Evaluation of the Appropriateness of Albumin Usage in a Teaching Hospital in Iran: The Impact of Clinical Pharmacist Intervention

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Keywords: Guideline, Albumin, Pharmacist, Drug Utilization Evaluation, Irrational Drug Use, Clinical Pharmacy

Abstract

Background: Albumin is a colloidal protein medication in which has a limited availability in market and it has a high cost. Albumin must be used in such approved indications as, large volume paracentesis, plasmapheresis, spontaneous bacterial peritonitis and hepato-renal syndrome.

Objectives: The aim of this study was to evaluate the appropriateness of albumin utilization in a teaching hospital in Iran before and after guideline implementation.

Methods: In this prospective study, a total of 100 patients were enrolled into the study in Loghman Hakim Teaching Hospital. The medical records of patients were reviewed and some information such as demographic parameters, albumin indication, albumin therapy duration, appropriateness of indication were recorded again. Then in post-intervention phase, albumin was administered after clinical pharmacist teaching and guideline implementation. After post-intervention period, demographic parameters, albumin indication, albumin therapy duration, appropriateness of indication were recorded again.

Results: In phase 1, albumin was mostly prescribed in inappropriate indications and internist physicians were the most physicians who ordered albumin and wound healing also was the most frequent indication for albumin therapy. This improvement also was significant (P < 0.05). Data showed that albumin indication in post-intervention was different from that in the pre-intervention phase. After clinical pharmacist intervention most of indications were appropriately.

Conclusions: This study demonstrated that in this hospital, albumin was prescribed inappropriately in most cases based on hospital guideline. This rate improved after clinical pharmacist intervention and resulted in significant reduction in albumin irrational utilization. It is advisable that albumin prescription must be monitored carefully by clinical pharmacists.

Keywords: Guideline, Albumin, Pharmacist, Drug Utilization Evaluation, Irrational Drug Use, Clinical Pharmacy

1. Background

Irrational medication use, as a global challenge to healthcare systems worldwide, especially hospitals, is reviewed by Drug Utilization Evaluation programs. Appropriate medication use is an issue of considerable concern owing to limited medical and financial resources, particularly in developing countries. The World Health Organization has suggested clinical practice guidelines as a regulatory strategy to improve the drug utilization pattern (1). Implementation of clinical practice guidelines will enhance medication consumption through minimizing inappropriate medication prescription, decreasing costs, and managing medication supplies (2, 3). Human albumin, one of the circulating blood proteins determining oncotic pressure and regulating body fluid distribution, which also carry substances such as hormones, bilirubin, and drugs, is limited in resources and high in costs (4). Human albumin use has been widely accepted indications such as therapeutic paracentesis, plasmapheresis, spontaneous bacterial peritonitis, and hepato-renal syndrome, as well as several more indications justified only if specific criteria are met (5). Regarding the broad spectrum of accepted human albumin indications, irrational utilization of albumin in some clinical settings is prevalent. The previous research found that nutrition support and hypoalbuminemia were the most common inappropriate uses of al-
bumin in our country (6). Previous studies in Iran showed that the percentage of inappropriate use of albumin is relatively high (7). Irrational albumin use in Iran is reported as high as 70% or more in previous studies (8, 9), and it is also reported that inappropriate albumin prescription could amount for 88.6% additional costs (10). It could be expected adherence to standard guidelines minimize the inappropriate use of albumin.

2. Objectives

Considering the high cost and limited resources of human albumin, our study aimed to assess the impact of the guideline implementation and clinical pharmacist’s intervention on the medication prescription and consumption pattern in the Loghman-Hakim Teaching Hospital in Iran.

3. Methods

3.1. Study design

This interventional study was conducted in the Loghman-Hakim Hospital from May 2017 to January 2018. Loghman-Hakim Hospital is a general tertiary educational hospital with 420 beds, 24 wards, 33 clinic units, and 14 paraclinical units affiliated with Shahid Beheshti University of Medical Sciences, Tehran, Iran, which was constructed in 1971. The study was approved by the Hospital Medical Ethics Committee and Institutional Review Board (IR.SBMU.PHARMACY.REC.1397.013), and written informed consent was obtained from the patients or their family members. One hundred patients who were candidate to receive albumin were included in the period of study. Inclusion criteria were as follows: patients hospitalized in internal, emergency, intensive care unit (ICU), neurosurgery and general surgery wards, who were candidates to receive albumin. In the pre-intervention phase, in a 5-month period, information about albumin prescription was gathered and then in the post-intervention phase, in a 8-month period, prescription was limited only after consultation of a clinical pharmacist and consisted of hospital clinical pharmacists based on the guidelines, thereafter. The medical team is included in, deputy of education, head of hospital wards and intensive care, clinical pharmacy, nephrology, gastroenterology, internal medicine, neurology, neurosurgery and surgery specialties. Supplementary file appendix 1 provides the Loghman-Hakim albumin indication guidelines.

3.3. Guidelines Implementation

In the pre-intervention phase of the study, all wards were allowed to prescribe and receive albumin according to the physician’s order with no limitation and consultation, to explore prescriptions pattern and data gathered on inappropriate medication use.

Thereafter, in the post-intervention phase, after coordination with hospital departments, after albumin request by the physician order, the request was examined based on the guidelines by a clinical pharmacist according to clinical and paraclinical findings. Clinical pharmacist was authorized to consult on approval or disapproval of the request. The physicians did receive educational courses on appropriate use of albumin in pre- or post-intervention phases by their request in a non-mandatory way. After the clinical pharmacist’s visit, a list of approved or disapproved patients, who were requested to use albumin for, was given to both the ward and hospital pharmacy. Figure 1 illustrates the flow chart of the clinical pharmacy unit guidelines.

3.4. Data Collection

Data collection was performed by a pharmacist under supervision of a clinical pharmacist and consisted of a checklist with the following items: (1) patient’s information (including demographics such as age, sex, height and weight, admitted ward, admission time); (2) patient’s nutritional status (including Nutritional Risk Screening (NRS) score, type of nutrition, times and amount of food; (3) albumin indication; (4) albumin order; (5) administration date and therapy duration; (6) clinical and paraclinical data (including albumin serum level and total protein, liver function test, complete blood counts, renal function tests, electrolytes and biochemistry, blood pressure and body temperature; (7) patient’s medication history; and (8) final decision.
3.5. Statistical Analysis

Statistical analyses were conducted as descriptive and analytical. Categorical variables were expressed as percentage. Chi-square or Fisher exact (if 20% of the variables have frequency of less than 5) were performed to analyze the correlation between these variables. Kolmogorov-Smirnov test was performed to examine the normal distribution of continuous data. Normally and non-normally distributed continuous variables were expressed as mean ± standard deviation (SD) and median (interquartile range), respectively. A comparison between parametric and non-parametric continuous variables was performed by independent t-test and Mann-Whitney, respectively. P value less than 0.05 was considered statistically significant in all analyses. All the above analyses were conducted by the Statistical Package for the Social Sciences (SPSS) version 21 soft-
ware (IBM Company, New York, NY, United States).

4. Results and Discussion

In pre-intervention and post-intervention phases, 72 and 28 patients were recruited to gather albumin prescription data, respectively. In addition, 81% and 19% of the patients were recruited from intensive care units (Neurosurgery ICU, General ICU and Emergency ICU) and internal ward, respectively. There were no significant differences regarding number of patients in different wards in pre- and post-intervention phases (P = 0.508). Albumin were prescribed mostly by internists in pre-intervention (33.34%) and post-intervention (46.42%) phase of the study. The mean ± SD age of the patients in pre- and post-intervention phases were 57 ± 18.12 and 56.03 ± 17.81 years, respectively with no statistically differences between two groups (P = 0.800). Furthermore, no differences were observed in sex distribution between the two groups (P = 0.487).

In the pre-intervention phase, the 3 most frequent indications were as follows: Wound healing (18.05%), Intracerebral hemorrhage (12.5%), and Edema (9.72%) and the post-intervention phase: Major surgery (42.21%), Edema (14.28%), Subarachnoid hemorrhage (14.28%). Figure 2 presents all albumin indications in two phases. Data showed that albumin indication in post-intervention was significantly different from that in the pre-intervention phase (P = 0.043). Only 13 out of 72 indications were correctly identified based on the hospital guidelines in the pre-intervention phase. However, 18 out of 28 indications in the post-intervention phase were correct. The number of correct indications was statistically different between the two groups (P < 0.001).

Regarding type of nutrition (Enteral nutrition, Nil Per Os or Per Os), frequency of physician specialty prescribing the medication, type of received intravenous fluid, receiving vasopressors and receiving inotropes, we did not identify statistically significant differences in pre- and post-intervention phases (P = 0.228, P = 0.531, P = 0.052, P = 0.985, and P = 0.256, respectively). Twenty nine percent of the patients received furosemide to treat edema in the pre-intervention phase, and 35% of the patients received this agent in the post-intervention phase. Comparing the number of patients and the dose of furosemide between the two groups, we did not identify a statistically significant difference (P = 0.452, P = 0.357, respectively). The mean furosemide dose in pre-intervention phase was 40.66 ± 49.26 and in post-intervention phase was 37.30 ± 16.04 mg per day. The patients in the post-intervention phase received albumin with a period of 5.5 ± 5.26 days, which compared to the pre-intervention phase, a period of 8.15 ± 7.72 days was shorter (P = 0.049). About one-third (32.62%) of total used vials were with correct indication in the post-intervention phase. On the contrary, in the pre-intervention phase, 6.28% were of total used albumin vials with correct indication. In the pre-intervention phase, 444 albumin vials and in post-intervention phase 249 albumin vials were consumed.

In comparison of albumin serum level before albumin transfusion, in pre-intervention phase higher levels were detected versus post-transplant phase (P = 0.028). Post transfusion albumin levels did not differ statistically significant in pre- and post-intervention phases (P = 0.058). Tables 1 and 2 show the important laboratory data of pre-and post-intervention phases and their distribution between two the groups. Apart from serum potassium (P = 0.022), total protein (P = 0.008), and initial albumin level (P = 0.028), other laboratory parameters were comparable between pre- and post-intervention periods.

Drug utilization program and guidelines implementation are proven tools to obtain standards in medication use in hospitals. Interventional strategies employed by the World Health Organization in promoting rational drug use as well as medication management in hospitals, including educating and administrative actions, provide better access to limited source medications and offer clinical and economic benefits to healthcare systems (11). In this study, in a teaching hospital over 9 months, we investigated clinical pharmacist’s intervention in albumin rational use as high-cost medication with limited resources. In the post-intervention phase, after clinical pharmacist intervention, we observed that albumin consumption and less misuses based on incorrect indications reduced.

In the past decades, in different healthcare systems, inappropriate albumin prescriptions was reported, which
Table 1. Pre- and Post-Intervention Phases Laboratory Data and Their Distribution Between Two Groups*  

| Laboratory Parameter | Pre-Intervention | Post-Intervention | P Value |
|----------------------|------------------|-------------------|---------|
| White blood cells ($\times 10^3$ cells/mm$^3$) | 12.60 ± 8.26 | 13.75 ± 7.67 | 0.388 |
| Hemoglobin (g/dL) | 22.18 ± 6.39 | 10.30 ± 2.03 | 0.833 |
| Blood urea nitrogen (mg/dL) | 31.98 ± 23.86 | 37.29 ± 27.83 | 0.397 |
| Serum creatinine (mg/dL) | 1.29 ± 0.99 | 1.41 ± 0.92 | 0.564 |
| Blood sugar (mg/dL) | 129.91 ± 45.07 | 138.51 ± 60.65 | 0.602 |
| Sodium (mEq/L) | 139.16 ± 5.68 | 137.82 ± 5.20 | 0.022 |
| Potassium (mEq/L) | 3.88 ± 0.62 | 4.20 ± 0.50 | 0.646 |
| Calcium (mg/dL) | 8.03 ± 1.14 | 8.35 ± 1.07 | 4.38 ± 16.95 |
| Alanine aminotransferase (Units/L) | 59.38 ± 91.38 | 43.50 ± 36.95 | 0.362 |
| Aspartate aminotransferase (Units/L) | 6.11 ± 84.59 | 6.33 ± 22.55 | 0.722 |
| International normalized ratio | 1.52 ± 0.64 | 1.47 ± 0.51 | 0.986 |
| Partial thromboplastin time (sec) | 34.37 ± 8.50 | 36.31 ± 10.35 | 0.340 |

*Values are expressed as mean ± SD.

Table 2. Total Protein and Albumin Serum Concentration in Pre- and Post-Intervention Phases*  

| Laboratory Parameter | Pre-Intervention | Post-Intervention | P Value |
|----------------------|------------------|-------------------|---------|
| Total protein concentration | 5.35 ± 0.84 | 4.82 ± 0.88 | 0.008 |
| Initial albumin level | 2.94 ± 0.63 | 2.62 ± 0.45 | 0.028 |
| End of the study albumin level | 3.48 ± 1.06 | 3.67 ± 0.58 | 0.058 |

*Values are expressed as mean ± SD.

was responsible for albumin irrational utilization at least in 50% of prescriptions in different countries (12-14). Owing to high cost and limited resources, albumin overuse could be a challenge to healthcare systems (12). It is indicated by the Iranian Food and Drug Organization in a 9-month period in 2008, 472,089 vials of albumin 20% were consumed, which amounted to approximately 21 million USD (15). Albumin usage also causes some serious concerns due to adverse effects. Severe anaphylactic reactions, coagulation abnormalities and electrolyte disturbances were reported with its usage. Some of these adverse reactions are caused by large replacement of volumes and need patients monitoring, and some of them occur rapidly and need immediate discontinuation. Furthermore, albumin should be used with caution in conditions which hypervolemia and hemodilution may increase the risk of adverse effects such as heart failure, hypertension, and pulmonary edema (16, 17). Most of the albumin vials in our study were prescribed by internists. It was noted in previous studies that, albumin prescription not based on guidelines could lead to false prescription (14). It was also stated before that we could decrease patients and health system costs by limiting albumin prescription (18-20). Clinical pharmacist interventions and guidelines implementation in our study lead to 46.23% reduction in albumin use, and it was close to previous data (19). In line with our data, albumin guidelines implementation in an ICU in a teaching hospital in the Unites States resulted in statistically significant reduction of albumin use (54%) and lower costs (56%) (21). In a study by Miguel et al., to determine the impact of education on albumin irrational use, after providing a set of guidelines on albumin indications, physicians could prescribe albumin only based on the guidelines and they received education about albumin rational use, which was provided by a clinical pharmacist. The study showed a 37.2% reduction in wrong prescription and 30% reduction in cost after education (22). In our study, we observed a reduction in wrong prescription after providing the albumin use guidelines, but we could not determine the financial impact.

In our study, in the pre-intervention phase, we observed that the three most frequent indications for albumin prescription were as follows: (1) wound healing, (2) ICH, (3) edema, and only 18.05% of prescriptions were correct based on the guidelines. Roberts et al. compared albumin to treat hypovolemia with low-cost fluid such as crystalloids in critically ill hospitalized patients with hypoalbuminemia. This study showed no evidence of reduced morbidity and mor-
Study, similar to our study, it was showed that, after pro-

2017, albumin pattern use in hospital was assessed. In this

satisfaction, guidelines provision and instruction to use) in

and reduced wrong prescriptions. In a 3-phase study (ob-

albumin use in our hospital changed prescription pattern

served in our study, guidelines implementation in human

is less than 3 g/dL (27-30). We also considered 17 more other

bumin would be used in these patients if serum albumin

cm H, if delayed vasospasm occurred. We indicated that al-

The goal of central venous pressure is 6 - 8 cm H and 8 - 12

min level is less than 3 g/dL and the aneurism is secured.

this regimen the albumin is indicated if the serum albu-

Hypertension and hemodilution may be considered. In

therapy which is involved the induction of Hypervolemia,

therapy, and it was previously shown that albumin would

be beneficial in these patients. In patients with symp-

tic paracentesis in patients with ascites; (2) plasmaphere-

sis as a replacement of plasma; (3) spontaneous bacterial

peritonitis in patients with cirrhosis; (4) diagnosis of sus-

pected hepato-renal syndrome; (5) treatment of confirmed

hepato-renal syndrome. In these five indications, albumin

showed its efficacy. However, in some indications such as

nutritional interventions in patients with serum albumin

above 2.5 g/dL for wound healing or in burnt patients in

the first 24 hours, albumin is not indicated and should not

be used. In the guidelines, we provided indications, which

albumin may be beneficial. For example, in patients with

subarachnoid hemorrhage, albumin is part of triple H

therapy, and it was previously shown that albumin would

be beneficial in these patients. In patients with symp-

omatic vasospasm, after securing aneurism the triple H

therapy which is involved the induction of Hypervolemia,

Hypertension and hemodilution may be considered. In

this regimen the albumin is indicated if the serum albu-

min level is less than 3 g/dL and the aneurism is secured.

The goal of central venous pressure is 6 - 8 cm H and 8 - 12

cm H, if delayed vasospasm occurred. We indicated that al-

bumin would be used in these patients if serum albumin

is less than 3 g/dL (27-30). We also considered 17 more other

indications, which albumin may be beneficial. As we ob-

served in our study, guidelines implementation in human

albumin use in our hospital changed prescription pattern

and reduced wrong prescriptions. In a 3-phase study (ob-

servation, guidelines provision and instruction to use) in

2017, albumin pattern use in hospital was assessed. In this

study, similar to our study, it was showed that, after pro-

viding the albumin indication guidelines, consumption

pattern changed and wrong prescription decreased (31).

Our data may not be generalizable to all hospitals in Iran,

and we need to investigate similar studies in different cen-
ters to provide general DUE program for albumin use in

Iran; however, this may lead to increase albumin rational

treatment and decrease costs of the healthcare system, which ir-

rational drug utilization imposes additional costs on the

healthcare system.

There were some limitations in our study: (1) small

sample size; (2) single centered study design; (3) in hol-

idays and night shifts due to absence of a clinical phar-

macist, some patients received albumin without consulta-
tion; (4) not including financial benefit of albumin utiliza-
tion program; and (5) in the study duration, to obey the

guideline was not mandatory and in some cases the med-
ication could be delivered to wards without clinical phar-

macist approval.

5.1. Conclusions

In conclusion, our study demonstrated that in

Loghman-Hakim Hospital, albumin utilization was irra-

tional and was not based on correct indications; theref-

ore, we reduced irrational prescriptions by providing and

using guidelines as well as correcting the prescriptions

under supervision of a clinical pharmacist. The use of

proper albumin indication guidelines in the medical

center based on documented and scientific indication will

improve drug utilization program along with cost saving.

Supplementary Material

Supplementary material(s) is available here [To read

supplementary materials, please refer to the journal web-

site and open PDF/HTML].

Footnotes

Authors’ Contribution: Interpretation of data: Maede

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drafting of the manuscript: Omid Moradi, Ali Saffaei, and

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Salamzadeh, Omidvar Rezaeimirghaed, and Zahra Sahraei;

study supervision: Zahra Sahraei and Jamshid Salamzadeh.

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References

1. Holloway K, Green T. Drug and therapeutics committees: a practical guide. 2003; 146 p.
2. Rosenberg W, Donald A. Evidence based medicine: an approach to clinical problem-solving. BMJ. 1995;310(6987):122-6. doi: 10.1136/bmj.310.6987.1222. [PubMed: 7742682]. [PubMed Central: PMC2549505].
3. Schifalaci MM, Shepard A, Kelley W. Evidence-based practice: cost-benefit of large system implementation. Qual Manag Health Care. 2012;21(5):74-80. doi: 10.1097/QMH.0b013e2824249df4. [PubMed: 22453818].
4. Moman RN, Varacallo M. Physiology. Albumin. 2019; 3:817-22. doi: 10.1186/s13054-014-0702-y. [PubMed: 24564759]. [PubMed Central: PMC4620749].
5. Treasure Island (FL): Stat Pears Publishing LLC; 2019.
6. Fairbairn GM, Bennardello F, Lattanzio A, Piccoli P, Rossetta G, Italian Society of Transfusion M, et al. Recommendations for the use of albumin and immunoglobulins. Blood Transfus. 2009;7(3):216-34. doi: 10.2450/2009.0994-09. [PubMed: 19657486]. [PubMed Central: PMC2792742].
7. Talasaz AH, Jahangard-Rafsanjani Z, Ziaie S, Fahimi F. Evaluation of the pattern of human albumin utilization at a university affiliated hospital. Arch Iran Med. 2012;15(2):85-7. doi: 10.22222/aom.22229577.
8. Rezapour A, Java-Noughabi J, Salehiniya H, Gholami K, Hadavand N. Albumin Usage in Iran. Arch Iran Med. 2009;22(13):1273-8. [PubMed: 19458115].
9. Kazemi Y, Hadavand N, Hayatshahi A, Torkamandi H, Gholami K, Hadjibabaei M, et al. Albumin Utilization in a Teaching Hospital in Tehran: Time to Revise the Prescribing Strategies. J Pharm Care. 2013;1(4):127-32.
10. Farsad B, Hadavand N, Masumi S. Albumin utilization review to evaluate The efficacy and cost, Perform as a Qualitative study in Special Wards in Shaheed Rajaei Cardiovascular, Medical & Research Center. Biosciences, Biotechnology Research Asia. 2008;3(3):1469-77. doi: 10.1005/bbra/2290.

Noort M et al. 6. 2012;31(3):209-90. doi: 10.1016/j.manm.2011.02.002. [PubMed: 22210555].
8. Mahmoudi L, Karamikhhah R, Mahdavinia A, Samiei H, Petramfar P, Niknam R. Implementation of Pharmaceutical Practice Guidelines by a Project Model Based: Clinical and Economic Impact. Medicine (Baltimore). 2015;94(42). e744. doi: 10.1097/MD.0000000000000744. [PubMed: 26496288]. [PubMed Central: PMC4620749].
9. Vazin A, Karimzadeh I, Karamikhhah R, Oveis Z, Mohseni S, Keykheie M, et al. Clinical and economical impacts of guideline implementation by the pharmaceutical care unit for high cost medications in a referral teaching hospital. BMC Health Serv Res. 2018;18(1):385. doi: 10.1186/s12913-018-2837-3. [PubMed: 30355280]. [PubMed Central: PMC5205144].
10. Zolfagharian F, Ghazanfari S, Elyasi S, Iranshi P, Saberi MR, Vahdati-Mashhadian N, et al. Drug utilization evaluation of albumin in a teaching hospital of Mashhad, Iran: an interventional pre-post design study. Int J Clin Pharm. 2017;39(4):704-11. doi: 10.1007/s11996-017-0458-y. [PubMed: 28540466].

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