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Original Article:

Enhancing the Rational Use of Albumin and Intra-venous Pantoprazole in Hospitals by Implementing Pharmaceutical Guidelines in Hospitals: A Quasi-experimental study

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ABSTRACT

Background: Irrational use of drugs is a serious global problem, especially in developing countries. Scientific evidence has announced albumin and intravenous pantoprazole as expensive drugs, i.e., relatively irrationally applied in hospitals without following the guidelines.

Objectives: Considering health cost management policy in Iran, this study aimed to evaluate the effects of implementing pharmaceutical guidelines to rationalize and reduce the use of albumin and intravenous pantoprazole and the related inappropriate costs.

Methods: This quasi-experimental study was conducted from January 2016 to October 2018 in two teaching Hospitals in Jahrom City, Iran. Pharmaceutical guidelines were implemented throughout the physical training as well as a pharmacist-led intervention and supervising. All inpatient prescriptions of the studied medicines were evaluated.

Results: Before conducting the intervention (June 2016), an average of 357 albumin vials were monthly used; after performing the interventions, 166 and 167 vials were used in 2017 and 2018, respectively. Reduced albumin use rate equaled 48%, i.e., significant (P=0.002). Annual cost-saving was estimated to be 25000 USD. In comparison to the previous year, there were 46% and 70% reductions in the mean number of pantoprazole vials prescribed in 2017 and 2018, respectively (P=0.005).

Consuming pantoprazole was measured to be 1457 vials per month in 2017 and 795 in 2018, i.e., significant (P=0.002). Cost-Saving in intravenous pantoprazole was estimated to be 16000 USD in 2017 and 25000 USD in 2018.

Conclusion: Prescription strategies, such as pharmaceutical guidelines with educational measures, pharmacist-led intervention, monitoring the prescribing drug, and feedback to prescribers can significantly decrease the inappropriate use of expensive drugs and their costs.

Introduction

The first conference concerning the Rational Use of Drug (RUD) was held in Nairobi in 1985, where the RUD was defined as "patients receive medications appropriate to their clinical needs, in doses that meet their requirements, for an adequate period, and at the lowest cost to them and their community" [1]. In other words, each individual receives a maximal curative benefit with minimal risk and cost.

Common types of Irrational Use of Drug (IRUD) include the inappropriate use of antibiotics, the overuse of injection when the oral drug would be more appropriate, multiple medicines per prescription, prescribing medicine regardless of clinical guidelines, failure to follow drug orders, and inappropriate self-medication [2]. IRUD is a serious global problem, especially in developing countries. It can greatly impact the patient (adverse drug reaction, drug resistance), the community, and the health system (the wastes of resources) [3]. This issue has a long history in Iran; as the World Health Organization (WHO) reported in 1999, the IRUD concerning factors, such as the economic benefit of, the pressure of patients on physicians for prescribing drugs, legal weaknesses, and self-medication [4].

Medicines account for 20%-60% of healthcare costs in Low- and Middle-Income Countries (LMICs) [5]. In Iran, the analysis of pharmaceutical markets between 1997 and 2010 indicated that medicine consumption sales value growth equaled 28.38% annually; while the annual growth of population was calculated as 1.53% [6]. Another research suggested a 107% increase in pharmaceutical costs from the beginning of the 2001s to the end [7].

In response to these rising, the Ministry of Health and Medical Education (MoHME) of Iran has adopted various cost containment strategies, including standard treatment guidelines. The guidelines are managerial interventions to help prescribers make decisions about appropriate interventions for specific clinical conditions. There is growing literature on the impact of some of these techniques on RUD and drug spending. A study indicated that IRUD can lead to higher pharmaceutical expenditures due to the prescription of unnecessarily expensive products [8]. Another study also declared pharmaceutical costs in healthcare could have been reduced by 70% if some managerial strategies had been implemented [9]. In a study in Iran, Rafsanjani et al. declared that implementing restrictive drug protocols, decreased pantoprazole

consumption by approximately $1.4 per hospital bed day and a 43% reduction in albumin expenditure [10].

In the first phase of implementing the cost management program in the hospital by the MoHME, Intravenous (IV) pantoprazole and albumin were candidates for cost savings. These drugs are expensive and the costliest medications in hospitals [11]. We will describe the irrationalized use of albumin and IV pantoprazole in hospitals by implementing pharmaceutical guidelines. Albumin is a biological drug with high consumption, i.e., not produced in Iran [12]. It is used to treat patients with hypovolemia (hemodialysis, acute liver failure, & high bilirubin in infants) [13]. There exist some favorable alternatives to albumin, as per the scientific literature, with a cost-reduction approach [14, 15]. Pantoprazole is a proton pump inhibitor prescribed to reduce gastric acid secretion and treat acute peptic ulcers and reflux esophagitis [16].

The present study aimed to rationalize and reduce the use of albumin and IV pantoprazole and assess the relevant inappropriate costs. This study was in line with the MoHME of Iran's policy on health cost management (Health Reform Plan).

Material and Methods

This quasi-experimental study was conducted from January 2016 to October 2018 in two teaching hospitals affiliated with Jahrom University of Medical Sciences, Sothern of Iran. Both hospitals had 200 active beds with 15 medical wards. This project was approved by the Ethics Committee of the MoHME in Iran (Code: IR.JUMS.REC.399.068).

After conducting the pharmaceutical guidelines [13, 17, 18] by specialist physicians in June 2016, we examined its effects on using these expensive drugs. The implementation of the guidelines include a few steps, as follows:

1. Training physicians

2. Supervising clinical pharmacists on daily orders according to the relevant indications checklist (appendix 1, 2)

3. Managing data in the prescribing drugs

4. Providing feedback to prescribers

In 3 years (2016-2018), we compared drug consumption data and the created drug costs. For this purpose, we used the pharmaceutical software data of each hospital dedicated to this measure. The study population consisted of all prescriptions at inpatients wards during the period. These

prescriptions were related to the numbers of 61377, 63847, and 63877 patients in the studied years, respectively.

The data collection was performed from January to February 2019. Descriptive statistics were presented as frequencies and mean in tables. Two-Way non-parametric Analysis of Variance (ANOVA) was applied in SPSS to assess the obtained results and compare values in the 3 years. The significance level was set at $P<0.05$. Besides, the estimated Odds Ratios (ORs) were presented with a 95% Confidence Interval (CI).

Results

The Mean±SD number of patients in the two studied hospitals per month in 2016, 2017, and 2018 were equal to 5114±250, 5320±278, and 5315±524 years, respectively. The minimum and maximum albumin use in the first 6 months of the year 2016 equaled 294 and 397 vials, in sequence, in December. After implementing the albumin guideline, the average drug use was measured as 166 and 167 vials in 2017 and 2018, respectively. Reduced albumin use in the years was approximately 48% and significant ($P<0.05$). Averagely, approximately 165 vials per month were prescribed appropriately (Table 1).

Annual cost saving from RUD in albumin was estimated to be USD 25000.

The reduced mean number of pantoprazole vials prescribed for patients in 2017 was calculated as 46%, compared to the previous year. This trend has continued in the following year (2018); we observed a 70% reduction in this respect. Change in the number of drugs prescribed in the study years was determined to be statistically significant ($P<0.05$). Consuming IV pantoprazole was measured to be 1457 vials and 795 vials per month in 2017 and 2018, respectively; it revealed a significant reduction ($P=0.002$) (Table 2). Cost-Saving from RUD in IV pantoprazole was estimated to be USD 16000 in 2017 and USD 25000 in 2018.

Declined albumin and IV pantoprazole prescription patterns used after the intervention are shown in Figure 1. The majority of prescribed albumin and pantoprazole vials were deemed to have been inappropriate. RUD was consistent in the years after the implementation of guidelines. Cost-saving respecting RUD in albumin and IV pantoprazole were approximately USD 50000 per year.

Based on trend analysis by joint point regression method, the average monthly changes in albumin consumption in

Table 1. The distribution of albumin use per month in the hospitals in 2016-2018

| Months | The Number of Albumin Vials Consumed | | | P* |
	2016	2017	2018	
January	294	177	141	
February	397	186	163	
March	345	417	168	0.042
April	376	75	198	
May	333	107	182	
June	395	148	175	
July	250	115	191	
August	233	165	140	
September	346	118	279	0.042
November	407	99	102	
December	189	183	115	
October	202	211	151	
Mean	314	166	167	0.002

* Friedman's two-way ANOVA

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Table 2. The distribution of IV pantoprazole use per month in the hospitals in 2016-2018

Months	The Number of IV Pantoprazole Vials Consumed			P*
	2016	2017	2018	
January	2874	1837	836	
February	3527	2228	865	
March	2945	2238	765	0.002
April	2738	2096	742	
May	2700	1482	681	
June	2836	1521	498	
July	2495	972	662	
August	2565	1011	748	
September	2244	1138	1122	0.006
October	2326	1153	722	
November	2546	852	1101	
December	2436	956	804	
Mean	2686	1457	795	<0.005

*Friedman's two-way ANOVA

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the first 17 months of the study presented a significant decrease of 5% (AMPC=-5; 95%CI: -6.6 to-3.4; P<0.001); it has been then almost constant. The average monthly change of pantoprazole consumption has been decreasing in 28 months. The largest decrease in the 10th to 28th months was approximately 7% (AMPC= -6.8; 95% CI: -7.3 to -6.3; P<0.001). Besides, from the 28th to the 36th month, it was almost constant (Table 3) (Figure 2, 3).

Discussion

The WHO reported that in numerous countries, 30% of patients in public sectors and 40% of patients in private sectors are treated per standard clinical guidelines [19]. Previous studies evaluated the clinical and economic impacts of pharmaceutical guidelines in Iran, suggesting that IRUD for albumin and pantoprazole ranged between 36% and 93% [12, 20, 21]. Albumin and IV pantoprazole IRUD in the studied hospitals, before our intervention (July 2016), has dramatically risen from 48% to 70% in 2015 and 2016, respectively. We attempted to reduce the irrational use of these expensive drugs and their costs by implementing pharmaceutical guidelines.

The WHO announced that only less than half of all countries are implementing the basic policies required to ensure the appropriate use of medicines [4]. Introducing evidence-based guidelines for the expensive drug, i.e., led to a steady decline in drug use in our study has been followed by implementing the Health Reform Plan in Iran [22].

Table 3. The trend analysis of albumin and IV pantoprazole consumption per month in hospitals in 2016-2018

Months	Albumin		Months	Pantoprazole	
	AMPC* (95% CI)	P		AMPC** (95% CI)	P
1-17	-5 (-6.6, -3.4)	<0.001	1-10	-1.6 (-3.2, -0.1)	<0.001
17-36	0.3 (-0.2, 0.7)	0.3	10-28	-6.8 (-7.3, -6.3)	<0.001
_____	_____	_____	28-36	1.7 (-0.5, 3.9)	0.1

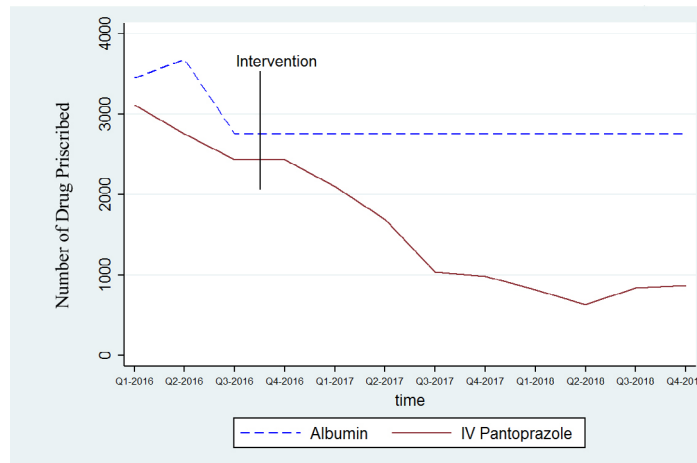* AAPC: Average Monthly Percent Change

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Figure 1. Albumin and IV pantoprazole use in hospitals in 2016-2018

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A pre and post-clinical pharmacists' interventional study was conducted by Vazin et al. to evaluate the use pattern and direct cost of 3 high-cost medications, including albumin and IV pantoprazole in a hospital in Shiraz City, Iran. The obtained results indicated that after the intervention, the administered medication and their cost significantly decreased by 50.76%. Moreover, the direct cost of albumin and IV pantoprazole significantly decreased by 55.8% and 83.92%, respectively [23]. Reduced mean frequency of albumin vial and IV pantoprazole in our study, compared to pre-intervention was measured as 48% and 70%, in sequence. Additionally, these findings were in line with those of a study by Rafsanjani et al. who found that protocol implementation in the hospital ward can decline 19% and 43% in IV pantoprazole and albumin vials prescription, respectively [10].

In our interventional study, the use of pharmaceutical guidelines led to the RUM and saving its cost in hospitals. This recommendation was previously made by a few similar studies to reduce IRUD in the world with drug use evaluation. Ala et al. evaluated using albumin in a teaching hospital in Tehran City, Iran. They described how to RUM and its cost-saving with pharmaceutical guidelines [24]. Another study evaluated the pattern of albumin use in a large university-affiliated hospital in Iran; the obtained data highly suggested a mandatory need for education physicians to revise the prescribing strategies for expensive drugs, like albumin [25]. In this regard, promoting rational prescribing with clinical guidelines in Bangladesh [2] and 12 developing countries [26] was reported.

A cost-saving of USD 50000 annually in the study hospitals by educational and management measures,
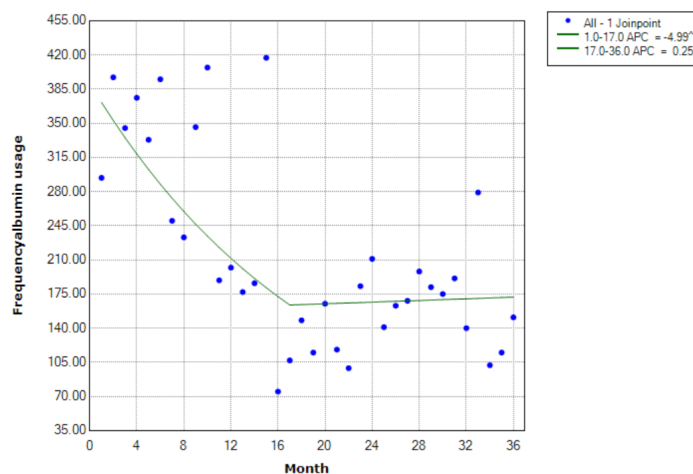

Figure 2. The average percentage of change per month in albumin usage in hospitals in 2016-2018
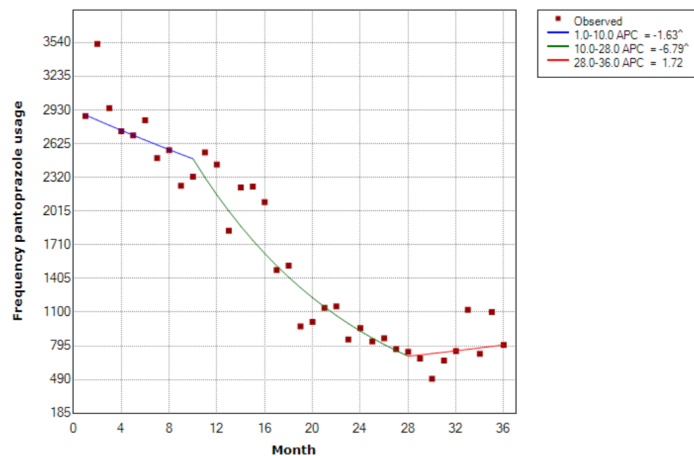
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Figure 3. Average percentage change per month in IV pantoprazole usage in hospitals in 2016-2018

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like pharmacist-led intervention, has resulted in only two expensive drugs. This intervention was performed in another research by Dastan et al. in a tertiary referral hospital in Iran. They introduced an evidence-based guideline for albumin via a pharmacist-led audit and feedback leading to a reduction of USD 38800 [27]. Similar findings announced a USD 77720 cost reduction for three medicines (albumin, IV pantoprazole, IV immune globulin) in a referral hospital in Shiraz City, Iran [23]. The cost reduction revealed a decrease in the antibiotic expenditure of approximately Euro 3.6 million in a study by Piovani and associates [28].

Conclusion

Prescription strategies, such as pharmaceutical guidelines with educational measures, pharmacist-led intervention, monitoring the prescribing drug, and feedback to prescribers can significantly decrease the inappropriate use of expensive drugs and their costs. However, most similar studies focusing on drug cost management were regionally conducted in Iran. Therefore, further studies are required at the national level to allow accurate assessment of the cost-effectiveness of these intervention strategies. In particular, Iran's health reform plan embodies such a policy.

This study overlooked examining the trend of the two expensive drug use in the studied years, regardless of the number and type of patients in the hospitals that may affect the extent of consumed medications.

Ethical Considerations

Compliance with ethical guidelines

This project was approved by the Ethics Committee of the MoHME in Iran (Code: IR.JUMS.REC.399.068).

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Authors' contributions

Data collection: Vahid Kohpeima Jahromi, Mohamad Rahmanian; Data analysis: Nader Sharifi; Writing and drafting the manuscript: Vahid Kohpeima Jahromi, Rahim Raoofi; Approval of the final manuscript: All authors.

Conflict of interest

The authors declared no conflict of interest.

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