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ORIGINAL ARTICLE

Impact of interventions targeting the inappropriate use of proton-pump inhibitors by clinical pharmacists in a hepatobiliary surgery department

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Abstract

What is known and Objective: At present, studies on the usage of proton-pump inhibitors (PPIs) have universal significance. In clinical practice, PPIs are widely used to treat a variety of acid-related diseases, but they can be inappropriately prescribed, leading to increased medical costs and patient harm. The study comprehensively evaluated the clinical effects of a clinical pharmacist intervention on inappropriate PPI prescriptions in a tertiary general hospital hepatobiliary surgery ward.

Methods: A retrospective, single-centre intervention study covering the periods of July-December 2018 and July-December 2019 was conducted. In the intervention group, clinical pharmaceutical care was initiated by a clinical pharmacist in the hepatobiliary surgery ward. Outcomes, including the clinical pattern of PPI utilization, the rate of inappropriate PPI use and safety outcomes, were compared between the two periods.

Results and discussion: In total, 1150 patients were admitted to the hepatobiliary surgery ward in our hospital in the study periods. Of these, 717 patients met the inclusion criteria for this study, and 420 and 297 patients were included in the pre-intervention and post-intervention groups, respectively. The PPI utilization rates before and after the intervention were 82.0% and 55.0%, respectively. The rates of inappropriate PPI use before and after the intervention were 48.9 and 22.7 per 100 patient-days, respectively. Clinical safety outcomes were nearly identical between before and after the intervention, but patients treated with PPIs were more likely to experience nosocomial pneumonia (2.4% vs. 0.6%).

What is new and Conclusion: The implementation of a clinical pharmacist intervention for PPI use decreased inappropriate PPI use during hospitalization without sacrificing clinical safety outcomes.

KEYWORDS

appropriate use of PPIs, clinical pharmacist, proton-pump inhibitors

1 | WHAT IS KNOWN AND OBJECTIVE

Proton-pump inhibitors (PPIs) are widely used to treat and prevent multiple gastric acid-related diseases.[1,2] PPI usage has grown over time in China and other countries.[3-12] Given their increasing use, the risks of PPIs and the problem of overuse have attracted the attention of physicians and industry.

Unreasonable PPI use can expose patients to harm. Several studies concluded that PPI usage increased the risk of various adverse effects.[13-16] It is thus essential to adopt an effective and rational approach to decrease inappropriate PPI use.

Many studies have demonstrated that clinical pharmacist interventions have a significant role in the rational use and costs of PPIs.[17-23] To date, little research has examined the effects of clinical pharmacist interventions on PPI use in hepatobiliary surgery wards. The only available study included patients undergoing elective surgery in a hepatobiliary surgery department.[24]

Hence, this study aimed to comprehensively evaluate the effectiveness of a clinical pharmacist intervention in a hepatobiliary surgery ward from the perspectives of PPI usage patterns, appropriateness and safety.

2 | MATERIALS AND METHODS

2.1 | Patients and setting

A single-centre retrospective pre- and post-intervention study was conducted in the Department of Hepatobiliary Surgery of Beijing Chaoyang Hospital (West Campus). The Department has 36 beds and handles approximately 1000 inpatient admissions annually. The study was divided into pre- and post-intervention stages according to the inclusion of pharmacists in the medical team. Patients who were admitted to this department in July-December 2018 and July-December 2019 were enrolled in the pre- and post-intervention groups, respectively. Patients receiving PPIs were eligible. The exclusion criteria were as follows: age <18 years, hospitalization for fewer than 3 days, presence of systemic diseases, transfer from or to other clinical departments for further treatment and use of PPIs within 14 days before hospitalization.

2.2 | Intervention

In the preintervention period, pharmacists were responsible for reviewing prescriptions remotely via the order management system. It was difficult to review inappropriate prescriptions. In the post-intervention period, a clinical pharmacist as certified by the Chinese Hospital Association was assigned to participate in the medical management of patients in the Department of Hepatobiliary Surgery. Specific daily pharmaceutical care mainly consisted of two parts. First, the clinical pharmacist participated in the daily medical rounds of all inpatients with the treatment team each morning. Subsequently, the clinical pharmacist reviewed the rationality of PPI use for each patient based on the daily rounds and made recommendations to the attending physician. In addition, the clinical pharmacist developed targeted educational interventions for physicians, rotation residents and nurses concerning the existing national guidelines and adverse effects of PPIs each quarter.

2.3 | Data collection

The data required in this study were gathered from the hospital information system and the EMRs by two clinical pharmacists who were blinded to the patients' group assignment. A structured data collection form was designed to recorded patients' demographic and medical characteristics, surgical variables and medicine orders in Excel.

2.4 | Evaluation criterion

2.4.1 | Determine the indication for PPI use

Based on the EMR review, the indication for PPI use for each patient was categorized as treatment or prevention.[25-28]

2.4.2 | Evaluate the appropriateness of PPI use

The evaluation criteria for PPI use followed those of Martindale: The Complete Drug Reference (39th), New Materia Medica, drug instructions, American Society of Health-System Pharmacists criteria and Expert consensus on the application of PPIs, as listed in Table 1.[29-32]

The purpose and appropriateness of PPI use were evaluated by two clinical pharmacists. Disagreements were explicitly resolved by a senior clinical pharmacist.

2.5 | Outcome measures

2.5.1 | Intervention analysis

In the post-intervention period, the clinical pharmacist reviewed each PPI-related order and issued a proposal, which was recorded and catalogued. Meanwhile, the frequencies of education on PPI use among patients and medical staff were recorded.

2.5.2 | Utilization pattern of PPIs for inpatients

The Anatomical Therapeutic Chemical Classification System and the defined daily dose (DDD) are recommended by the World Health Organization for measuring drug utilization in countries.[33] PPI utilization was analysed using the consumption, prescribing

TABLE 1 Appropriate indications and recommendations for PPIs

Indications for PPIs	Recommendation
Peptic ulcer disease	Standard dose QD; gastric ulcer 6-8 wk, duodenal ulcer 4-6 wk. For large ulcers patients, can extend the period
Gastroesophageal reflux disease(GERD)	Initial treatment: Standard dose QD, 8 wk Maintenance treatment: Standard dose or half dose QD, use for a long time Refractory GERD: Standard dose BID
Non-variceal upper gastrointestinal (GI) bleeding	①Before endoscopy: High dose ②After Endoscopic haemostasis treatment: For high-risk patients[a]: extend the period of high dose treatment, then standard dose BID 3-5 d, When the disease stabilizes, PO Standard dose QD until ulcer healing For low-risk patients[b]: Standard dose QD until ulcer healing
Zollinger-Ellison syndrome	Standard dose BID, then increase dose to 120 mg BID
Helicobacter pylori infection	PO Standard dose BID, 2 wk
Dyspepsia	Standard dose QD, 4-8 wk
Chronic gastritis	Mucosal erosion and/or acid-related symptoms, Standard dose QD, 4-6 wk
Pancreatitis	Severe pancreatitis: double dose QD, or standard dose BID; Patients without abdominal pain, blood routine, amylase normal can stop the drug Acute pancreatitis and chronic pancreatitis: standard dose QD/BID
Stress ulcer prophylaxis for high-risk patient[c]	IV Standard dose, When the patient is stable enough to tolerate adequate enteral nutrition or has taken food, the clinical symptoms begin to improve or the patient is transferred to the common room, the drug may be taken orally or gradually withdrawn
Prevention of NSAIDs (antiplatelets)-related ulcer for risk patient[d]	Standard dose QD until drug requiring prophylaxis is stopped
Prevention of chemotherapy-induced gastric mucosal injury	If there is stomach discomfort, PPIs can be applied in antiemetic regimen until the end of chemotherapy

Note: Standard dose: (a) for oral administration: omeprazole 20 mg daily, esomeprazole 20 mg daily, pantoprazole 40 mg daily, lansoprazole 30 mg daily and rabeprazole 20 mg daily; (b) for intravenous administration: omeprazole 40 mg daily, esomeprazole 40 mg daily, pantoprazole 40 mg daily, lansoprazole 30 mg daily and rabeprazole 20 mg daily;

High dose: IV 80 mg by fast infusion during 30 min then 8 mg hourly for 72 h.

Abbreviations: BID, twice a day; NSAIDs, non-steroidal anti-inflammatory drugs; PPI, proton-pump inhibitor; QD, once a day.

[a]Forrest grade Ia-IIb, difficulty in endoscopic haemostasis or uncertain efficacy of endoscopic hemostasis, combined use of antiplatelet drugs or NSAIDs.

[b]Forrest grade IIc-III.

[c]Coagulopathy (eg platelet count of <50 000/mm^3, INR ≥ 1.5); Mechanical ventilation for >48 h.

[d]NSAIDs and patient history of ulcer/GIB; NSAIDs and patient age > 60 y; NSAIDs and patient age > 60 y; NSAIDs plus concomitant use of any of the following drugs: corticosteroids, antiplatelets, and/or anticoagulants.

rate, DDD, defined daily cost (DDC), drug utilization index (DUI), prescribed daily dose (PDD) and DDD/100 patient-days before and after the intervention.[3,34] The variables were calculated and defined (Appendix A).

2.5.3 | The incidence of inappropriate PPI utilization

The rationality of PPIs was separately evaluated according to the purpose of use, including the indications, daily dose, duration, route of administration and inappropriate treatment continuation on discharge.

The incidence of inappropriate PPI usage was described as the number of days of inappropriate use per 100 patient-days rather than number of inpatients to accurately verify the incidence and minimize the influence of variation in the duration of therapy.[35]

2.5.4 | Clinical safety outcomes

The clinical safety outcomes included medical quality indices and adverse drug reactions. The medical quality indices were as follows: clinical cure rate, case fatality rate and average length of stay. The adverse reactions to PPIs included the incidence of nosocomial pneumonia, *C Difficile* infection and GI bleeding during SUP.

2.6 | Statistical analysis

Microsoft Office Excel® 2013 (Redmond) was used to collect the medical data for statistical analysis.

Qualitative and quantitative data were expressed as frequencies (percentage) and the mean ± SD. For qualitative data, the

chi-squared test or Fisher's exact test was used for analysis as appropriate. For quantitative data, if the data were normally distributed, then Student's *t*-test was applied. If the data were skewed, then the two-sample Wilcoxon rank-sum test was applied. Statistical significance was indicated by $P < .05$ in all analyses. IBM SPSS Statistics version 25 was used to analyse all statistical data.

3 | RESULTS

In total, 1150 patients were screened for inclusion during the study periods. Of these, 717 patients were finally included in our study and evaluated for PPI utilization. Among the included patients, 420 were assigned to the preintervention group, and 297 were assigned to the post-intervention group. Figure 1 describes the procedure of patient selection.

3.1 | Demographic status and patient characteristics

The patient demographics and characteristics are presented in Table 2. There were no significant differences between the two groups regarding the proportion of patients >65 years old, the gender distribution, the frequency of underlying disease and the use of parenteral nutrition. The PPI utilization rate during hospitalization in the hepatobiliary surgery unit was significantly reduced after the intervention (82.0% vs. 55.0%, $P < .001$).

The majority of patients received PPIs for prevention (Table 3). Among patients treated preventatively, the most common indication was stress ulcer, followed by dyspepsia for cancer and medication-induced ulcers. Many inpatients in both groups received PPIs without a clear indication. After implementation of the intervention, the proportion of patients treated with PPIs without an indication was significantly decreased (45.5% vs. 24.6%, $P < .001$). The proportion of patients receiving PPIs for treatment purposes was not changed by the intervention.

3.2 | Intervention analysis

A review of all PPI-related medication orders identified 356 pharmacist recommendations, 87.6% of which were accepted by the physicians (Table 4). During the intervention period, 215 patients received PPI education from a clinical pharmacist. Physicians (including rotating residents) and nurses were educated quarterly about the clinical practice guidelines and adverse effect of PPIs.

3.3 | Utilization patterns of PPIs by inpatients

Concerning PPI use in the hepatobiliary surgery unit, five PPIs were used in our hospital: omeprazole, esomeprazole, lansoprazole, pantoprazole and rabeprazole. The total DDD (14 304.67 vs. 6686) and DDD/100 patient-days (291.52 vs. 219.79) were substantially decreased by the intervention. Meanwhile, the DUIs of injectable omeprazole and oral

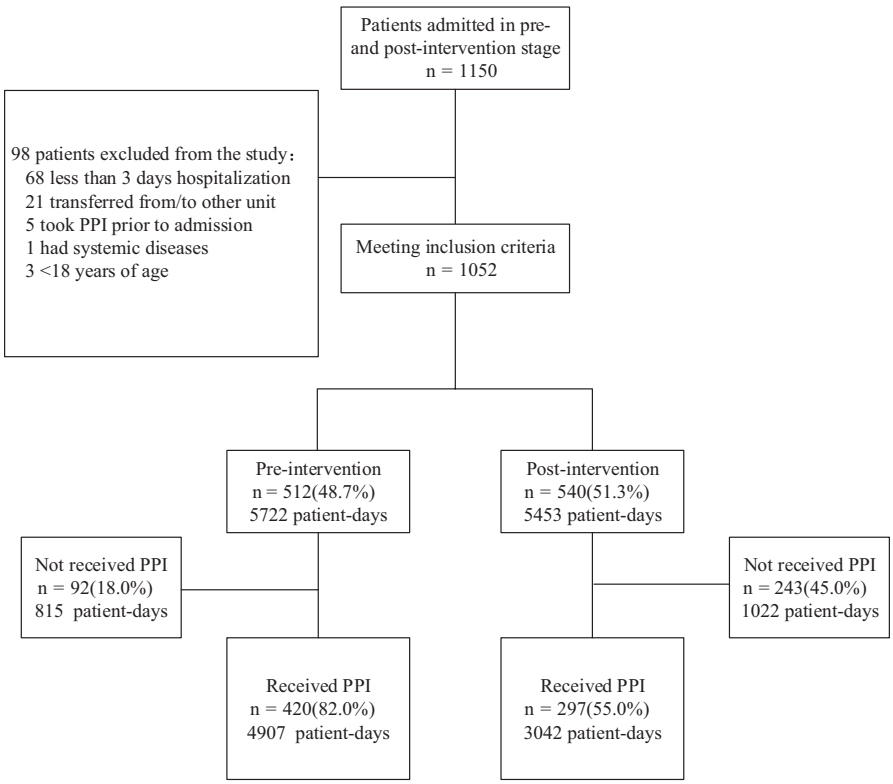

FIGURE 1 Patient selection flow chart

TABLE 2 Demographic and general characteristics of the included patients

Variable	Preintervention (n = 420, 82.0%)	Post-intervention (n = 297, 55.0%)	*P* value
Age ≥ 65 y (n, %)	114 (27.1)	98 (33.0)	.091
Gender, male (n, %)	211 (50.2)	162 (54.5)	.255
Underlying diseases (n, %)			
HTN	164 (39.0)	121 (40.7)	.648
HLP	51 (12.1)	41 (13.8)	.512
DM	97 (23.1)	86 (29.0)	.076
CAD	55 (13.1)	38 (12.8)	.906
OMI	4 (1.0)	2 (0.7)	1.000
AF	10 (2.4)	10 (3.4)	.430
CKD	3 (0.7)	1 (0.3)	.873
Parenteral nutrition (n, %)	323 (76.9)	214 (72.1)	.140

Abbreviations: AF, atrial fibrillation; CAD, coronary artery disease; CKD, chronic kidney disease; DM, diabetes mellitus; HLP, hyperlipidaemia; HTN, hypertension; OMI, old myocardial infarction.

esomeprazole declined from 3.94 to 2.82 and from 1.30 to 0.8, respectively, after the intervention. The PDDs of injectable omeprazole and oral esomeprazole declined from 78.86 to 56.38 mg and from 39.11 to 23.93 mg, respectively, after the intervention.

The injectable form of omeprazole was the most commonly used drug. After implementation of the intervention, the use of injectable omeprazole decreased (99.6% vs. 96.4%, $P < .001$). The number of PPIs prescribed, which accounted for 100% of the total volume, was increased after implementation of the intervention (2 vs. 5, Table 5). Changes in the varieties of PPIs and the proportion of tablet dosage forms grew after the intervention.

3.4 | The incidence of inappropriate PPI utilization

A comparison of the incidence of inappropriate PPI utilization between the two study groups is provided in Table 6. Cases of PPI usage without indications were directly classified as inappropriate PPI utilization, and PPI usage with indications was further analysed concerning the rationality of drug use. Inappropriate PPI use was decreased by the intervention (48.9% vs. 22.7%, $P < .001$). In the two groups, the lack of an indication was the most frequent cause of inappropriate PPI utilization, followed by inappropriateness of the daily dose, duration, route of administration and drug-drug interactions. The proportion of patients who were prescribed PPIs without any indication in the preintervention phase was 32.2%, vs 14.2% ($P < .001$) in the post-intervention phase. There were significant differences in the daily dose, duration and route of administration between the pre- and post-intervention groups for prevention indications (all $P < .001$), whereas no differences in these variables between before and after the intervention were noted for treatment indications.

The proportion of patients who inappropriately continued PPI therapy after hospital discharge was 0.5% in the preintervention group, compared with 0.7% in the post-intervention group. One patient (1.1%) in the preintervention group failed to receive a PPI despite having a proper indication. No such error occurred in the post- intervention group.

TABLE 3 Associated indications for PPI use

Indications (n, %)	Preintervention (n = 420)	Post-intervention (n = 297)	*P* value
Treatment			
Gastroesophageal reflux	8	5	.827
Helicobacter pylori infection	1	0	1.000
Gastric or duodenal ulcer	1	2	.762
GI bleed	7	2	.403
Pancreatitis	23	27	.061
Total	40 (9.5)	36 (12.1)	.233
Prevention			
SUP	162 (38.6)	181 (60.9)	<.001*
Medication-induced ulcers	5 (1.2)	2 (0.7)	.758
Chemotherapy-induced gastric mucosal injury	22 (5.2)	26 (8.8)	.064
Total	189 (45.0)	188 (63.3)	<.001*
No indications	191 (45.5)	73 (24.6)	<.001*

Abbreviations: GI, gastrointestinal; PPI, proton-pump inhibitor; SUP, stress ulcer prophylaxis.
*$P < .05$.

TABLE 4 Clinical pharmacist intervention analysis

Pharmaceutical care	Number	Accepted number (n, %)
Recommendations		
Start	15	13 (86.7)
Discontinuation	136	119 (87.5)
Dosage adjustment	78	70 (89.7)
Change route	124	107 (86.3)
Order entry error	3	3 (100)
Total	356	312 (87.6)
Education times		
Physician	Once a quarter	2 (100)
Nurse	Once a quarter	2 (100)
Patient	215	215 (100)

3.5 | Clinical safety outcomes

As shown in Table 7, there were no significant differences in medical quality indices and adverse drug reactions between the pre- and post-intervention groups. However, patients who received PPIs had a higher risk of nosocomial pneumonia, but not *C difficile* infection or GI bleeding, than those who did not receive PPIs.

4 | DISCUSSION

Previous reports described the improper use of PPIs in the ICU or in general medicine and surgery wards.[2,4-12] In the current study, the data clearly reflected and quantified the extent of inappropriate PPI use in a hepatobiliary surgery unit. Inappropriate PPI use significantly decreased after implementation of the clinical pharmacist intervention.

The results illustrated that the clinical patterns varied greatly. The DDD and DDDs/100 patient-days of PPIs decreased in the hepatobiliary surgery ward after the intervention, and the varieties and dosage forms of PPIs were also changed by the intervention. After the intervention, the DUI and PDD of PPIs were close to 1 and 40 mg, respectively. However, the DUI was higher than that reported by Jie Ying and colleagues,[3] indicating that additional improvements are needed to ensure the appropriate usage of PPIs.

An important issue identified in this study was the high proportion of hospitalized patients who were inappropriately treated with PPIs (48.9 per 100 patient-days). This proportion was higher than those previously reported in the USA (14.4, 26.8 and 20 per 100 patient-days).[22,35,36] The reason for the higher rate of irrational PPI use was that our study cases covered all indications for PPIs, whereas prior studies only examined specific indications for SUP.

The problem of inappropriate PPI use mainly focuses on the indications. PPIs were used for SUP among hospitalized patients who were no indication. In a cohort study of critically ill patients, the use of PPIs for SUP did not significantly reduce the incidence of GI bleeding and mortality, but the risk of hospital-acquired pneumonia was increased.[37] Recently published studies revealed that for low-risk patients, a reduction of bleeding risk may be unnecessary. Variable quality evidence suggested no notable effects of GI bleeding prophylaxis on mortality or in-hospital morbidity outcomes.[38] Thus, PPI prescriptions without indications result to unnecessary costs and risks to patients despite their minimal or non-existent therapeutic benefit.

Meanwhile, PPIs were inappropriately prescribed to prevent chemotherapy-induced emesis in patients with cancer. Antacids

TABLE 5 PPI utilization patterns before and after the intervention

	Preintervention (n = 420, 4907 patient-days)			Post-intervention (n = 297, 3042 patient-days)					
Metric	O^I	ESO^T	Total	O^I	ESO^I	P^I	ESO^T	P^T	Total
DDD (mg)	20	30	—	20	30	40	30	40	—
Total doses (mg)	284 920	1760	286 680	136 880	200	400	2920	5120	145 520
Total sale (CNY)	333 855.01	825.82	334 680.83	151 015.14	500.60	72.00	1 369.00	599.04	153 555.78
Medication days (d)	3613	45	3658	2286	5	10	122	128	2551
DDDs (n, %)	14 246* (99.6)	58.67 (0.4)	14 304.67	6444* (96.4)	6.67 (0.1)	10 (0.1)	97.33 (1.5)	128 (1.9)	6686.00
DDC (CNY)	23.44	14.08	—	23.44	75.09	7.20	14.07	4.68	—
DUI	3.94	1.30	—	2.82	1.33	1	0.80	1.00	—
PDD (mg)	78.86	39.11	—	56.38	40.00	40.00	23.93	40.00	—
DDDs/100 patient-days	291.52			219.79					

Abbreviations: DDC, defined daily cost; DDD, defined daily dose; DUI, drug utilization index; ESO, esomeprazole; I, injection; O, omeprazole; P, pantoprazole; PDD, prescribed daily dose; PPI, proton-pump inhibitor; T, tablet.

*$P < .001$.

TABLE 6 The incidence of inappropriate PPI utilization

	Preintervention (n = 420, 4907 patient-days)		Post-intervention (n = 297, 3042 patient-days)		*P* value
① Inappropriateness in indication (d, %)	1580 (32.2)		431 (14.2)		<.001*
② Inappropriateness in others (d, %)	Treatment	Prevention	Treatment	Prevention	—
Daily dose	0	782	0	96	—, <.001P*
Duration	4	611	2	45	1.000T, <.001P*
Route	9	223	6	89	.890T, <.001P*
Interaction	1	5	0	3	1.000T, 1.000P
Total	14 (0.3)	804 (16.4)	8 (0.3)	252 (8.3)	.854T, <.001P*
Total inappropriate utilization (d, %)	2398 (48.9)		691 (22.7)		<.001*
Inappropriate on discharge (n, %)	2 (0.5)		2 (0.7)		1.000
Inappropriateness not receiving PPIs (n, %)	1/92 (1.1)		0/243 (0)		.613

Abbreviation: PPI, proton-pump inhibitor.
[T]Comparison between the treatment groups.
[P]Comparison between the prevention groups.
*$P < .05$.

TABLE 7 Clinical safety outcomes

Variable	Receiving PPIs n = 717		No receiving PPIs n = 335	*P* value
	Preintervention n = 420	Post-intervention n = 297		
Medical quality indices				
Clinical cure rate (n, %)	402 (95.7)	288 (97.0)	——	.384
Case fatality rate (n, %)	7 (1.7)	3 (1.0)	——	.678
Average length of stay (d)	10.83 ± 8.75	9.95 ± 7.62	——	.162
Adverse drug reactions				
Nosocomial pneumonia (n, %)	12 (2.9)	5 (1.7)	2 (0.6)	.309[a], .045[b,*]
CDI (n, %)	21 (5)	17 (5.7)	15 (4.5)	.670[a], .570[b]
GI bleeding of SU (n, %)	4 (1.0)	1 (0.3)	0 (0)	.603[a], .296[b]

Abbreviations: CDI, *Clostridium difficile* infection; GI, gastrointestinal; SU, stress ulcer.
[a]Comparison between before and after the intervention.
[b]Comparison of treatment with and without PPIs during the study period.
*$P < .05$.

are not essential for preventing chemotherapy-induced emesis. If patients with cancer have dyspepsia, antacid therapy (H2 blockers or PPIs) can be considered because patients sometimes have difficulty discriminating heartburn from nausea. Emesis should be prevented using a combination regimen of olanzapine, an NK1 receptor antagonist, a 5-HT3 receptor antagonist and dexamethasone.[27]

The quality of clinical care was not significantly changed by the intervention. However, the results illustrated that patients treated with PPIs had a higher risk of nosocomial pneumonia. This is consistent with the findings of Anstey et al[18] The clinical pharmacist intervention targeting the rational use of PPIs did not deteriorate the quality of clinical care. On the contrary, such interventions can prevent the occurrence of adverse drug reactions.

Many previous studies described the responsibilities and roles of clinical pharmacists in various clinical specialties.[39-41] Under the Chinese chief pharmacist system, a consensus has been reached that clinical pharmacists can use their unique experience in pharmaceutical care and pharmacology to participate in the clinical treatment of patients and facilitate the rational use of drugs.[42,43]

In this study, the clinical pharmacist was only authorized to provide recommendations to the physicians or refuse to dispense drugs when inappropriate PPI prescriptions were received. In fact, only 87.6% of the recommendations were accepted by physicians. This is different from the results of studies in the USA and Iran,[19,35,36] in which clinical pharmacists were authorized to modify prescriptions for SUP. However, clinical pharmacists in China are not authorized to prescribe drugs. If physicians decline to accept their recommendations, the intervention will not achieve its purpose, which explains why the rate of inappropriate PPI use remained higher in this study than in previous research.

Some limitations of this study should be noted. First, this was not a randomized controlled study, and thus, some bias was unavoidable. Second, this study was retrospective, and it relied on clinical documentation, which can lead to variability based on the accuracy of documentation.

5 | WHAT IS NEW AND CONCLUSIONS

These findings highlight the role and significance of clinical pharmacists in the rational use of drugs. Intervention by clinical pharmacists helps to improve the awareness and prescribing behaviours of clinicians to achieve rational drug use, thereby effectively, safely and economically preventing and treating diseases. This successful strategy can be applied to the rational administration of other types of drugs or other hospital departments.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest relevant to this article.

AUTHOR CONTRIBUTIONS

YZ, QG and LHL designed the experiments and wrote the manuscript. LR and XZ collected data and prepared the tables and figures of the manuscript. JPY and HY evaluated the rationality of PPI use based on the aforementioned criteria. YZ and JK analysed the analysis and performed statistical analyses. YZ wrote the article. All authors revised and approved the final version of the manuscript.

ETHICS APPROVAL

The study was approved by the HPATC and Hospital Ethics Committee prior to its initiation. The committees permitted clinical pharmacists to make recommendations to the physicians but not to modify physicians' order when inappropriate prescriptions occurred.

PATIENT CONSENT STATEMENT

Because of to the retrospective nature of the study, the requirement for informed consent was waived.

PERMISSION TO REPRODUCE MATERIAL FROM OTHER SOURCES

Previously published illustrations were not used in this study, and permission was not required from the copyright holder.

DATA AVAILABILITY STATEMENT

All data generated or analysed during this study are included in the paper.

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APPENDIX A

Calculation and definition of variables

DDD = the assumed average maintenance dose per day for a drug used for its main indication in adults. The DDD is not restricted by the indication classification, dosage form or ethnic group.

DDC = total sales of the drug/DDD. DDC represents the price level of the drug and the average daily cost of the drug for the patient. A higher DDC indicates a greater financial burden, whereas a lower value indicates an obvious cost advantage for clinical practice.

DUI = DDD/actual medication days. DUI can be used as a metric to determine whether a clinical medication is reasonable. A DUI >1.0 indicates that the prescribed daily dose exceeds the DDD, and thus, the medication is unreasonable.

PDD = total dose/actual medication days. PDD is the average daily dose prescribed, as obtained from a representative sample of prescriptions.

DDD/100 patient-days = (DDD × 100)/total patient-days in the same period. This variable denotes the intensity and extensity of inpatient exposure to PPIs.