



Albumin Utilization in a Teaching Hospital in Tehran: Time to Revise the Prescribing Strategies

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ABSTRACT

Background: Since albumin imposes a relatively high cost to a healthcare system, drug use evaluation for this drug is much more important. This study wants to evaluate pattern of albumin use in a large university affiliated hospital in Tehran, Iran.

Methods: A concurrent, cross-sectional study was performed in “Shaheed Rajaei” Cardiovascular, Medical and Research Center. All inpatient adults that were prescribed albumin during the study period were evaluated to register the indications for albumin usage according to the evidence-based guidelines.

Results: Only for five patients (4%) the albumin prescriptions were justifiable. Of these cases, intractable edema was the leading cause of albumin misuse (73 patients; 60.8%). The total 1468 vials of Albumin were prescribed for 120 patients during the study period. The most common reasons to prescribe albumin were acute normovolemic (34%), cardiac failure (0.83%), resistance edema with Albumin>2g/dL (61%), nephrotic syndrome (0.83%), plasmapheresis (1.67%), ascetic (1.67%).

Conclusion: These data, together with previous national studies highly suggest a mandatory need for educational measures for practicing physicians along with strict regulations for prescription strategies regarding expensive drugs such as albumin.

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Introduction

Recently, the increased drug expenditures have become significant issue in managing health care systems. Indeed, financing of health care is based on a fee-for-service

system and hence cost control strategies play an important role in rational usage of drugs. This control should be greater on expensive drugs (1, 2).

To achieve this goal, drug use evaluation (DUE) should be considered in any healthcare system to ensure appropriate and proficient drug use (3, 4). This evaluation means tight regulation of drug prescription regarding correct indications, continuous monitoring of the patient during treatment and possibilities for cessation of a certain treatment. These successive checkpoints in

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drug use evaluation require utilization of high quality evidenced-based guidelines for appropriate drug usage as well as repeated assessments of drug use with the accepted guidelines. The process of drug use evaluation is of a great importance for high-priced drugs and narrow therapeutic index, also spectrum broad antibiotic agents (1, 2)

Human albumin is an expensive drug that requires extensive purification processes and since its arrival to the market in the 1940s, the rising demand for the drug has raised serious questions regarding its appropriate indications. The problem in albumin usage roots in many pathophysiological justifications for its prescription that was not verified in randomized clinical trials. Role of albumin in management of critically ill patients, where most of its usage is confronted, is not well-supported by high quality clinical evidence. It has been stated that less expensive alternatives such as crystalloid solutions could be used in many clinical settings (5).

Correct indications are those supported by Meta analysis as well as well-designed randomized controlled trials. Incorrect indications are those which have reached no agreement, and the studies are inconsistent and contradictory. Moreover, those usages that could not increase survival of the patients or do not provide a clear advantage to the patients are also inappropriate prescriptions (6). Since albumin imposes a relatively high cost to a healthcare system, drug use evaluation for this drug is much more important. This importance will be doubled if one considers controversial pattern of usage for this drug.

This study wants to evaluate pattern of albumin use in a large hospital affiliated to Tehran University of Medical Sciences. Moreover, we look for adherence of the physicians to evidenced-based guidelines in albumin prescription in an inpatient setting.

Patients and Methods

Study participants

This cross-sectional study was conducted between September 2012 and June 2013 at "Shaheed Rajaei" Cardiovascular, Medical and Research Center which is a Iran University of Medical Sciences affiliated center and is served as a nation-wide referring facility for cardiovascular diseases. Adult patients (more than 14 years old) who receiving albumin in this period of time were included in this study. A daily evaluation of all the physician orders of albumin in this hospital has been carried out in our study.

Data recruitment and studied variables

In the participating hospital, albumin which is prescribed by the attending physician will be requested from the inpatient pharmacy. Upon reviewing albumin requests from the data bank of the pharmacy, a list of

potential study participants was generated by a clinical pharmacist. A form which is consisted of patients' demographic information including age, gender, reason of hospitalization, and type of surgical intervention, concurrent use of furosemide as well as laboratory findings comprising liver function tests, total protein and albumin levels, hematocrit and serum creatinine levels was recorded.

Then, it is enriched with the prescription details including the cause of the prescription, the amount and length of usage.

Criteria for defining appropriate use of albumin

To address appropriateness of the albumin usage, no national guideline was available and hence the most up-to-date and comprehensive evidenced-based guidelines were utilized (7, 8). The correct and appropriate usages were defined when the prescription was corresponded the accepted indications. The indications were listed in Table 1.

Statistical analysis

Data recruited from the standard forms were gathered and analyzed using IBM SPSS software version 20.0. For descriptive assessment, mean and standard deviations of continuous variables along with their range were provided. For nominal variables, number and percentages were reported.

Results

Patients' demographics

During the study period, a total of 120 patients with a mean age of 57.5 ± 16.5 years received albumin. Of these, 70 (58.3%) were male and 50 (41.6%) were female. The total number of vials used was 1468 and the patients received a mean number of 12.3 vials ranging from 1 to 68 vials. Our findings showed that albumin treatment course in our patients were 6.2 days.

Since the participating hospital was a tertiary center for cardiovascular diseases, the distribution of albumin prescriptions were mostly encountered in Intensive Care Unit (ICU) and Cardiovascular Care Unit (CCU). Our analysis showed that as much as 77.9% of the patients receiving albumin were admitted to the care units (46.2% in ICU and 31.7% in CCU).

Distribution of underlying reason of albumin prescription

Prescriptions were most frequent after coronary artery bypass grafting (CABG) (40.8%) and decompensate heart failure with edema (15.8%). Valvular replacements, pending heart transplantation and other etiologies were amongst next frequent underlying diseases (see Table 2 for more details).

Table 2 also summarizes the mean plasma levels

Table 1. Indication for the use of albumin (7).

Indication	Notes	GOR*
<i>Appropriate indications (for which there is widespread consensus)</i>		
Paracentesis	5 g of albumin/L ascitic fluid removed, after paracentesis of volumes > 5 L.	1C+
Therapeutic plasmapheresis	For exchanges of > 20 mL/kg in one session or > 20 mL/kg/week in more than one session.	2C+
Spontaneous bacterial peritonitis	In association with antibiotics.	1C+
<i>Occasionally appropriate indications (when other criteria are fulfilled)</i>		
Heart surgery	Last-choice treatment after crystalloids and non-protein colloids.	2C+
Major surgery	Albumin should not be used in the immediate post-operative period. Only indication for use: serum albumin < 2 g/dL after normalisation of circulatory volume.	2C+
Cirrhosis of the liver with refractory ascites	Generally ineffective, except in patients with serum albumin < 2 g/dL.	2C
Contraindications to the use of non-protein colloids	Pregnancy and breastfeeding; Prenatal period and early infancy; Acute liver failure; Moderate-severe renal failure (particularly when anuria/oliguria); Dialysis treatment in the presence of severe abnormalities of haemostasis and baseline albumin < 2 – 2.5 g/dL; Intracranial hemorrhage; Hypersensitivity	2C
Hemorrhagic shock	Only in the case of : Lack of response to crystalloids or colloids; Contraindication to the use of non-protein colloids.	1A
Hepatorenal syndrome	In association with vasoconstricting drugs	2B
Nephrotic syndrome	Only in patients with albumin < 2 g/dL with hypovolaemia and/or pulmonary oedema.	2C
Organ transplantation	In the post-operative period after liver transplantation to control ascites and peripheral oedema, to replace the loss of ascitic fluid from the drainage tubes, if albumin < 2.5 g/dL with a haematocrit > 30%.	1C
Burns	In the case of burns of > 30% body surface area, after the first 24 hours.	2C+
<i>Dose</i>		
The dose needed to obtain a serum albumin ≥ 2.5 g/dL is calculated using the following formula: Dose (g) = [desired albumin concentration (2.5 g/dL) – actual albumin concentration (g/dL)] x plasma volume (0.8 x kg)		

GOR* = Grade of Recommendation

of AST (aspartate aminotransferase), ALT (alanine aminotransferase), alkaline phosphatase, albumin, total protein, hematocrit and creatinine of the study participants. Of these variables, although serum albumin is the most important index that may help in decision making for albumin use, only for 44 patients (36.7%) this value was measured. More interestingly, in our study, albumin levels showed a mean value of 3.5 ± 0.4 g/dL (range 2.2–4.5 g/dL) which is well above the accepted cutoff for any prescription (2.0 g/dL).

Adherence of albumin orders to valid guidelines

According to current guidelines, only for five patients

(4%) the albumin prescriptions were justified. Of these patients, two received albumin after plasmapheresis; one patient needed albumin because of nephritic syndrome with concurrent hypoalbuminemia and the remaining two patients with ascites received albumin after massive paracentesis (Figure 1).

On the other hand, in 95% of the patients, albumin prescription was not in accordance with the current evidenced-based guidelines. Of these cases, intractable edema was the leading cause of albumin misuse (73 patients; 60.8%). The only accepted usage in a setting of intractable edema is confirmed presence of hypoalbuminemia along with the underlying edema. This

Table 2. Patients' demographics and underlying diseases of the study participants.

Variable (N=120)	Results*
Age, years	57.5±16.5 (14.0-90.0)
<i>Admission ward</i>	
Intensive care unit	77 (46.2)
Cardiovascular care unit	38 (31.7)
Other wards	5 (4.2)
<i>Underlying disease</i>	
Decompensate CHF	49 (40.8)
Admission during the course of CABG	19 (15.8)
Admission during the course of MVR	18 (15.0)
Other etiologies	28 (23.3)
Number of used albumin vials	12.3±13.9 (1-68)
Concurrent use of furosemide	75 (62.5)
<i>Lab values</i>	
Serum albumin	3.5±0.4 (2.2-4.5)
Total protein	6.3±0.9 (3.7-8.3)
Serum creatinine	1.4±0.8 (0.6-4.1)
Hematocrit	32.5±7.1 (22.0-53.0)
AST	94.4±157.2 (10-785)
ALT	69.1±153.8 (7-791)
ALP	305.6±153.4 (85-568)

CHF: Congestive Heart Failure; CABG: Coronary Artery Bypass Graft; MVR: Mitral Valve Replacement; ALT: Alanine transaminase; AST: Aspartate transaminase; ALP: Alkaline phosphatase

*Mean±SD (range) for continuous variables; Frequency (%) for nominal variables.

is while in the majority of these 74 patients (42 patients; 57.5%), no albumin measurement had been carried out. In all remaining cases (32 patients; 42.5%), serum albumin level showed to be above the cutoff (i.e. >2g/L).

Moreover, for 40 patients (34.2%), the reported indication was filed as correction of acute hypovolemia which also could be categorized as an incorrect indication. These data are summarized in figure 1.

Discussion

Our findings in the current study underscore the importance of drug utilization review in prescribing of albumin. Indeed majority of the cases received albumin in an inappropriate setting. High costs of albumin in our country, as stated by official authorities (9), signify importance of the issue. Although the same results were consistently reported for the misuse of albumin (10,11) but our study had two intriguing differences. First, with the aid of a concomitant registration, rather than a widely used conventional retrospective design, we were able to minimize the confounding nature of recall

bias. Moreover, simultaneous open discussion with the practicing physician helped us to fully understand his/her underlying justification for drug prescription. The cross-sectional recruitment of data also helped us to follow the course of therapy and monitor possible changes in motives for albumin prescriptions. Our study also focused in a hospital with a large load of patients requiring cardiovascular interventions. A prospective study conducted by Jahangard and colleagues in a large teaching hospital affiliated by Tehran University of Medical Sciences (Shariati Hospital) has shown that most prevalent inappropriate use of albumin is seen in patients after variety of cardiac surgeries (9). Our results in the current study not only confirm the previous results but also show that the ratio of inappropriate utilization of albumin would be much larger in a tertiary cardiovascular setting. This ratio reached 95% in our cases, whereas the reported ratio for other studies never reached this level (9-11).

There has been widespread debate over correct indications of albumin use. Although many guidelines are available for the use of albumin, but two major problems were faced in our study. To the best of our knowledge, there are no national evidenced-based guidelines that clearly state proper indications of albumin use in Iran. Moreover, most of the present guidelines from Europe and United States do not provide "clear" indications (12-14). Indeed defining a precise clinical setting in which albumin use is justifiable is not that straightforward. However, in this study, after reviewing a variety of current guidelines, we came up to an evidenced-based guideline (7). The possible inconsistencies between the studies when providing appropriate indications could be minimized considering the level of recommendation in evidence-based guidelines.

In our study, we found that 95% of albumin usage was inappropriate. This result is in line with majority of published data. The rate of inappropriate albumin use varies among studies. In a study conducted in Southeast Asia, as much as 35.6% of prescription showed to be incorrect (10). Of these patients, edema, anemia and indications related to management of patients after CABG were among most frequent inappropriate prescriptions. Some other studies reported the misuse ratio to be much higher. A multicenter study conducted in Spain showed that only 8.1% of prescriptions (corresponding to 9.8% of all used vials) were in accordance with accepted indications (11). In that study, use of albumin as the first line (before any other crystalloid or colloid solutions) for correction of volume depletion was the major cause of inappropriate prescription (as much as 30.9%). This data is comparable to our results. As stated in our findings, most of incorrect use of albumin was encountered in correction of hypovolemia after cardiac surgery. Indeed rushing into albumin before a full trial of conventional

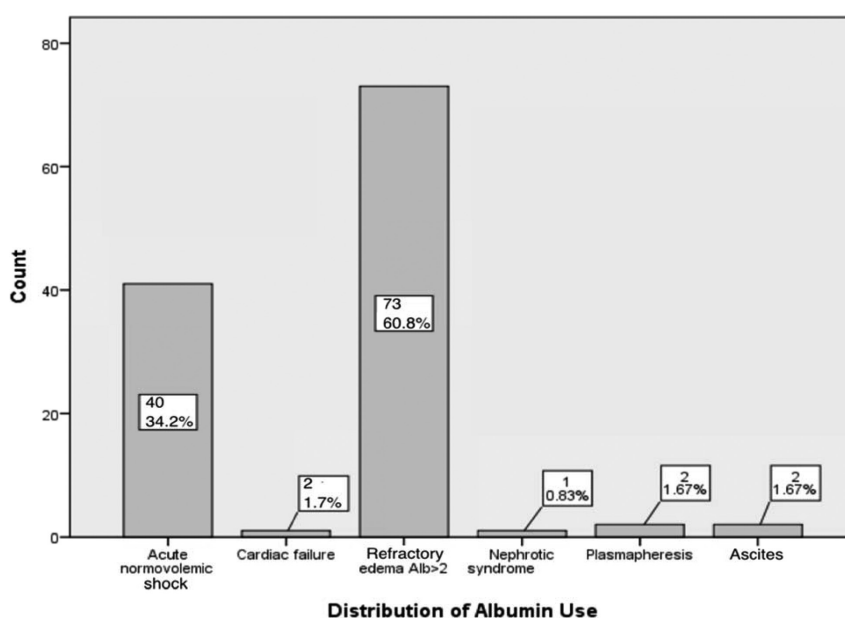


Figure 1. Graphical representation of appropriate and inappropriate prescription of albumin.

crystalloid solutions is one of the major pitfalls in albumin prescription.

Our study also showed that in most cases, no correct estimate of patients' albumin level was available before initiation of albumin injections. A threshold value of 2.0 g/dL for definition of hypoalbuminemia is a well-accepted cutoff (14), although few studies suggest a more rigid cutoff (15). Considering either cutoff as the starting point for prescription of albumin, we showed that in more than 60% of our patients, no albumin measurement was ordered.

Most of the authorities including Belgian consensus conference on albumin use suggest that when hypovolemia or shock is suspected, human albumin should only be used after an abundant amount of synthetic colloids is infused (12-16).

In conclusion, our study could be summarized in two major findings. Inappropriate human albumin use, despite its high cost, is fairly common. The misuse is more prominent when including patients of the study suffers from cardiovascular compromises. Secondly, we showed that although albumin prescription might fall into appropriate use when a laboratory diagnosis hypoalbuminemia is established, but most of the prescriptions were ordered before any confirmatory tests that show serum albumin levels were conducted. These data, together with previous national studies highly suggest a mandatory need for educational measures for practicing physicians along with strict regulations for prescription strategies regarding expensive drugs such as albumin. Thus far it is well established that educational

interventions may help improvement in adherence of physicians for albumin prescription (15).

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