Human Albumin Utilization in Patients Admitted to a University-affiliated Hospital in Iran

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A B S T R A C T

Background: As an essential human protein and an expensive biological drug, albumin is, in several cases, prescribed without an appropriate indication. This study determined the compatibility of albumin administration with the current standard protocols in a university-affiliated hospital in Iran.

Methods: A total of 151 patients admitted to a university-affiliated hospital in Iran from June 22, 2016, to 2017 participated in the present cross-sectional study. The demographic information of the patients (age, gender, and ward), the reason for albumin prescription, and details of its use were recorded (the total amount prescribed, the duration of albumin therapy, dosage, or frequency). The compliance of the albumin administration with the current guidelines (appropriate vs. inappropriate) was checked and confirmed by a senior clinical pharmacist.

Results: Sixty-six (43.7%) patients were female and 85 (56.3%) were male. The Mean±SD age of the patients was 53.98±25.34 years. Among the patients receiving albumin, patients with infectious diseases, burn injuries, and operations were the most frequent cases. Generally, 171 vials were administered inappropriately during the study. Also, the inappropriate administration of albumin was most common among infectious disease specialists, followed by internists and general surgeons, resulting in $35878.5 wastage (each vial is around $33.5 in Iran).

Conclusion: The logical administration of albumin should be based on the appropriate guidelines and clinical needs of the patients. In a majority of the cases, albumin was prescribed inappropriately and at an alarming rate. These results indicate the need for educational programs and appropriate policies for physicians prescribing albumin.

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1. Introduction

Studies on Drug Utilization Evaluation (DUE) are cost optimization initiatives for expensive drugs that may have alternative options [1]. DUE intends to describe, review, and improve the quality of drug use [2-6]. The world health organization defines rational drug use as follows: "Patients will receive the appropriate drug with their clinical needs, with doses in a suitable period, and with the lowest cost applied to them and society" [7]. As an essential human protein that has many physiological roles and an expensive biological drug, albumin is, in several cases, prescribed without an appropriate indication.

Nevertheless, several specific standards have been developed for albumin administration in clinical practice [1, 8, 9]. Guidelines do not recommend albumin as the first-line treatment for nutritional intervention, hypoalbuminemia, pancreatitis, volume replacement/expansion, and renal failure [10, 11]. On the other hand, it has been reasonably discussed as the best choice prescribed product in critically ill patients and subjects in need of intensive care [12]. Several alternatives for albumin are economical and less risky compared with albumin.

The indications for the administration of these alternatives should be clearly defined; so, the best results could be achieved at the patient's bedside. However, albumin production imposes high costs on the healthcare system and is accompanied by limitations. The high risk of contamination during injection and increased mortality are other disadvantages of albumin administration, which mandate its cautious use in clinical settings [13]. This study aimed at investigating the compatibility of albumin administration with the standard protocols for the logistic use of albumin in a university-affiliated hospital in Iran.

2. Methods

This descriptive study was conducted on 151 hospitalized patients in a university-affiliated hospital in Iran for 12 months from June 22, 2016, to 2017. The data were collected in a designed checklist (Indication checklist) with two separate sections. The first section comprised of patients' demographic characteristics (age, gender, ward of admission, etc.), the prescribing physicians' specialty, and the reason for the prescription of albumin (20% (50 CC) injectable vial). In the second section, the details of albumin use were recorded (the total amount prescribed, the duration of albumin therapy, dosage, and frequency). Reasons for the prescription of albumin

were recorded, using the information in patients' files and consulting with the physicians, who delivered treatment to the patients. Serum albumin levels, serum creatinine, calculated creatinine clearance, alanine transaminase and aspartate aminotransferase, total and direct bilirubin, sodium, potassium, magnesium, calcium, and urinalysis were also examined.

Accordingly, decisions on the appropriateness of albumin administration were made and confirmed by a senior clinical pharmacist. The indications were evaluated as appropriate or inappropriate according to the guidelines [6, 7]. The following items were regarded as inappropriate in our study: 1. Albumin above 2.5 g/dL (unless indicated); 2. Hypoalbuminemia in the absence of edema or acute hypotension; 3. Malnutrition; 4. The improvement of wound healing; 5. Non-hemorrhagic shock; 6. Diuretic-treatable ascites; 7. Burn-injury in the first 24 hours; 8. Protein-losing enteropathy; 9. Acute or chronic pancreatitis; 10. Hemodialysis; 11. Brain ischemia; 12. Normovolemic hemodilution in operation; and 13. Ovarian irritability syndrome [14-16]. The extra cost imposed by inappropriate indications for albumin were also calculated, using the following formula: cost of an albumin vial × the number of vials used without a proper indication. The data were analyzed with SPSS V. 16. Descriptive data were expressed as frequency and Mean±SD.

3. Results

A total of 151 patients were included in this study; 66 (43.7%) patients were female and 85 (56.3%) were male. The Mean±SD of the patients was 53.98±25.34 years ranging from 10 months to 95 years. Patients with infectious diseases, burn injuries, and operations were the most frequent subjects receiving albumin (Table 1).

The highest number of patients receiving albumin was in the infectious diseases' Intensive Care Unit (ICU) (n = 26). Also, the highest number of albumin administration was in the burn injury ward (100%), followed by internal medicine ward (90%), surgical ICU (86%), and emergency ICU (86%). According to Table 2, the most common indication for albumin administration was burn injuries. However, the most common indication, which led to the inappropriate administration of albumin, was hypoalbuminemia.

Table 3 presents the individualized consumption of albumin for different wards. According to Table 3, 1071 vials had an inappropriate indication for administration. Considering the cost of each vial of albumin in Iran ($33.5), $35878.5 was spent on albumins that were administered

20

Gharekhani A., Albumin Utilization in Hospitalized Patients in Iran. JPPM. 2018; 4(1-2):19-24.

Table 1. Frequency of diseases treated with albumin

Illness	No. (%)
Infectious diseases	38 (25.2)
Burn	32 (21.2)
Abdominal operation	16 (10.6)
Liver disease	14 (9.3)
Cancer	14 (9.3)
Kidney diseases	10 (6.6)
Lung diseases	10 (6.6)
Gastrointestinal bleeding	5 (4)
Poisoning	5 (3.3)
Other reasons	6 (3.3)

out of indication. The highest number of inappropriate administrations was in the surgical ICU (n=18) and infectious diseases ICU (n=14). The inappropriate administration of albumin vials was the highest in the infectious diseases' ICU (413 vials), followed by internal medicine ICU (246 vials) and surgical ICU (171 vials).

4. Discussion

The irrational consumption of medications is one of the critical issues in the health care system. The logical use of medication should be based on the appropriate guidelines and clinical needs of patients [17]. Human albumin is a medication commonly used in critically ill patients. However, its out-of-indication use is a major health problem imposing medical complications on the patients and the financial burden on the health

Table 2. Frequency of albumin administration and its compliance with standard guidelines

Indication	Total Administration	%	Inappropriate Administration	%
Edema	29	19.2	9	31
Ascites	8	5.2	2	25
Nutritional support	6	3.9	6	100
Burn	33	21.8	11	33.3
Spontaneous bacterial peritonitis	6	3.9	0	0
Operation	25	16.5	4	16
Plasmaphresis	2	1.3	0	0
Nephrotic syndrome	5	3.3	3	60
Hepatic failure	3	1.9	3	100
Hepatorenal syndrome	2	1.3	0	0
Hypo-albuminemia (2.5<Alb<3)	13	8.6	13	100
Albumin ≤2.5	18	11.9	0	0
Other indications	1	0.66	0	0

Gharekhani A., Albumin Utilization in Hospitalized Patients in Iran. JPPM. 2018; 4(1-2):19-24.

21

Table 3. Frequency of hospitalized patients in each ward

Ward	No. (%)			Total Vials	Inappropriate Vials (%)	Total Cost ($)	The Extra Cost Imposed ($)
	Patients	Appropriate Administratio	Inappropriate Administration				
Infection disease ICU*	26 (17.2)	14 (53)	12 (47)	692	413 (59.6)	23182	13835.5
Internal medicine ICU	21 (13.9)	12 (57)	9 (43)	430	246 (57.2)	14405	8241
Surgical ICU	21 (13.9)	18 (32)	39 (68)	538	171 (31.7)	18023	5728.5
Burn ICU	19 (12.5)	12 (63)	7 (37)	109	24 (22)	3651.5	804
Poisoning ICU	5 (3.3)	3 (60)	2 (40)	66	37 (56)	2211	1239.5
Emergency ICU	7 (4.6)	6 (86)	1 (14)	116	1 (0.8)	3886	33.5
Women's burn	5 (3.3)	4 (80)	1 (20)	40	15 (37.5)	1340	502.5
Men's Burn	2 (1.3)	2 (100)	0	8	0	268	0
Children's burn	6 (3.9)	3 (50)	3 (50)	26	17 (65.3)	871	569.5
Women's Internal	8 (5.2)	4 (50)	4 (50)	115	15 (13)	3852.5	502.5
Men's Internal	11 (7.2)	7 (64)	4 (36)	67	37 (55.2)	2244.5	1239.5
general Internal	10 (6.6)	9 (90)	1 (10)	141	16 (11.3)	4723.5	536
Infectious disease	4 (2.6)	1 (25)	3 (75)	73	49 (67.1)	2445.5	1641.5
Men's operation	4 (2.6)	3 (75)	1 (25)	64	11 (17.1)	2144	368.5
Urology	1 (0.66)	0	1 (100)	19	19 (100)	636.5	636.5
Dermatology	1 (0.66)	1 (100)	0	18	0	603	0
Total	151	99	52	1451	1071	84487	35878.5

*ICU: Intensive Care Unit

care system [12]. In spite of standard guidelines for the clinical administration of albumin, physicians do not observe appropriate indications [18, 19].

In this study, the highest prevalence of albumin administration was in patients admitted to the infectious diseases ward, followed by internal medicine, operation, and burn injury wards, which accounted for 25% of all prescriptions. Internists and infectious disease specialists were the most frequent users of albumin. We also found that most inappropriate prescriptions were made by infectious disease specialists, where 50% of the prescriptions by these specialists could be considered inappropriate. Similarly, in a study conducted in Northeastern Iran, burn, ICU, internal, and surgical wards were the most frequent users of albumin among hospital wards [19]. However, in another study in Fars province, Iran, the use of albumin was the highest in the internal medicine ward, followed by emergency medicine, pediatric diseases, and ICU wards [20].

The high administration of albumin in the surgical ward mandates an appropriate educational strategy about albumin use guidelines for surgeons. Burn, edema, and operation were the most common indications for albumin administration in Sina Hospital. In a study conducted in 2014, Fuerte et al. showed that the most common indication for albumin administration was non-hemorrhagic septic shock, followed by operation, suggesting high consumption of albumin in infected patients, especially patients with septic shock [21].

In a study by Ala et al. [22], 63% of albumin administration was according to the standard guidelines, which was significantly more than the rate of appropriate administration in our study; it could be because of the lack of proper observance of the standard protocols for prescribing albumin. On the other hand, the results could be influenced by the difference in sample size and the sampling method between the two studies. In a study performed in 2012, Talasaz et al. [23] also reported that

63.8% of the cases of albumin administration were in accordance with the current guidelines, which is more than that of reported in our study. In the Talasaz et al.'s study, albumin was most commonly used for patients undergoing heart operation; whereas, in our study, the majority of albumin injections were for patients with infectious diseases. However, the findings of other studies were in line with our results. Albumin was prescribed inappropriately in more than 50% of cases, wherein some studies, it was as high as 70% [19, 24].

Most patients, who received albumin in ICU, were in critical condition and needed special treatment. Caironi et al. investigated the effect of the administration of albumin on critically ill patients. They showed that damage to patients is unlikely after the administration of albumin. However, it is not necessary to prescribe it in all terminally or critically ill patients. Thus, it should be used for certain groups of patients, where there is evidence of positive albumin impact [25].

In the present study, all albumin prescriptions for nutritional support, hypoalbuminemia, and hepatic impairment lacked proper indication. On the other hand, prescriptions for spontaneous bacterial peritonitis, hepatorenal syndrome, albumin less than 2.5 g/dL, and plasmapheresis were consistent with the current standard guidelines. In another study performed by Kazemi et al. [24], 61% of all albumin injections were for patients with edema with albumin less than 2 g/dL. However, in 57.5% of these patients, serum albumin levels were not measured. This study reported the highest frequency of albumin administration in the surgical wards, where the frequency neared as much as 25% of total prescriptions. Yet, 16% of these prescriptions were inappropriate.

In a similar study that was carried out in Imam Reza Hospital of Tabriz by Shafiee et al. [26], about 76% of albumin injections lacked appropriate indications, imposing an extra cost of $274,607 on patients and health care system. In comparison to this study, the inappropriate use of albumin during hospitalization was significantly lower than that of Shafie et al.'s study; it could be primarily because of the controlled administration and delivery of albumin by the hospital and structural differences between Imam Reza and Sina Hospitals (the number of bedridden wards and ICUs). As the highest amount of albumin administration in both studies was for patients admitted to the ICUs, the resulting difference is justifiable.

In the present study, several cases of inappropriate albumin administration for patients with aluminum phosphide poisoning (rice pill), fat embolism, and enteropathy due to inflammatory bowel disease were excluded. However, this study had several drawbacks. We could not perform a before-after study to assess the effects of the implementation of guidelines on the use and administration of albumin in our region. Conducting such a study would reasonably yield more definitive results about the impacts of DUE studies on the albumin consumption in this region.

5. Conclusions

The present study showed high consumption of albumin in Sina Hospital of Tabriz, where around half of the prescriptions in this hospital could be considered inappropriate. Also, the most common ward, in which albumin was prescribed inappropriately, was the infectious diseases ward. This imposed a high extra cost on both patients and the health care system. The implementation of the current standard protocols will prevent similar inappropriate prescriptions and reduce the irrational drug consumption costs and its possible side effects.

Ethical Considerations

Compliance with ethical guidelines

This study was approved by the Ethics Committee of A university-affiliated hospital in Iran (under TBZMED.REC.1394.1021 code), and the anonymity of the patients and clinical data was guaranteed. All the procedures were in accordance with the ethical standards of the responsible committee on human experimentation (institutional or regional) and with the Helsinki Declaration of 1975 as revised in 2013 (available at http://jamanetwork.com/journals/jama/fullarticle/1760318).

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Authors contributions

Conceptualization: Afshin Gharekhani; Methodology: Afshin Gharekhani, Hamid Noshad, Soheil Teimouri; Investigation: Afshin Gharekhani, Sepideh Rahigh-Aghsan, Abasad Gharedaghi; Witing – original draft: Sepideh Rahigh-Aghsan; Writing – review & editing: Sepideh Rahigh-Aghsan, Afshin Gharekhani, Hamid Noshad, Soheil Teimouri.

Gharekhani A., Albumin Utilization in Hospitalized Patients in Iran. JPPM. 2018; 4(1-2):19-24.

23

Conflict of interest

The authors declared no conflict of interest.

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24

Gharekhani A., Albumin Utilization in Hospitalized Patients in Iran. JPPM. 2018; 4(1-2):19-24.