Original Article

Impact of Protocol Implementation on Rationalization of Albumin Use in a Tertiary Care Teaching Hospital in Tehran, Iran

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ABSTRACT

Objective: With respect to the high cost and limited availability of albumin, its use must be restricted to indications strongly supported by solid scientific evidence. It was anticipated that with the implementation of the National Health Reform Plan (NHRP), the consumption of albumin would increase as the result of decreasing patients' out-of-pocket costs. This study aimed to evaluate the efficacy of protocol implementation on the rationalization of albumin use in surgery wards of Cancer Institute of Imam Khomeini Hospital Complex, Tehran, Iran. **Methods:** This pre-post interventional study was conducted in 32-month phases from January to November 2014 in an Iranian University hospital. The first phase was before the implementation of NHRP, the second phase was after NHRP, and the last one was after the intervention. The first and second phases were conducted retrospectively. Data extraction was performed by a hospital pharmacist. During the third phase, the physicians were mandated to adhere to a local albumin protocol which had been prepared by clinical pharmacy service and approved by drug and therapeutic committee. Appropriateness of prescriptions regarding indication, dose, and duration based on local guideline was compared among groups. **Findings:** Although hospital bed-days of care remained consistent among phases, albumin was prescribed for 40, 45, and 8 patients during first, second, and third phases, respectively. This shows about 80% reduction of drug prescriptions in the last phase. The mean duration/dose of albumin in inappropriate indications reduced significantly from 11.3 ± 8.2 days/24.7 ± 21.2 vials in the second phase to 2.6 ± 1.7 days/5.6 ± 3.5 vials in the third phase, respectively ($P = 0.001$ and $P = 0.003$). **Conclusion:** Interactive collaboration through guideline implementation seems effective in rationalizing the use of high-cost medications such as albumin.

Keywords: *Albumin, cost, drug utilization evaluation, practice guideline*

Received: March 2018.
Accepted: July 2018.

Introduction

Albumin, as the major contributing factor in determining oncotic pressure of blood, regulates fluid distribution between plasma and tissue compartment. Albumin also serves as a carrier for endogenous and exogenous substances such as hormones, bilirubin, and various drugs. In parallel with these main effects, novel capacities, including antioxidant, anti-inflammatory, immune-modulatory, and endothelial stabilization effects, have been attributed to albumin.[1]

Access this article online

Quick Response Code:

Website: www.jrpp.net

DOI: 10.4103/jrpp.JRPP_18_38

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How to cite this article: Ebrahimpour S, Nosrati M, Mohammadi M, Kamyab H, Sarayani A, Mahmoodzadeh H, *et al.* Impact of protocol implementation on rationalization of albumin use in a tertiary care teaching hospital in Tehran, Iran. J Res Pharm Pract 2018;7:182-7.

Besides widely accepted indications of albumin, which consists of paracentesis, plasmapheresis, spontaneous bacterial peritonitis, and volume resuscitation in acute care, there are several indications in which albumin use is justified only if specific criteria are met.[2] With respect to the broad spectrum of conditionally accepted indications of albumin, there is an intense tendency toward irrationally high utilization of albumin in some clinical settings. The previous research found that nutrition support and hypoalbuminemia were the most common inappropriate uses of albumin in our country.[3,4]

Considering the high cost and limited availability of albumin, overutilization imposes substantial economic burden on the healthcare system. The National Health Reform Plan (NHRP), commenced since May 2014 in Iran, aimed at reducing patients' out-of-pocket costs. The plan attempted to pay the costs not covered by the four main health insurance organizations in Iran and also to finance the healthcare costs of patients not covered by any of the insurance organizations.

The high cost of albumin has always been a barrier to its liberal prescription, and physicians had to consider some prerequirements such as measurement of serum albumin and unresponsiveness to other preferred interventions. Before NHRP implementation, albumin ranked first in the costs associated with medications in our teaching hospital. It was anticipated that the costs also would increase considerably with the implementation of NHRP and with reducing the concerns about patients' payments. These events necessitated more vigilant monitoring of high-cost medications such as albumin. With regard to previous successful experiences with rationalizing drug utilization through the implementation of local guidelines,[3] we were motivated to evaluate the efficacy of preparation of a local guideline on regulating albumin consumption.

Methods

This study was a pre-post interventional study performed in four surgical wards of Cancer Institute of Imam Khomeini University Hospital (affiliated with Tehran University of medical sciences, Tehran, Iran). The study was conducted in 32-month phases, and all patients with albumin prescription in each phase were recruited into the study. Albumin was available as 20% (50 ml) vials in all phases of the study. Phase 1 (pre-NHRP) was conducted in January–February 2014, before NHRP implementation. The second phase (post-NHRP) was run after the implementation of NHRP in June–July 2014. During these two phases, medical records of all patients who received albumin were investigated retrospectively by a hospital pharmacist under the supervision of a clinical pharmacist. Relevant data, including age, gender, vital signs, serum levels of albumin and total protein, and dose (vial number), duration, and indication of albumin, were extracted. Additional information, including data related to costs, hospital bed-days of care, and parenteral nutrition products, was obtained from the hospital information system.

Before enrollment of Phase 3, a local evidence-based protocol for albumin use was prepared by two clinical pharmacists. The draft was sent to the heads of surgery wards, additional comments were obtained, and the protocol was modified accordingly if there was strong evidence. The revised version was sent back to the heads for final confirmation [Table 1]. The protocol was then discussed and approved by drug and therapeutic committee (DTC). After approval, educational programs for attending physicians, medical residents, and pharmacists were held in the form of oral presentations. Hard copy of the albumin request form was also sent to the wards.

Phase 3 of the study (after DTC intervention) was executed in October–November 2014. During this phase, it was mandatory for physicians to fill the albumin request form for each patient and send it to the pharmacy. The request forms were evaluated by the pharmacist based on the approved protocol and the patient's medical records. Appropriate prescriptions were filled by the pharmacy. In case of uncertainty of appropriate indication, albumin was delivered to the ward until the clinical pharmacist could call the physician for the resolution of ambiguity. The physician's order was carried out if he/she still insisted on the prescription.

Appropriateness of albumin prescription was evaluated according to the approved local guideline of our institution. For patients who were treated inappropriately, the mean duration of albumin use and the mean number of albumin vials were compared among the study groups. The number of albumin prescriptions, adjusted per 1000 hospital bed-days of care, was also compared. Albumin doses more than 10% above or under the recommended doses were considered inappropriate.

Data analysis was conducted using the SPSS statistics software (Version 21.0. IBM Corp. Armonk, NY, USA). Normal distribution of data was analyzed using the Kolmogorov–Smirnov test. Qualitative data were stated as numbers and frequencies (*n*; %) and quantitative data as a mean ± standard deviation.

The Kruskal–Wallis *H* test was run to compare the duration and number of albumin vials in the three phases of the study with respect to the nonnormal distribution

Table 1: Institutional protocol for Albumin use

Indication	Criteria and dosing
Paracentesis[5]	6-8 g albumin/L ascitic fluid removed for paracentesis volumes>4-5L
Liver transplantation[2]	If the following criteria are met:
	Serum albumin <2.5 g/dL
	Hematocrit >30%
Liver resection (>40%) or extensive intestinal resection[2]	If after volume resuscitation serum albumin is <2 g/dL
Spontaneous bacterial peritonitis[6]	If serum creatinine >1 mg/dL, blood urea nitrogen >30 mg/dL, or total bilirubin >4 mg/dL
	1.5 g/kg up to 150 g within 6 h of suspicion and 1 g/kg on 3rd day, maximum 100 g
Hepatorenal syndrome[6]	Diagnosis
	1 g/kg of body weight per day up to a maximum of 100 g/day) for at least 2 days
	Treatment
	In combination with vasoconstrictor agents
	1 g/kg/day, maximum 100 g, for 2 days, then 20-40 g/day
	Treatment can be continued until midodrine and octreotide are administered
Heart surgery[2]	Fluid resuscitation in patients unresponsive to crystalloids
Acute respiratory distress syndrome[7]	25 g in combination with furosemide; if needed, may repeat at 8 h for 3 days
Edema[8-11]	Resistant to treatment with diuretics in patients with serum albumin <2 g/dL
Hypovolemia[2]	In patients unresponsive to crystalloids
	5% albumin: IV: Initial: 12.5-25 g (250-500 mL); repeat after 15-30 min as needed
Plasma exchange[12]	For exchanges of >20 mL/kg in one session or >20 mL/kg/week in more than one session
	Equal to removed volume (albumin 5% in combination with normal saline in 70:30 ratio)
Burn[2]	If all of the following criteria are met:
	Burn >50% BSA
	After the first 24 h of burn
	Hypovolemia unresponsive to crystalloids
Diarrhea[2]	In patients who cannot tolerate enteral feeding and in the presence of all following criteria:
	Diarrhea volume >2 L/day
	Serum albumin <2 g/dL
	Continuing diarrhea in spite of the administration of short-chain peptides and mineral formulas

BSA=Body surface area

of these data. $P < 0.05$ was assumed as statistically significant difference in all tests. The mean albumin costs associated with inappropriate prescriptions were compared among the three study phases using the one-way ANOVA test.

Results

Albumin was prescribed for 93 patients during the aforementioned phases of the study (44.1% were male). The mean age of the patients was 58.6 ± 14.2 years.

Albumin was prescribed for 40, 45, and 8 patients in Phases 1, 2, and 3, respectively, and hospital bed-days of care were 4396, 5934, and 5043 for corresponding phases. This revealed that the number of albumin prescriptions per 1000 hospital bed-days of care reduced from 9.1 in Phase 1 and 7.6 in Phase 2 to 1.5 in Phase 3, which corresponds to 82.5% and 80.3% reductions, respectively ($P = 0.002$).

The indication was appropriate in eight patients during Phase 1 and one patient in each of the other phases (10.7% of all patients). Albumin was dosed correctly only in 4 of 10 patients with appropriate indication (40.0%). In six patients of Phase 1 and eight patients of Phase 2, it was not feasible to ascertain the appropriateness of prescription based on medical records (15.0% of all patients). Nutritional support and hypoalbuminemia were the most common inappropriate indications in all phases [Table 2].

The mean durations of inappropriate albumin use were 7.28 ± 6.0, 11.3 ± 8.2, and 2.6 ± 1.7 days for Phases 1–3, respectively. The Kruskal–Wallis H test delineated that there was statistically significant difference in mean durations of albumin use among the study periods (χ^2 (2) = 15.2, $P < 0.001$, with a mean rank of 42.25 for Phase 1, 56.21 for Phase 2, and 18.94 for Phase 3). The pairwise comparisons showed the statistically significant

Table 2: Frequency of appropriate and inappropriate indications of Albumin in three phases of the study including before National Health Reform Plan, after National Health Reform Plan, and after Drug and Therapeutics Committee intervention

Indication	Phase 1: Pre-NHRP (*n*=40 requests)		Phase 2: Post-NHRP (*n*=45 requests)		Phase 3: After DTC intervention (*n*=8 requests)	
	Patients, *n* (%)	Vials, *n* (%)	Patients, *n* (%)	Vials, *n* (%)	Patients, *n* (%)	Vials, *n* (%)
Appropriate indications						
Paracentesis (>4 Liters)	2 (5.0)	18 (2.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Liver resection	1 (2.5)	7 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hepatorenal syndrome	1 (2.5)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Nonhemorrhagic shock	1 (2.5)	74 (12.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Resistant edema	3 (7.5)	41 (6.8)	1 (2.3)	27 (2.4)	1 (12.5)	4 (8.8)
Total	8 (20.0)	141 (23.5)	1 (2.3)	27 (2.4)	1 (12.5)	4 (8.8)
Inappropriate indications						
Hypoalbuminemia	7 (17.5)	91 (15.1)	11 (24.4)	218 (19.7)	0 (0.0)	0 (0.0)
Nutritional support	15 (37.5)	272 (45.2)	16 (35.5)	426 (38.4)	5 (62.5)	37 (82.2)
Combined hypoalbuminemia and nutritional support	2 (5.0)	40 (6.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Anastomosis leak	2 (5.0)	21 (3.5)	5 (11.1)	157 (14.2)	0 (0.0)	0 (0.0)
Edema with serum albumin <2 g/dL with or without diuretic	0	0	2 (4.5)	24 (2.2)	0 (0.0)	0 (0.0)
Paracentesis (<4 L)	0	0	2 (4.5)	96 (8.6)	2 (25.0)	4 (8.8)
Total	26 (65.0)	424 (70.5)	36 (80.0)	921 (83.1)	7 (87.5)	41 (91.2)
Unknown indications	6 (15.0)	36 (6.0)	8 (17.7)	160 (14.4)	0 (0.0)	0 (0.0)

NHRP=National Health Reform Plan; DTC=Drug and Therapeutics Committee

difference between post-NHRP and after DTC intervention phases (P = 0.001) [Figure 1a]. Noteworthy, the difference was marginally significant between pre- and post-NHRP periods (P = 0.05).

The mean numbers of inappropriately used albumin vials were 16.1 ± 15.8, 24.7 ± 21.2, and 5.6 ± 3.5 for Phases 1–3, respectively. The Kruskal–Wallis H test revealed that there was a significant difference in the mean number of albumin vials among three phases of the study (χ^2 (2) = 12.3, P = 0.002, with a mean rank of 42.50 for Phase 1, 54.74 for Phase 2, and 21.19 for Phase 3). The *post hoc* analysis also indicated that the mean vial number significantly differed between the post-NHRP and after DTC intervention phases (P = 0.003) [Figure 1b].

Total number of inappropriately prescribed albumin vials were 424 in Phase 1, 921 in Phase 2, and 41 in Phase 3, which correspond to direct drug costs of 614.8 million IRR (≈16,394 USD), 1.34 billion IRR (≈35,612 USD), and 59.4 million IRR (≈1585 USD), respectively. This shows that DTC intervention led to about 90% reduction in drug costs compared with the post-NHRP phase. Correspondingly, the mean albumin costs associated with inappropriate prescriptions differed significantly among groups as determined by the one-way ANOVA test (F[2,90] = 4.9, P = 0.009). The Hochberg's GT2 *post hoc* test revealed that the mean drug cost per patient was significantly lower after DTC intervention compared with the post-NHRP period (217.7 ± 133.9 USD and 952.9 ± 810.7 USD, respectively; P = 0.021).

The number of patients who received albumin for the management of hypoalbuminemia or for nutritional purposes decreased from 27 patients (644 vials) in Phase 2 to 5 patients (37 vials) in Phase 3. This was coincident with doubling the number of patients who received parenteral nutrition in aforementioned phases (21 patients in Phase 2 and 40 patients in Phase 3). The costs associated with albumin in these patients were 933.8 million IRR (24,900 USD) in Phase 2 and 53.6 million IRR (1430 USD) in Phase 3. Corresponding costs for parenteral nutrition were 148.9 million IRR (3972 USD) in Phase 2 and 286.3 million IRR (7634 USD) in Phase 3. The actual cost saving is calculated by subtracting the cost of parenteral nutrition from the costs saved by reduced albumin use. The saving was calculated to be 743 million IRR (19800 USD) in Phase 3 compared to Phase 2.

Discussion

In 2008, Iranian Food and Drug Organization of the Ministry of Health publicized that albumin ranked first in the highly paid medications in hospital settings.[3] The hypothesis behind our study was that with the initiation of NHRP and reduction of patients' out-of-pocket costs, albumin use would increase considerably.

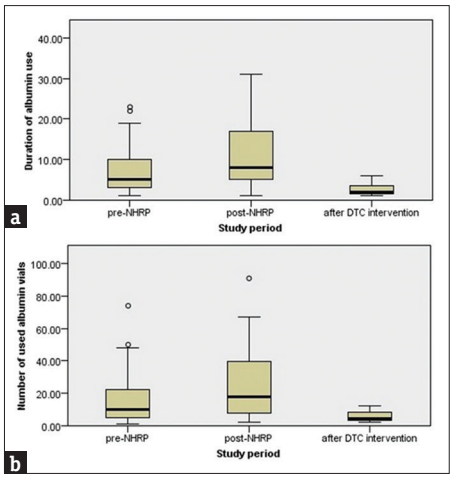

Figure 1: (a) Comparison of duration of albumin use in inappropriate indications in three phases of the study. The mean duration of albumin use was significantly lower in "after Drug and Therapeutic Committee intervention" phase compared with "post-National Health Reform Plan" phase. (b) Comparison of number of used albumin vials in inappropriate indications in three phases of the study. The mean number of albumin vials was significantly lower in "after Drug and Therapeutic Committee intervention" phase compared with "post-National Health Reform Plan" phase

The most interesting finding of the current study was that albumin had been prescribed inappropriately in 65% of patients in pre-NHRP phase and this also increased considerably with conduction of NHRP (80%). This finding is in agreement with the results of other studies performed in similar settings. In the study by Laki *et al*., albumin was ordered inappropriately in 58% of patients before implementation of an institutional guideline.[13] Comparable results were also reported by Zolfagharian *et al*. and Mahmoudi *et al*. which showed 62% and 51.2% inappropriate prescriptions, respectively, before protocolization of albumin use.[4,14] The mean duration and mean vial number of inappropriate albumin use increased in post-NHRP period compared with pre-NHRP, although the difference was marginally significant only for the mean duration of use. These findings suggest that the initiation of NHRP and subsequent reduction of patients' out-of-pocket costs provided the basis for prolongation of albumin use but not its prescription rate. This reflects that the main determinant of albumin use was the physicians' attitude toward an indication of albumin not the imposed patient's out-of-pocket cost. With the reduction of costs imposed directly on patients, the physicians seem to interested in prolongation of therapy with albumin.

Although hospital bed-days of care remained nearly unchanged during all phases, about 80% of reduction was observed in the number of albumin prescriptions in Phase 3 compared with Phases 1 and 2. The most frequent inappropriate indications in all study phases were nutritional support and hypoalbuminemia, which was in agreement with previous studies.[3,4] Besides the substantial reduction of the number of albumin prescriptions in Phase 3, the mean duration of albumin use for incorrect indications also showed a significant reduction ($P < 0.001$). It should be noted that comparing the percentages of inappropriate uses in the three phases of the study is misleading. For example, in the case of nutritional support, the number of prescriptions was 15, 16, and 5 in Phases 1 through 3, respectively, which reflects substantial reduction; however, the percentages show rising trend. The increased percentages are due to the reduction of the total number of prescription not the increased number of inappropriate prescriptions. It is somewhat surprising that the number of patients under total parenteral nutrition was doubled in Phase 3 compared with Phase 2. In total, this is consistent with our finding that the most common inappropriate indication of albumin was nutritional support, which was replaced by total parenteral nutrition in Phase 3.

According to the process approved by DTC, if the hospital pharmacist did not find the albumin indication in accordance with the protocol, a clinical pharmacist was contacted. The clinical pharmacist then visited the patient to ensure the appropriateness of prescription. In case of confirmed inappropriate indication, albumin was delivered to the ward until the physician could be convinced. Therefore, the patients would receive albumin for even some days until the pharmacist, and the attending physician could reach an agreement.

Of note, our study was conducted in only four wards of the hospital, and it was feasible for the pharmacy service to evaluate prescriptions and to perform interventions if needed. In addition, debating inappropriate prescriptions with physicians was a time-consuming process, especially at times, they were not available. If it was planned to expand the local protocol to all of our hospital wards, more pharmacists were needed to be involved particularly with regard to the remaining 60 wards. The use of an online audit program to request albumin from the hospital pharmacy seems to be more effective to maximize physicians' adherence to implemented guidelines. Obviously, using such online programs could be suggested to save time and workforce and also to optimize guideline adherence by physicians.

It is interesting to note that in the 10 patients with appropriate indication in all study phases, only four received albumin with the correct dose and duration. Therefore, even if the indication is correct based on local guidelines, continued surveillance is needed to ensure appropriate treatment.

Considering that the duration of albumin use in most of its indications is determined based on

clinical conditions of the patient, serial rechecks performed every 24–48 h is recommended to reassure appropriate use. It would be favorable if the hospital information systems could be programmed to alarm on prescheduled times and necessitate reordering for albumin prescription in case of prolonged use. Such programs make the extensive supervisions possible without imposing extra works compared with manual systems.

Giving feedback to the medical staff on the results of study in the form of benchmarking tables, charts, E-mails, and pamphlets help them to remain adherent to local guidelines.

The persuasive nature of our study caused limitations in stringent conduction of the local guideline. It seems that the use of more restrictive methods will result in more favorable outcomes.

Due to the retrospective design of Phases 1 and 2, the current study was unable to determine the appropriateness of prescriptions in a number of patients only based on medical records.

An issue that was not addressed in this study was that the outcomes were not measured, and the effect of the intervention on patients' outcome such as postsurgery recovery, length of hospital stay, and mortality rate could not be determined.

In parallel with the main finding of the study, which showed that the implementation of local guideline was effective in rationalization of albumin use, the following conclusions could also be drawn. First, the implementation of NHRP resulted in marginal increase in duration of albumin use. Therefore, besides of appropriateness of indication, the duration of albumin use should also be considered and managed by designed protocols. Second, providing alternative treatments such as parenteral nutrition could be effective in reducing albumin use for nutritional support. Third, with respect to significant workload of implementing a local protocol, online audit program should be considered.

Authors' Contributions

Zahra Jahangard-Rafsanjani, Habibollah Mahmoodzadeh, Haniyeh Kamyab, and Amir Sarayani designed the study. Kheirollah Gholami, Zahra Jahangard-Rafsanjani, and Marzieh Nosrati were involved in study conduction and data extraction. Sholeh Ebrahimpour and Mehdi Mohammadi prepared the manuscript and performed the data analysis. All authors read and approved the manuscript.

Acknowledgments

The authors would like to appreciate DTC members of Imam Khomeini Hospital Complex for their collaboration.

Financial support and sponsorship

This study was financially supported by the Research Council of Tehran University of Medical Sciences.

Conflicts of interest

There are no conflicts of interest.

References

1. Caraceni P, Domenicali M, Tovoli A, Napoli L, Ricci CS, Tufoni M, *et al.* Clinical indications for the albumin use: Still a controversial issue. Eur J Intern Med 2013;24:721-8.
2. Liumbruno GM, Bennardello F, Lattanzio A, Piccoli P, Rossettias G; Italian Society of Transfusion Medicine and Immunohaematology (SIMTI), *et al.* Recommendations for the use of albumin and immunoglobulins. Blood Transfus 2009;7:216-34.
3. 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;15:85-7.
4. Zolfagharian F, Ghazanfari S, Elyasi S, Iraji 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;39:704-11.
5. Runyon BA; AASLD. Introduction to the revised American association for the study of liver diseases practice guideline management of adult patients with ascites due to cirrhosis 2012. Hepatology 2013;57:1651-3.
6. Caraceni P, Tufoni M, Bonavita ME. Clinical use of albumin. Blood Transfus 2013;11 Suppl 4:s18-25.
7. Martin GS, Mangialardi RJ, Wheeler AP, Dupont WD, Morris JA, Bernard GR, *et al.* Albumin and furosemide therapy in hypoproteinemic patients with acute lung injury. Crit Care Med 2002;30:2175-82.
8. Eadington DW, Plant WD, Winney RJ. Albumin in the nephrotic syndrome. BMJ 1995;310:1333.
9. Fliser D, Zurbrüggen I, Mutschler E, Bischoff I, Nussberger J, Franek E, *et al.* Coadministration of albumin and furosemide in patients with the nephrotic syndrome. Kidney Int 1999;55:629-34.
10. Na KY, Han JS, Kim YS, Ahn C, Kim S, Lee JS, *et al.* Does albumin preinfusion potentiate diuretic action of furosemide in patients with nephrotic syndrome? J Korean Med Sci 2001;16:448-54.
11. Hari P, Bagga A. Co-administration of albumin and furosemide in patients with the nephrotic syndrome. Saudi J Kidney Dis Transpl 2012;23:371-2.
12. Winters JL. Plasma exchange: Concepts, mechanisms, and an overview of the American society for apheresis guidelines. Hematology Am Soc Hematol Educ Program 2012;2012:7-12.
13. Laki B, Taghizadeh-Ghehi M, Assarian M, Heidari K, Torkamandi H, Javadi MR, *et al.* Effect of hospital-wide interventions to optimize albumin use in a tertiary hospital. J Clin Pharm Ther 2017;42:704-9.
14. Mahmoudi L, Karamikhah R, Mahdavinia A, Samiei H, Petramfar P, Niknam R, *et al.* Implementation of pharmaceutical practice guidelines by a project model based: Clinical and economic impact. Medicine (Baltimore) 2015;94:e1744.