Advances in Pharmacology and Therapeutics Journal
Shahid Sadoughi University of Medical Sciences, Yazd, Iran

SHAHID SADOUGHI UNIVERSITY OF MEDICAL SCIENCES

Original Article

Pattern of albumin consumption in patients hospitalized in intensive care unit of two teaching hospitals in Iran

Running Title: Drug use evaluation of albumin in intensive care units

Hadis Valapour[1], Mohammad Hossien Jarrahzadeh[2], Seyed Mojtaba Sohrevardi*[1]

[1]School of Pharmacy, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.
[2]School of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.

ARTICLEINFO

Received: 6/02/2021

Accepted: 9/14/2021

Corresponding author
School of Pharmacy, Shahid Sadoughi University of Medical Sciences, Yazd, Iran
Tel: +989134512422
E-mail
smsohrevardi@yahoo.com

Abstract

Aims: The goal of this study was to evaluate the consumption pattern of human albumin according to the available and reliable guidelines.

Methods: This research was a descriptive-analytical study. The study sample consisted of patients admitted to the intensive care units (ICUs) of Shahid Sadoughi and Rahnemoon Yazd Teaching Hospitals. In this study, 67 patients were selected. The study was carried out over three months. During the study, the albumin request by ICUs was investigated. Along with observing albumin orders' para-clinic findings were evaluated. The specific form of albumin consumption and prescription prepared by the Hospital Steering Board of Pharmacy was completed for each patient individually.

Results: In this study, 65.7% of prescribed albumin was infused for approved cases by the US food and drug administration (FDA). Administration after burn injury with 32.8% and hypoalbuminemia with 19.4% of cases were the most frequently reasonable prescribed albumin. About 34.3% of prescribed albumin (18 cases) did not have FDA-approved indications. Albumin infusion after patients edema in 14.9% of cases, nutritional support 6 % and Major surgery 6% have been the most frequently incorrect prescribed albumin.

Conclusion: Based on the findings of this study, the prescription of albumin in patients admitted to ICUs of Sadoughi and Rahnemoon teaching hospitals from October to December 2015 was not completely in accordance with the guidelines. So , consulting with relevant health care professionals can be helpful to improve the proper administration of this essential and expensive drug.

Keywords: Albumin; Hospitals; Intensive care unit; Medication therapy management; Patients

Citation: Valapour H, Jarrahzadeh MH, Sohrevardi SM. Pattern of albumin consumption in patients hospitalized in intensive care unit of two teaching hospitals in Iran. Adv Pharmacol Ther J. 2021;1(1): 23-30. https://doi.org/10.18502/aptj.v1i1.7957.

Introduction

Paying attention to prescription and consumption patterns of medications is important. Inappropriate and too much prescription of medicine besides incidence of medication-induced adverse events can lead to the financial burden on the patients (1). Trying to rationalize medication use has always been considered one of the most important pharmaceutical policies. According to the World Health Organization (WHO), to achieve a rational use of medication, medication with a good therapeutic effect is required to meet the clinical needs in a specific geographic area with the least side effects and lowest cost. In addition, the dose and duration of antibiotic use are of utmost importance (2, 3).

Albumin is a biological and relatively expensive medication simultaneously (the price per 20% vial was 1,150,000 Rials at the study time) and is prescribed too much. Since the arrival of albumin to the pharmaceutical market, it has always had a series of defenders and detractors (4, 5). On the other hand, the albumin production capacity in the country is low. In comparison, only the capacity of one company producing biological products in China is four times more than the maximum amount of albumin production in our country (6). Due to the mobilization plan and increased production line capacity of refinery and blood research, the albumin production line has been suspended since 2003, and the country consuming albumin is imported from foreign companies.

Another problem is the inadequate distribution of the products produced by the company. They were being informed on how to prescribe and use albumin (as a vital and strategic product) in medical centers of Iran is essential and needs a serious and immediate review. The use of albumin should be following valid protocol. In addition, the percentage of errors and their causes should be clarified and modified (7).

Drug utilization evaluation (DUE) means a progressive and appropriate program that examines and analyzes drug use patterns compared with standard criteria in a medical center (8, 9). According to the WHO, DUE studies include the investigation of distribution, prescription, and use of drugs in society, emphasizing the medical, social, and economic outcomes. The successful implementation of a DUE study will ensure the appropriate, safe, and effective medication use. Among the objectives of the DUE programs are assuring rational use of medicines, improving patients' health, forecasting and timely prevention of side effects, identifying the pattern of drug use in the community, and reducing the cost of treatment (10). It should be noted in this regard that various indices, including the Anatomical Therapeutic Chemical (ATC) classification system and the Defined Daily Dose (DDD), have been provided by WHO for the statistical study of drugs. In evaluating the consumption pattern, issues such as the number of prescribed drugs or a drug group, drug prescription patterns among physicians, the comparison of the treatment process with standard treatment strategies, and therapeutic use of expensive drugs are considered. Implementing a basic DUE program in the hospital includes planning, data collection and analysis,

interventions, and evaluation of the DUE program. To choose medicine for assessments, we mostly consider some criteria such as medication cost, adverse drug reaction, and a narrow therapeutic index (11, 12). This study aimed to investigate the albumin use pattern in patients admitted to the intensive care units (ICUs) of Shahid Sadoughi and Rahnemoon University Hospitals in Yazd, Iran.

Materials and methods

This research was a descriptive-analytical study. The study sample consisted of patients admitted to the ICU section of Shahid Sadoughi and Rahnemoon University Hospitals from October to December 2016 and was under treatment with albumin. According to Talasaz et al. (13), and considering 45% pattern, 1% accuracy test compliance, and confidence level of 95%, 67 patients were recruited in this study. The Ethics Committee approved the study protocol of Shahid Sadughi University of Medical Sciences (IR.SSU.MEDICINE.REC.1394.290).

Research method

This cross-sectional observational study was conducted for three months in the Sadoughi and Rahnemoon University Hospitals. By tracking albumin orders, finding patients' demographic data, and visiting them in the relevant ward (unit), the para-clinic findings were evaluated. The hospital Pharmacy committee prepared the specific form for consumption, and prescription (Directions for Use) was completed for each patient individually. For each patient, demographic characteristics (age, sex), pregnancy, duration of hospitalization, cause of admission, the amount of albumin use and its time, the cause of albumin prescription, adverse reactions, and infusion (injection) rate were recorded. Also, during the prescription period questioning the related doctor and the nurse and the observation of the patient, cause adverse outcomes, and its cause (in case of side effects) was examined and recorded. Each patient receiving albumin to find the criteria for prescribing and medication use albumin to what extent are run was evaluated separately and finally collected information into were entered into a form prepared by the researcher and were compared with existing standards regarding albumin use pattern. In this study, to determine the prescription conditions and non-prescription of albumin, the guidance provided in **Table 1** was used.

Data analysis

The collected data were entered into SPSS version 20, and after determining normality using the chi-square test and Fisher exact test were analyzed.

Results

In the current study, 58.2% of the patients were males, and 41.8% were females. The mean age of female patients was 60±26.3 years old, and that of men was 53.87±24.42 years old. The general mean age of the patients was 56.43± 25.22 years old.

Based on the findings of this study, 88.1% of the patients had no complications after albumin infusion (injection), 6% had increased saliva, and 6% experienced nausea.

Table 2 shows adverse events in hospitalized patients concerning patients' sex. The greatest impact was seen in women, which caused nausea. The chi-square test results also showed that there

 DOI: https://doi.org/10.18502/aptj.v1i1.7957

was no significant difference between male and female patients in terms of the presence of side effects (P>0.05). According to **Table 3**, the mean number of vials of prescribed albumin for approved and not approved cases by the FDA was 8.96±11.44, which was 6.16±6.76 days at a speed of 1-2 ml per minute on average. Generally, 600 vials of albumin were used within 834 days. Among the total number of prescribed vials, 440 vials (73.3%) were used for males and 160 vials (26.7%) for women. Mann-Whitney U test results showed that despite more prescribed vials for men than women, this difference was not significant statistically (P>0.05) **Table 4, 5**.

Table 1. The prescription and non-prescription condition of albumin(14) (GUIDELINES FOR USE OF ALBUMIN, Feb 27, 1995)

For the following albumin administration is correct (approved by FDA)
Hemorrhagic shock
Non-Hemorrhagic shock
Burning (decrease in plasma volume)
Ischemia or cerebral hemorrhage
Nutritional supports
Heart surgery
Hyperbilirubinemia in newborns
Acute nephropathy and nephrotic syndrome, hypoalbuminemia
Ascites, cirrhosis, spontaneous bacterial peritonitis, hepatorenal syndrom
Organ transplants
Plasmapheresis
Albumin is inappropriate for other administration

Table 2. The presence of adverse events in hospitalized patients with resect to sex (N: Number).

		side effect				**Total**
		Not		**Increased saliva**	**Nausea**	
Sex	Male	N	36	2	1	39
		% of total	53.7%	3%	1.5%	58.2%
	Female	N	23	2	3	28
		% of total	34.3%	3%	4.5%	41.8%
Total		N	59	4	4	67
		% of total	88.1%	6%	6%	100%

Table 3. Descriptive statistics of prescribed albumin vials in patients

	Number	Total	Minimum	Maximum	Mean	Standard Deviation
The number of vials of albumin	67	600	1	55	8.96	11.44
Albumin prescription duration(day)	67	834	١	28	6.16	6.76

Table 4. Comparison of vials prescribed in patients with respect to sex

	Sex	Number	Ranks average	Ranks sum	P value
Prescribed albumin	Male	39	36.6	1427.5	0.19
	Female	28	30.38	850.5	
Total		67			

Table 5. Descriptive statistics of prescribed vials and their prescription duration in approved and unapproved patients according to FDA

		Total	Minimum	Maximum	Mean	Standard Deviation
Approved	Albumin vial number	493	1	55	11.2	13.38
	Albumin prescription duration (day)	323	1	28	7.34	7.78
Non-Approved	Albumin vial number	107	1	12	4.65	3.69
	Albumin prescription duration (day)	90	1	14	3.91	3.26

The average number of vials of albumin prescribed for approved cases by the FDA was 11.20±13.38, which on average it was infused at a speed of 1-2 ml per minute.

According to **Table 6**, 493 vials of albumin (82.2%) were generally used within 323 days for approved cases by the FDA, and 107 vials of albumin (17.8%) were used within 90 days for non-approved cases by FDA.

According to **Table 7**, the average number of vials of albumin prescribed for non-approved cases by the FDA except burning was 8.64±12.53, which were infused within 5.95±7.23 days and at average the speed of 1-2 ml per minute. Generally, 190

 DOI: https://doi.org/10.18502/aptj.v1i1.7957

(64%) vials of albumin were used within 131 days for approved cases by FDA except burning. In addition, in burn patients (approved by FDA), the average number of administered vials of Albumin was 13.77±13.99, which on average were infused within 8.73±8.23 days and at the speed of 1-2 ml per minute. In general, 303 (50.5%) vials of albumin were administered in patients with a diagnosis of burning within 192 days, 190 vials of albumin (31.7%) were administered in patients without burning (approved by FDA), and 107 (17.8%) vials of albumin were used in non-approved patients by FDA.

Table 6. Frequency of vials prescribed in approved and non-approved patients

	Frequency	Percentage
Approved cases by FDA	493	82.2
Non-approved cases by FDA	107	17.8
Total	600	100

Table 7. Descriptive statistics of prescribed vials and their prescription duration in approved cases by FDA other than burning

		Total	Minimum	Maximum	Mean	Standard Deviation
Patients without burning	Albumin vial number	190	1	50	8.64	12.53
	Albumin prescription duration (day)	131	1	26	5.95	7.23
Burn patients	Albumin vial number	303	1	55	13.77	13.99
	Albumin prescription duration (day)	192	1	28	8.73	8.23

Discussion

This study aimed to investigate the consumption pattern of albumin in patients hospitalized in ICUs of Shahid Sadoughi and Rahnemoon University Hospitals of Yazd from October to December 2015. In this study, 88.1% of patients had no complications after albumin infusion, 6% had increased salivation, and 6% had nausea. In Ala et al.'s study (2015), 3 patients experienced side effects such as headache, hypotension, and rash, which were eliminated by decreasing albumin injection speed (15). According to the results of the chi-square test, there was no significant

difference between men and women in terms of the presence of side effects (P>0.05). In this study, the mean number of vials of prescribed albumin for approved and not approved cases by the FDA was 8.96±11.44. On average, albumin was infused 6.16±6.76 days at a speed of 1-2 ml per minute. Generally, 600 vials of albumin were used within 834 days. The average number of vials of albumin prescribed for approved cases by the FDA was 11.2±13.38, which on average it was infused at a speed of 1-2 ml per minute. The mean number of prescribed vials of albumin for non-approved cases by FDA was 4.65±3.69, which on average was infused within 3.91±3.26 days at a speed of 1-2 ml per minute. Generally, for cases approved by the FDA, 493 vials of albumin (82.2%) within 323 days, and for non-approved patients by FDA, 107 vials of albumin (17.8%) within 90 days were used. After separating burn cases, the average number of vials of albumin prescribed for approved cases by the FDA was 8.64±12.53, which on average was used 5.95±7.23 days at a speed of 1-2 ml per minute.

In total, 190 (64%) vials of albumin for approved cases by the FDA except burning were used within 131 days. In addition, the average number of administered (prescribed) vials of albumin was 13.77±13.99 in patients diagnosed with burning (approved by FDA). On average, it was used in 8.73±8.23 days at the speed of 1-2 ml per minute. In a nutshell, 303 (50.5%) vials of albumin were used in burn patients within 192 days, 190 vials of albumin (31.7%) were used in non-burn patients (approved by FDA), and 107 (17.8%) vials of albumin were used in patients with non-approved diagnosis by FDA.

In this study, among prescribed cases of albumin, diagnosis of 34.3% (18 cases) were not approved by FDA. Albumin infusion after patients' edema in 14.9% of cases, nutritional support 6 % and Major surgery 6% have been the most frequently incorrect prescribed albumin based on albumin prescription and administration guidelines. In the present study, the use of albumin to provide nutritional support only in patients with diarrhea more than 2 liters per day and serum albumin less than 2 grams per deciliters were considered rational. In this study, the serum albumin level before administration of albumin and infusion of nutritional support was not measured in patients. This means that the conditions for nutritional support were met, and the use of albumin was incorrect.

In a study by Talasaz et al. (2012), albumin was improperly prescribed for 36.2 cases. They found that hypoalbuminemia and nutritional support were the most conditions in which the albumin was used improperly (13). In contrast, hypoalbuminemia was mentioned as a proper case of albumin prescription in the present study. This discrepancy can be due to the use of two different albumin prescription and administration guidelines in two studies. According to the current research, albumin prescription conditions in the nutritional support were not intended, and albumin was prescribed improperly in Talasaz et al.'s study.

In Ala et al.'s study (2015), 37% did not use the American Society of Hospital Pharmacist (ASHP) protocol for the administration of albumin (15). In this study, serum levels of albumin were measured before administration of albumin only in 22 cases

 DOI: https://doi.org/10.18502/aptj.v1i1.7957

(32.8%) out of 67 cases, which its average was 2.5 mg per deciliter. The amount of serum level of albumin after the administration was not measured in patients, either. In Ala et al.'s study (2015), at least one day before the albumin start, plasma albumin was not checked in 16% of cases. Unlike the present study, serum albumin was measured during treatment in 72% of the patients (15).

Among the prescribed vials, 440 vials (73.3%) were for males, and 160 vials (26.7%) were for women. According to Mann-Whitney U test results, this difference was not significant (P>0.05). The main limitation of this study was the small sample size and heterogeneity of the studied patients.

Conclusion

According to the results of this study, the administration of albumin in patients admitted to ICUs of Shahid Sadoughi and Rahnemoon University Hospitals was not fully following the guidelines. Therefore, consulting with relevant health care professionals can be helpful to improve the proper administration of this sensitive and expensive drug. Future studies are recommended to investigate the consumption pattern of albumin in patients hospitalized in the ICUs using a larger population.

Conflict of interests: Authors have no conflict of interest.

Funding: No funding sources.

Acknowledgments: This work was supported by the School of Pharmacy, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.

References

1. Sepehri G, Dadolahi Y. Characterization of drug prescribing practices among dentists in Kerman province, 2001. journal of Dental School. 2006;24(1):94-101
2. Ogawa H, Yoshihara A, Amarasena N, Hirotomi T, Miyazaki H. Association between serum albumin and periodontal disease in community-dwelling elderly. J Clin Periodontol. 2006 May;33(5):312-6.
3. Don BR, Kaysen G. Serum albumin: relationship to inflammation and nutrition. Semin Dial. 2004 Nov-Dec;17(6):432-7.
4. Kshirsagar AV, Craig RG, Beck JD, Moss K, Offenbacher S, Kotanko P, et al. Severe periodontitis is associated with low serum albumin among patients on maintenance hemodialysis therapy. Clin J Am Soc Nephrol. 2007 Mar;2(2):239-44.
5. Mitzner S, Klammt S, Stange J, Schmidt R. Albumin regeneration inliver support-comparison of different methods. Ther Apher Dial. 2006 Apr;10(2):108-17.
6. Iwasaki M, Yoshihara A, Hirotomi T, Ogawa H, Hanada N, Miyazaki H. Longitudinal study on the relationship between serum albumin and periodontal disease. J Clin Periodontol. 2008 Apr;35(4):291-6.
7. Vaziri P, Vahedi M, Abdollahzadeh S, Abdolsamadi H, Hajilooi M, Kasraee S. Evaluation of salivary albumin in diabetic patients. Iranian journal of public health. 2009;38(3):54-9.
8. Novak M. Classification and epidemiologyof periodontal disease. In: Newman MG, Takei H, Klokkevold PR, editors. Carranza's clinical periodontology. 10 ed. St. Louis: W.B. Saunders Co; 2006. p. 100-6.
9. Mellanen L, Sorsa T, Lahdevirta J, Helenius M, Kari K, Meurman JH. Salivary albumin, totalprotein, IgA, IgG and IgM concentrations and occurrence of some periodontopathogens in HIV-infected patients: a 2-year follow-up study. J Oral Pathol Med. 2001 Oct;30(9):553-9.
10. Ozturk A, Ozkan Y, Akgoz S, Yalcin N, Aykut S, Ozdemir MR. The effect of blood albumin and total lymphocyte count on short-term results in elderly patients with hip fractures. Ulus Travma Acil Cerrahi Derg. 2009 Nov;15(6):546-52.
11. Phillips A, Shaper AG, Whincup PH. Association between serum albumin and mortality from cardiovascular disease, cancer, and other causes. Lancet. 1989 Dec 16;2(8677):1434-6.
12. Mojon P, Budtz-Jorgensen E, Rapin CH. Relationship between oral health and nutrition in very old people. Age Ageing. 1999 Sep;28(5):463-8.
13. 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 Feb;15(2):85-7.
14. GUIDELINES FOR USE OF ALBUMIN, Adapted from the original published guidelines developed by the University Hospital Consortium and published in Archives of Internal Medicine, Vol 155, Feb 27, 1995, [Revised – 2005 & 2010
15. Ala S, Salehifar E, Chalaki V. Evaluation of Albumin Use in a Teaching Hospital. J Mazandaran Univ Med Sci. 2015;25(129):137-41.