the intensive care unit or medical/surgical unit from September 1, 2015 to August 31, 2016. The primary outcome was the number of patients who inappropriately received albumin based on national guidelines and FDA approved indications. Secondary outcomes included the number of patients who received the incorrect concentration or dose of albumin based on indication, as well as the cost associated with inappropriate albumin prescribing. Descriptive statistics were used to report outcomes.

**Results:** There were 68 instances (45%) where albumin was prescribed inappropriately according to guideline recommendations. Of the 82 instances where albumin was used appropriately, 18 patients received an incorrect dose (22%), and 6 received the inappropriate concentration of albumin (7%). The cost for the 150 patients included in the study associated with inappropriate albumin prescribing was approximately \$13,000.

**Conclusions:** This study identified areas for pharmacist intervention to ensure appropriate albumin utilization, as well as proper dosing for the most frequently incorrectly dosed indications, including hepato-renal syndrome, spontaneous bacterial peritonitis, and paracentesis. This study also identified an unexpected indication with significant inappropriate albumin utilization, perioperative hypotension, which is an area for further intervention to monitor and decrease use.

### Keywords

Serum Albumin; Critical Care; Drug Utilization Review; Guideline Adherence; Clinical Audit; Pharmacy Service, Hospital; Cost Savings; Hospital Costs; Clinical Audit; United States

## INTRODUCTION

Albumin is used throughout intensive care units (ICU) and medical/surgical floors. Albumin use is recommended over crystalloids in certain settings, such as large volume paracentesis, hepatorenal syndrome, and spontaneous bacterial peritonitis (SBP) treatment.<sup>1</sup> However, there is little data proving mortality benefit of albumin as the initial resuscitation fluid over less expensive crystalloids.<sup>2-4</sup> Fluid therapy practice standards have considerable variation in terms of volume and choice of fluid administered.<sup>5</sup> The Colloids Versus Crystalloids for the Resuscitation of the Critically Ill (CRISTAL) randomized trial determined there was no mortality benefit at 28 days when using colloids such as albumin, versus crystalloids such as normal saline or Ringer lactate solution in patients with hypovolemic shock.<sup>2</sup> Raghunathan *et al.* also determined giving colloids in addition to crystalloids resulted in increased cost per day without improved survival.<sup>3</sup> The Surviving Sepsis Campaign guidelines reflect the findings of these studies by recommending crystalloids as the preferred fluid therapy.<sup>4</sup>

Inappropriate fluid selection can have a large economic impact on institutions.<sup>3,5-9</sup> In a sequential multifaceted intervention to decrease albumin use in eight ICUs at two hospitals in an academic healthcare system, no statistically significant difference was found in ICU mortality or in-hospital mortality before and after the interventions.<sup>6</sup> These findings reinforce the notion that aligning clinical practice with evidence-based literature can both lower the economic impact of albumin, and also maintain the integrity of patient-centered care.

One component lacking from many studies regarding institutional albumin utilization is an assessment of the appropriateness of albumin orders.<sup>6</sup> Examples of inappropriate albumin prescribing, not supported by national guidelines or evidence-based literature, include first line for intradialytic hypotension (IDH)<sup>10,11</sup>, paracentesis of less than 5 liters<sup>1</sup>, and septic shock responsive to crystalloids.<sup>2-4,9</sup> A randomized, double-blind, crossover trial in 72 chronic hemodialysis patients was conducted to determine whether 5% albumin was more effective than normal saline for the treatment of IDH. The results showed that 5% albumin was no more effective than normal saline, and the investigators recommended that normal saline should be used as the initial fluid treatment for IDH.<sup>10</sup> A similar study by Emili *et al* evaluated the safety and efficacy of a stepwise protocol utilizing normal saline, mannitol, and albumin designed to minimize albumin use for IDH treatment. They found that of the 433 instances where the protocol was used, hypotension was reversed without the need for albumin in 91% of cases.<sup>11</sup>

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Table 1. Assessment of albumin orders by indication				
Indications <sup>a</sup>	Number of orders (%)	Inappropriate indication	Inappropriate dose	Inappropriate concentration
SBP	12 (8)	0	8	1
Large volume paracentesis	4 (3)	0	1	1
Paracentesis < 5 L	4 (3)	4	... <sup>b</sup>	...
HRS	16 (11)	0	9	4
IDH	4 (3)	4	...	...
Persistent hypotension despite adequate fluid resuscitation	41 (27)	0	0	0
Hypotension without adequate fluid resuscitation	32 (21)	32	...	...
Plasmapheresis	4 (3)	0	0	0
ARDS	5 (3)	0	0	0
Enhanced diuresis	10 (7)	10	...	...
Hypoalbuminemia	2 (1)	2	...	...
Perioperative hypotension	16 (11)	16	...	...
Total	150 (100)	68	18	6

<sup>a</sup> SBP =spontaneous bacterial prophylaxis, HRS =hepato-renal syndrome, IDH =intradialytic hypotension, ARDS =acute respiratory distress syndrome.

<sup>b</sup> Orders that were classified as an inappropriate indication were not evaluated for appropriateness of dose or concentration.

Enhanced diuresis and perioperative hypotension are two other controversial instances where albumin is used. Two studies, one in medical ICU patients and one in patients with cirrhosis and ascites, have shown no benefit to the addition of albumin to enhance diuresis.<sup>12,13</sup> Regarding perioperative hypotension, The British Consensus Guidelines on Intravenous Fluid Therapy for Adult Surgical Patients lists either crystalloid or colloid as potential fluids to correct hypotension, but does not comment on which order they should be used in.<sup>14</sup>

Given the widespread use of albumin in different hospital areas, practice variation regarding fluid selection, and the high cost of albumin as compared to therapeutic alternatives, a unique opportunity for pharmacist intervention presents itself to align clinical practice with evidence-based literature and lower the economic impact of albumin by decreasing its use in inappropriate settings.

The purpose of this study was to assess adherence to current national guidelines in the literature for appropriate albumin use at an academic medical center. Albumin orders were assessed for appropriateness using Food and Drug Administration (FDA) approved labeling and national guidelines including the American Association for the Study of Liver Diseases (AASLD) and the Society of Critical Care Medicine's Surviving Sepsis Campaign.

## METHODS

This study was conducted as a retrospective chart review in an urban academic medical center in the United States.

### Selection of Participants

Inclusion criteria for this study consisted of discharged patients at least 18-years-old admitted to the ICU or medical/surgical unit from September 1, 2015 to August 31, 2016. During this period of time, an electronic list of patients was generated consisting of patients that were

prescribed and administered at least one dose of albumin. A sample size of 150 patient charts was selected prior to Institutional Review Board submission. The electronic list generated 192 patient charts that met the inclusion criteria. In order to stay with the pre-determined sample size, a random numbers table was used to select a sample of 150 patient charts to be evaluated for the appropriateness of albumin orders.

### Definitions

Hypotension was defined as a mean arterial pressure (MAP) less than 65 mmHg, a systolic blood pressure less than 90 mmHg, or if MAP was greater than or equal to 65 mmHg while on vasopressors. The Surviving Sepsis Guidelines were utilized to determine the definition of adequate volume resuscitation, 30 mL/kg of crystalloid.<sup>4</sup> A diagnosis of HRS or the attempt to rule out HRS, and diagnosis of SBP or empiric SBP treatment was determined by physician documentation in the electronic medical record. The term perioperative was defined as the period of time from when the patient entered the preoperative unit, to when the patient left the post-anesthesia care unit. Appropriate dosing regimens were determined using the corresponding evidence-based literature and guidelines per indication.

### Outcome Measures

The primary outcome of interest was the number of patients who received albumin that was not indicated based on national guidelines or FDA approved indications. Secondary outcomes included the number of patients who received the inappropriate concentration of albumin according to indication, the number of patients who received the inappropriate dose of albumin according to indication, and the wholesale acquisition cost (WAC) associated with inappropriate albumin prescribing.

Table 2. Location of albumin administration			
Location	Number of albumin orders	Appropriate indication	Inappropriate indication
Intensive care unit	80	48	32
Medical/surgical unit	41	26	15
Emergency department	8	6	2
Dialysis	3	0	3
Perioperative	18	2	16

Table 3. Wholesale acquisition cost (WAC) associated with inappropriate albumin prescribing			
Albumin Product	Amount of inappropriately prescribed albumin	Cost in USD/unit <sup>a</sup> (WAC)	Cost in USD (WAC)
Albumin 5% (Albutein <sup>®</sup> )	1,315 g	48.51/unit	5,103.25
Albumin 25% (Albutein <sup>®</sup> )	2,230.7 g	44.00/unit	7,852.06
Total	3,545.7 g	...	12,955.31

<sup>a</sup> Unit = 12.5 g of albumin.  
<sup>b</sup> Not applicable.

## Statistical Analysis

Data was extracted from electronic medical records for patients included in the study during the one year study period. Descriptive statistics were used to report outcome measures. This retrospective study was deemed exempt by the Institutional Review Board.

## RESULTS

Of the 192 patient charts that met the inclusion criteria, 150 were randomly selected to be included in the analysis. Patient ages ranged from 20 to 89 years, with a median (interquartile range) of 57 years (48 to 67 years). The majority of patients were male (n=97, 65%). Regarding the primary outcome of interest, 68 patients (45%) received albumin that was not indicated based on guidelines or FDA approved indications. Of the 82 patients that received albumin based on an appropriate indication, 18 (22%) received the inappropriate dose, and 6 (7%) received the inappropriate concentration of albumin (Table 1). The majority of albumin orders were administered in the intensive care, medical/surgical, and perioperative units (Table 2). It was calculated that 3,545.7 grams of albumin was used inappropriately, and the cost (WAC) associated with this inappropriate albumin prescribing was USD 12,955.31 (Table 3).

## DISCUSSION

In this study, we determined whether a patient received albumin for either an appropriate or an inappropriate indication. The distinction between appropriate and inappropriate indications was based on evidence-based literature and national guidelines. Appropriate indications included: SBP, large volume paracentesis, HRS, persistent hypotension despite adequate fluid resuscitation, plasmapheresis, and acute respiratory distress syndrome (ARDS). Inappropriate indications included paracentesis less than five liters, intradialytic hypotension, hypotension without adequate fluid resuscitation, enhanced diuresis, hypoalbuminemia, and perioperative hypotension.

Table 1 details the classification of the 150 orders into their respective appropriate or inappropriate indications. Sixty-eight (45%) of the orders were classified as inappropriate indications, with the three most frequent being hypotension without adequate fluid resuscitation, perioperative hypotension, and enhanced diuresis. Perioperative hypotension was an unexpected indication identified, making up almost one-fourth of the inappropriate orders. Of the appropriate indications, HRS and SBP were frequently ordered with an incorrect dose or with the incorrect concentration of albumin.

Limitations of this study include those that are inherent to a retrospective study, namely relying of the accuracy of

documentation in the electronic medical record. One area where this lack of information was notable was the documentation of the amount of intravenous fluids used in the perioperative units. Another limitation was that this study was performed at a single medical center. The inclusion of additional sites may have yielded more indications for albumin not seen at our institution (i.e. ovarian hyperstimulation syndrome).

Defining adequate fluid resuscitation for the purposes of classifying albumin orders was another potential limitation in this study. The quantity of 30 mL/kg of crystalloid was derived from the Surviving Sepsis Campaign recommendations. However, a timeline for when this resuscitation occurred in relation to albumin administration needed to be established. There is little guidance in the literature defining this time period. The criteria used in this study to determine adequate resuscitation was for a patient to receive 30 mL/kg of crystalloid within 24 hours prior to albumin administration. However, there are some populations where risk and benefit should be weighed when administering these large amounts of fluid, such as heart failure patients. Although the Surviving Sepsis Campaign does not comment on these patient populations, perhaps a patient's overall volume status may be a determinant of appropriate albumin use.

Using this information, a pharmacy driven protocol outlining appropriate albumin use was implemented at our institution to align clinical practice with evidence-based literature and lower the economic impact of albumin, while maintaining the integrity of patient-centered care. Implementation strategies used include a pocket reference card for physicians and pharmacists with the dosing regimens for SBP, HRS, and paracentesis, prescriber education, formulary restrictions, and criteria based ordering. Data will be collected after sufficient implementation of these strategies to assess the impact of this pharmacist driven initiative to decrease albumin use.

Table 4 shows a pocket reference card created to aid in dosing for these indications.

## CONCLUSIONS

This study used evidence-based literature to assess adherence of albumin orders to current national guidelines. The results demonstrated a high rate of inappropriate

Table 4. Dosing "Pocket" Reference <sup>1</sup>		
Indication	Strength	Dose
SBP	25%	Day 1: 1.5 g/kg Day 3: 1 g/kg
HRS	25%	1 g/kg body weight daily up to maximum of 100 g
Paracentesis > 5 L	25%	5-10 g/L removed; or 50 g total

albumin prescribing within our institution. These results reveal potential areas for pharmacist intervention to decrease the amount of inappropriate albumin prescribing, as well as to ensure that the correct dosing and concentration be used with frequently incorrectly dosed indications such as SBP, HRS, and paracentesis. This study also identified an unexpected indication with significant inappropriate albumin utilization, perioperative hypotension, which is an area for further intervention to monitor and decrease use.

## CONFLICT OF INTEREST

No conflicts of interest to disclose.

## FUNDING

None.

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