

Investigation on Intervention Effects of Applying Proton Pump Inhibitors in Inpatients

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Research article

Keywords: inpatient, proton pump inhibitor, rational use

Posted Date: October 11th, 2019

DOI: <https://doi.org/10.21203/rs.2.15963/v1>

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Abstract

Background. To investigate the intervention effect of clinical pharmacists on irrational use of proton pump inhibitors (PPIs) in clinicians.

Methods. A cross-sectional study was used to through the hospital information management system survey, before intervention (July 15th, 2016, Aug 15th, 2016 and Sep 15th 2016) and dry prognosis (July 15th, 2017, Aug 15th, 2017 and Sep 15th, 2017) all the use of PPIs inpatients related information. According to the guidelines of "drug instructions" and "experts on stress ulcer prevention and treatment experts", the standard of drug use was formulated, and the use of PPIs before and after intervention was evaluated and analyzed in accordance with the standard, and the results of intervention were evaluated.

Results. The total number of hospitalized patients surveyed before the intervention was 1,693, the average utilization rate of proton pump inhibitors was 27.05% and the coincidence rate was 52.40%. The total number of hospitalized patients investigated after the intervention was 2,095, the average utilization rate of proton pump inhibitors was 8.54%, and the coincidence rate was 68.16%. Before and after the intervention, there was no difference in gender ratio and age distribution, the decrease of the utilization rate and the improvements of the qualified rate after intervention were statistically significant.

Conclusion. According to the standards of PPIs, clinical pharmacists strictly implement the special prescription review system and other intervention measures, which can significantly improve the level of PPIs rational clinical medication.

Background

Proton pump inhibitors (PPIs) are highly specific inhibitors of gastric acid secretion, which can specifically block the terminal part of gastric acid secretion from the gastric parietal cells, thereby reducing gastric acid secretion, and are effective gastric acid secretion inhibitors. As a therapeutic and preventive drug, PPIs have a wide range of clinical indications, and their use rate is rapidly increasing [1, 2]. However, with the widespread use of the clinic, the overuse of PPIs, the interaction of drugs, and the safety of long-term medication have received much attention.

In China, there are six PPIs including omeprazole, lansoprazole, pantoprazole, rabeprazole, esomeprazole and ilaprazole available as both oral enteric-coated tablets and intravenous injections and as both generics and originators [3]. Only omeprazole is listed in the catalogue of national essential medicine. Generic PPIs are available with lower cost than originators, and oral PPIs have similar in treatment effectiveness to injectable PPIs on equivalent doses. Nevertheless, previous studies indicated considerable use of injectable and originator PPIs. The "Consensus Review for SUP and Treatment" and "Prevention and Treatment of Stress Related Mucosal Disease" were published in 2015 in China to promote the rational prophylactic use of PPIs and improve the prevention of stress ulcers [4]. In addition, it also has been reported that the problem of clinical overuse in China and abroad is prominent [5,6]. To this end, this study is conducted to explore the intervention effect of clinical pharmacists on the irrational application of PPIs and provides a scientific basis for clinical safe drug use.

Methods

Data collection

Through the hospital information management system survey, we collected all the use of PPIs inpatients related information before intervention (July 15th, 2016, Aug 15th, 2016 and Sep 15th 2016) and dry prognosis (July 15th, 2017, Aug 15th, 2017 and Sep 15th, 2017).

A cross-sectional study was conducted to retrospectively analyze the situation before and after the intervention. The names, gender, clinical diagnosis, surgical name, PPIs usage and dosage of patients with PPIs before intervention were collected to analyze the clinical use of PPIs. In view of the problems existing in the pre-intervention investigation and analysis, the PPIs drug product specification was used as a standard, and the "experts on stress ulcer prevention and treatment experts" (2015 edition) is used to formulate clinical preventive use standards for PPIs, and to strictly control the indications and medications for preventive use [4]. For the course of treatment, patients with preventive medication must have clinical indications for preventive medication.

The injection time of proton pump inhibitors

Patients can prevent the use of PPIs for injection: 1. advanced age (age \geq 65 years); 2. severe trauma (cranial trauma, burns, chest, abdominal complex, difficult major surgery, etc.); 3. combined with shock or persistent hypotension; 4. Severe systemic infection; 5. complicated with multiple organ dysfunction syndrome, mechanical ventilation > 3 days; 6. severe jaundice; 7. combined with coagulation mechanism disorder; 8. organ transplantation; 9. long-term application of immunosuppressive agents and parenteral nutrition; 10. there was a history of ulcers during the year; 11. large areas of cerebral infarction, cerebral hemorrhage, severe craniocerebral trauma, and severe intracranial infection. In addition, focus on monitoring, reviewing, finding problems, and correcting the medical records of preventive PPIs.

Observation index

The number of patients in the two stages was collected. The PPIs used data of 5 types, cases, and the data of top 5 departments using PPIs.

Statistical analysis

Statistical analysis was performed using SPSS 17.0. The measurement data were expressed as mean \pm standard deviation. The *t* test was used for comparison between the two groups. The count data was expressed by the number of cases or rate (%) and χ^2 test was further used, and the difference was statistically significant at $P < 0.05$.

Results

Before the intervention, the total number of hospitalizations was 1693, and the average PPIs utilization rate was 27.05%. Among them, the reasonable use rate of PPIs was 52.40%, and the unreasonable use rate was 47.60%. Unreasonable main performance is 65.60% of drugs without indication, 22.02% of preventive drugs, and 11.02% of combination drugs. The top 5 departments with digestive medicine included gastroenterology, spinal joint surgery, intensive care, oncology, and traditional Chinese medicine. After the intervention, the total number of hospitalizations was 2,095, and 179 cases of PPIs were used, with an average utilization rate of 8.54%. Among them, 122 cases were evaluated as PPIs with a reasonable rate of 68.16%. Unreasonable in 57 cases, the unreasonable rate was 31.84%. Among them, the average utilization rate of the top five departments before the intervention changed: 42.74% in the department of gastroenterology, 93.78% in the department of spinal surgery, 33.85% in the Oncology, and 34.75% in the department of Traditional Chinese Medicine (Table 1).

The frequency of use of PPIs, the use of PPIs in hospitalized patients involved 48 varieties of 5 varieties, the highest frequency of use was 267 cases of omeprazole sodium for injection, accounting for 55.28%; followed by 165 cases of pantoprazole sodium for injection, accounting for 34.16%; the frequency of use of PPIs. After intervention, the PPIs used in hospitalized patients involved 182 cases of 4 varieties. The highest frequency of use was 126 cases of omeprazole sodium for injection, accounting for 69.23%; followed by pantoprazole for injection. 45 cases of sodium, accounting for 24.73% (Table 2).

For the comparison of patients' condition and average usage rate before and after intervention. There was no significant difference in gender ratio ($p = 0.334$) and age mean ($p = 0.826$) before and after intervention. There were also no significant difference in the average length of stay ($p = 0.598$), cure rate ($p = 0.090$) and mortality ($p = 0.449$) among the current patients before and after the intervention. The average usage rate ($p < 0.001$) and reasonable rate ($p = 0.010$) of PPIs in inpatients before and after intervention were statistically significant (Table 3).

Discussion

Clinical implications

Gastric acid secretion is an inherent physiological function of the human body. It is associated with many physiological activities. Only when it is necessary to prevent and treat certain digestive diseases, it is necessary to increase the pH value in the stomach. PPIs is a relatively safe type of acid suppression preparations, but overuse can also cause electrolyte metabolism disorders such as calcium and magnesium [7], and increase the risk of infection and other adverse consequences [8], which should be paid enough attention. Indications for the use of drugs for digestive tract gastric acid-related diseases are not accurate enough, which may lead to therapeutic abuse of PPIs [9]. Fear of gastrointestinal bleeding, lack of attention to side effects of acid suppression, and unfamiliar indications for emergency ulcer prevention are the main causes of preventive abuse of PPIs [10]. The development of PPIs clinical drug standards, strict control of preventive drug indications, strict implementation of special prescription review system and other interventions can effectively reduce the use of PPIs, improve the rational use of PPIs, save resources, and reduce medical costs and risks [11].

In this study, the average use rate of PPIs before intervention was 27.05%, which was basically consistent with the literature reports [12]; irrational use of drugs was 47.60%, higher than reported in the literature (34.00%) [13]. Among the patients with irrational use of drugs, 65.60% of the drugs were not indicated, and the preventive drug was not suitable for 22.02%, indicating that the clinical drug indications were not well mastered. After the intervention, the average utilization rate of PPIs was 8.54%, and the total ratio of irrational medication was 31.84%. After the intervention, the average use rate and irrational drug use ratio of PPIs decreased significantly ($P < 0.05$). Among the patients with irrational medication, the preventive medication was not suitable for 50.88%, and the indication was 45.61%, indicating that the rationality of clinical medication was improved after the intervention of clinical pharmacists.

Preventive overuse of PPIs is a worldwide problem [14]. In this study, the top 5 departments with the average pre-intervention rate, except for the department of gastroenterology, were mostly preventive PPIs. In addition, there are also indications, super-instructions, such as diagnosis of knee arthritis, cervical spondylosis, treatment with injection of omeprazole. After the intervention, the average utilization rate of the department was reduced by nearly 50%, and the average use rate of the spine joint surgery decreased by 93.78% dramatically.

Before and after the intervention, the PPIs used involved five varieties of specifications, the highest frequency of use was omeprazole for injection, followed by pantoprazole for injection. Omeprazole is the first generation of PPIs, which is characterized by large differences in the bioavailability of the drug, and is susceptible to food or other drugs. Pantoprazole is a third-generation PPIs drug. Compared with omeprazole, pantoprazole has high bioavailability and remains stable, independent of food intake and antacids, through cytochrome P450 enzymes. Other drugs that metabolize have less interaction than omeprazole, and pantoprazole is superior to omeprazole in terms of safety and efficacy. The results of the survey showed that the frequency of use of the first-generation PPIs was the highest, both before and after the intervention, and the third-generation PPIs with higher efficacy and safety were only half the former. It shows that most of the time clinicians choose drugs according to their habits, and there are still insufficient concerns about the safety and effectiveness of drugs. Clinical pharmacists should increase their medical advice and prescription comments in this regard and make proper guidance.

In addition, the average use rate of PPIs was 94.3% before the intervention, which was significantly higher than that reported in the literature (43.24%) [15]. For inpatients, the medication is well compliant, making physicians more inclined to use injections. Studies have shown that gastric juice $\text{pH} > 4$ can achieve the purpose of preventing stress ulcers [16], most PPIs oral preparations were given the usual amount, gastric juice within 24h of 90% of patients can reach this pH, if administered half an hour before breakfast and dinner, the ratio of pH in the stomach will be higher [17]. For patients without oral disorders, elective surgery, and indications for prevention of stress ulcers, oral medications can be used for prevention purposes. For postoperative patients, once enteral nutrition is acceptable, preventive use of PPIs should be discontinued [9]. Compared with oral administration, the intravenous administration process is more complicated, requiring open venous access, nursing manual care, increasing medical safety risks and medical costs, and oral administration is convenient to use, reducing labor costs and saving medical resources. Excessive use of injections not only increases the medical burden and medical risks, but also increases the workload of clinical treatment and increases the economic burden of patients, which should be taken seriously.

The age and gender distribution of patients before and after intervention were similar ($P > 0.05$). After the intervention, the use rate of PPIs was greatly reduced, and the reasonable rate was significantly increased ($P < 0.05$). There was no significant difference in the

average length of stay, cure rate and mortality ($P>0.05$), indicating that the significant reduction in the use of PPIs in inpatients after intervention did not affect the patient's treatment effect.

The intervention of clinical pharmacists promotes the rational use of PPIs, but there are still problems such as insufficient mastery of medication indications and irrationality of drug selection. In the future work, clinical pharmacists should strengthen the training of relevant knowledge and skills of clinicians and improve the rational use concept of clinicians; conduct regular special investigations, increase the evaluation of relevant doctors, and make timely feedback of problems to improve medical safety and reduce medical risks. Constrained by the research methods, this survey failed to evaluate the clinical course of treatment and adverse reactions of PPIs and needs further investigation.

Perceived limitations

One of major limitations of this study was the results still retained sufficient statistical power to evaluate the presence of any subgroup differences among the various factors for improvement the level of PPIs rational clinical medication given the rather large sample size. Secondly, due to the selected study subjects are based on the volunteers, the potential selection bias is inevitable because the participants who made a roust decision to be in the study hospitals. Voluntary bias could be viewed as the fact that a special sample could contain only those study subjects who are totally willing to join to the investigation and who participate and find the topic specially interesting are much possible of one's own free for that study, same to those who are look forward to be estimated on a positive level [18]. Thirdly, the generalization and external validity for the results should be further discussed. Finally, this study only obtained subjects from one teaching hospital in China as the target population. Therefore, the results of this study should not be extrapolated to hospitals in other regions of China. Future studies with random sampling approach of hospital selection over a wider range of regions would make the study more representative.

Conclusions

In conclusion, the active intervention of clinical pharmacists on the irrational use of drugs by clinicians can effectively improve the rational use of drugs by clinicians, reduce irrational drug use behavior, improve efficacy, and reduce medical safety hazards, which is worth promoting.

Abbreviations

PPIs: proton pump inhibitors

Declarations

Ethical approval and consent to participate

Declarations

All procedures were approved in accordance with the guidelines of our institutional ethics committee of Hechi Third People's Hospital, Guangxi, China (No. Z2016785) and adhered to the tenets of the Declaration of Helsinki. All study participants' information were anonymous. Subjects were asked to sign a letter of authorization before study. The anonymity and confidentiality of participants were ensured by using numerical codes for clinical information and destroying all the data at the end of investigation. The data supporting the conclusions of this article are included within the article.

Consent to publish

Not applicable

Availability of data and materials

All data underlying the findings are within the paper.

Competing interests

The authors declare that they have no competing interests *Funding*

There was no additional financial support from public or private sources *Authors' contributions*

Guotong Qing, Jian Wu, Runfong Wei, Di Wu, and Yipping Gou conducted the study and drafted the manuscript. Lizheng Huonh and Shenjun Wu participated in the design of the study and performed statistical analyses. Zhu Liduzi Jiesisibieke and Ching-Wen Chien conceived the study, and participated in its design and coordination. All of the authors read and approved the final manuscript.

Acknowledgments

This article was given the guidance and help of Professor Yueming Jiang, Guangxi Medical University, China and Dr Tao-Hsin Tung, Cheng-Hsin General Hospital, Taipei, Taiwan. The authors appreciate the Sunflower Statistical Consulting Company, Kaohsiung, Taiwan for statistical advice.

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Tables

Table 1 Summary of changes in the use of PPIs in the five clinical departments before intervention [n(%)]

Department	Before Intervention				After Intervention			
	Total Inpatients(n)	Usage of PPIs (%)	Drug Evaluation		Total Inpatients (n)	Usage of PPIs (%)	Drug Evaluation	
			Reasonable(%)	Unreasonable (%)			Reasonable(%)	Unreasonable (%)
Gastroenterology	83	100.00	77.11	22.89	117	57.26	83.58	16.42
Spinal joint surgery	94	95.74	22.22	77.78	102	1.96	100.00	0.00
Intensive care medicine	15	80.00	100	0.00	13	69.23	77.78	22.22
Oncology	46	56.52	69.23	30.77	75	22.67	70.59	29.41
Chinese medicine	92	38.04	28.57	71.43	152	3.29	0.00	100.00
Total	1693	27.05	52.40	47.60	2095	8.54	68.16	31.84

Table 2 Comparison of frequency of use of PPIs before and after intervention n(%)

Drug Name	Before Intervention	After Intervention
Omeprazole sodium for injection	267(55.28)	126(69.23)
Pantoprazole sodium for injection	165(34.16)	45(24.73)
Rabeprazole sodium enteric capsule	42(8.70)	4(2.20)
Omeprazole enteric capsule	6(1.24)	7(3.85)
Pantoprazole sodium enteric-coated tablets	3(0.62)	0(0)

Table 3 Statistical analysis of the general condition of patients and the use of PPIs before and after intervention

Items	Before Intervention	After Intervention	p-value
Average age (yrs)	56.03	56.50	0.826
Male/Female	253/206	92/89	0.334
Average length of stay (days)	7.83	7.70	0.598
Cure Rate (%)	47.91	46.54	0.090
Mortality (%)	0.37	0.45	0.449
Usage Rate (%)	27.05	8.50	<0.001
Reasonable Rate (%)	52.40	68.16	0.010