Retrospective Clinical Research Report

Journal of INTERNATIONAL MEDICAL RESEARCH

Journal of International Medical Research
48(10) 1–15

DOI: 10.1177/0300060520954729
journals.sagepub.com/home/imr
SAGE

Continuous improvement on the rationality of prophylactic injectable PPIs usage by a clinical pharmacist-led guidance team at a Chinese tertiary teaching hospital

Yun Hong, Ziqi Ye, Zhe Gao and Yuefeng Rao

Abstract

Objective: We aimed to evaluate the effects of a clinical pharmacist-led-guidance-team (CPGT) on improving rational prophylactic injectable proton pump inhibitor use (PIPU) and to explore the application of the Plan–Do–Check–Act (PDCA) method in promoting rational PIPU.

Methods: We conducted a retrospective study among 814 patients at a Chinese tertiary teaching hospital from January 2017 to December 2018. We enrolled 98 patients before the PDCA; 297 and 419 patients were included in first- and second-round PDCA cycles, respectively. The CPGT established the criteria for PIPU and conducted interventions, including medical record reviews, provision of feedback, clinician education, and outcome analysis. We analyzed the appropriateness and costs of PIPU before and after establishment of the PDCA cycle.

Results: Implementation of continuous CPGT-led intervention and a PDCA cycle significantly decreased the rate of irrational PIPU (53.06% vs. 8.57%), including duration, administration route, indication, and dosing frequency. Costs of total (USD 211.28 ± 162.33 vs. 53.17 ± 22.32) and inappropriate (USD 76.70 ± 59.78 vs. 2.25 ± 3.86) PIPU per patient were significantly reduced. The target compliance rate was 107.56%.

Conclusion: A CPGT can have an effective role in improving rational PIPU and optimizing administration through a PDCA cycle, to attain improved clinical and economic outcomes.

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Keywords
Prophylactic injectable proton pump inhibitor use, clinical pharmacist, intervention, Plan–Do–Check–Act, prescription evaluation, rational drug use

Date received: 27 February 2020; accepted: 6 August 2020

Introduction

Proton pump inhibitors (PPIs) are the first choice of treatment for esophagitis and peptic ulcer disease.[1,2] PPIs are also one of the most widely prescribed medicines in hospitals. A study in the United States showed that the proportion of prescriptions for PPIs doubled from 1999 to 2012.[3] In China, the annual use of PPIs has exceeded that of hypertension drugs and diabetes drugs and is second only to antibacterial drugs. In practice, however, not all PPIs are used following evidence-based guidelines, and irrational use is common.[4–6] Nearly USD 2 billion is spent globally every year for unnecessary PPI treatment, and inappropriate use of injectable PPIs (I-PPIs) accounts for 56% of all inappropriate PPI use.[7] In recent years, the irrational use of PPIs has become common in China, mainly involving unapproved indications and excessive dosages.[8,9] In addition, the negative effects of PPI use are generally underestimated owing to marketing and reporting bias in published trials. Widespread and inappropriate use of PPIs is likely to translate into serious long-term adverse effects such as increased gastrointestinal tract infections (e.g., *Clostridium difficile*-associated diarrhea), reduced intestinal absorption of vitamins and minerals, pneumonia, increased fracture risks,[10–14] kidney damage[15,16] and liver adverse effects.[17] These have undoubtedly given rise to new problems and challenges in the utilization of PPIs.

PPIs are available as both oral tablets and intravenous injections. Oral therapy is seen as highly effective,[18] similar in effectiveness to I-PPIs at equivalent doses.[19] However, I-PPIs have a considerably higher cost than oral equivalents and limited medical justification for their routine use. In recent years, we have become aware that utilization of I-PPIs has increased rapidly, especially in stress ulcer prophylaxis (SUP). Studies have shown that most I-PPI prescriptions in hospitals are inappropriate, leading to increased health care costs and potential adverse effects.[20] In 1985, the World Health Organization (WHO) put forward the concept of rational drug use. Developed countries began to explore rational use of medicines earlier than other countries. Therefore, the rational use of PPIs, especially for I-PPI, is an urgent problem in China.[9,21] Measures are critically needed to improve I-PPI use and to reduce unnecessary drug costs.

"Plan–Do–Check–Act (PDCA) circulation" was proposed in the 1950s by Dr Edwards Deming, an American expert in quality management.[22] PDCA divides the process of management into four parts. A PDCA cycle involves the process of finding and solving problems in the quality management of various fields. PDCA is also applicable for continuous improvement of medical quality management. In this paper, we report the use of the PDCA method by a clinical pharmacist-led guidance team (CPGT) to continuously improve rational prophylactic injectable proton

pump inhibitor use (PIPU) in a Chinese tertiary teaching hospital, and we present with a cost analysis. This work may serve as a basis for a feasible service mode for clinical pharmacists.

Methods

Study design and participants

This retrospective study was conducted in a Chinese tertiary teaching hospital with 2500 beds. The study included four consecutive steps of the PDCA cycle, for eight stages of prescription evaluation (PE) (Figure 1). The study data were collected from inpatient records. The information of patients and data related to I-PPI administration were acquired from electronic medical records (EMRs). Patients were excluded for any of the following reasons: age under 18 years or over 80 years, died during hospitalization, had taken PPIs within 2 weeks prior to hospitalization, treating peptic ulcers, gastroesophageal reflux disease, *Helicobacter pylori* infection, Zollinger–Ellison syndrome, upper gastrointestinal bleeding, or functional dyspepsia.

The ethics committee of The First Affiliated Hospital, College of Medicine, Zhejiang University, approved this study. All patients enrolled in this study agreed to the use of their information for this study. Detailed patient information was kept private and is unavailable to the public.

Plan

Data collection and statistical analysis. The rate of I-PPI prescriptions was expressed as defined daily doses (DDDs)/100 inhabitants per day, and expenditures were used for measuring drug utilization and expenditure. The Chinese currency (renminbi, CNY) was used to determine expenditure for I-PPIs over time (7.0 CNY equals 1 USD). We did not adjust for currency inflation or deflation in computing the actual changes during this period. We investigated and

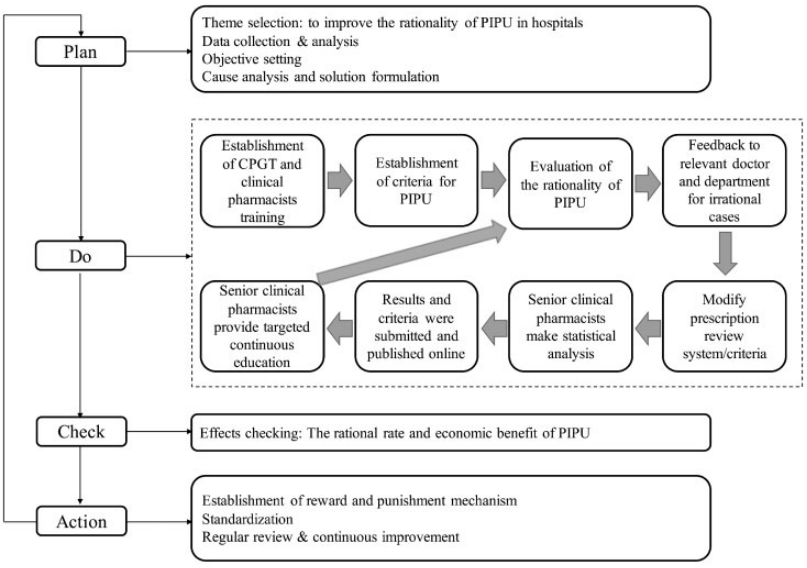

Figure 1. Process of pharmacist-driven intervention in improving rational PIPU using Plan–Do–Check–Act circulation.
CPGT, clinical pharmacist-led guidance team; PIPU, proton pump inhibitor use.

ranked I-PPI DDDs from October 2016 to March 2017 (3 months was considered a stage) as the pre-intervention period in our hospital, and selected 11 departments with the highest I-PPI DDDs for which "prophylaxis" was the purpose. We randomly selected cases from these departments and evaluated the rates of rational PIPU. Randomization was computer-generated. G*Power 3.1.9.4 (http: //www.softpedia.com/get/Science-CAD/G-Power.shtml) was used to perform power calculation and for sample size determination.

Statistical analysis was performed using chi-square and Student t tests with IBM SPSS software version 19.0 (IBM Corp., Armonk, NY, USA). Categorical variables are expressed as number and percentage; continuous variables are expressed as mean and standard deviation. Variables that are not continuously distributed were analyzed with the non-parametric Mann–Whitney U test. Statistical significance was defined as two-sided $P < 0.05$.

Objective setting. The objective of this study was to increase rational PIPU through PDCA and to evaluate the effects of intervention by a CPGT. The target value and target compliance rate were calculated using the following equation:

$$\text{Target value} = \text{Current rate} + \text{Improved value}$$

$$\text{Improved value} = \text{Current rate} \times \text{Intervention department} \times \text{Intervention coverage}$$

$$\text{Target compliance rate} = \text{Completion value}/\text{Target value}$$

Cause analysis and solution formulation. Based on the results of prescription evaluation of PIPU for patients before PDCA and the 80/20 rule, we created a fishbone diagram to analyze the causes of each factor; the main causes were identified for improvement (Figure 2). Ultimately, selection and integration of countermeasures according to the main causes were performed, including: 1) setting up evaluation criteria, 2) carrying out personnel training, 3) conducting special PE, and 4) carrying out clinical education.

Do

Establishment of the CPGT. We established a multidisciplinary CPGT for this study, which included clinical pharmacists, gastroenterologists, administrators in the department of medical affairs and the information department, as well as members of the pharmaceutical and quality management committee. The group was in charge of drafting and determining evaluation rules and presiding over the process to ensure that the work was carried out smoothly. Clinical pharmacists who had completed at least 1 year of residency in a ward and had taken training courses to become familiar with guidelines related to PIPU, were included in this study. Senior clinical pharmacists were in charge of carrying out a series of professional training sessions for the relevant departments to help them quickly become familiar with the criteria of rational I-PPI use.

Establishment of criteria for PIPU. According to the guidelines for I-PPI, the American Society of Health-System Pharmacists therapeutic guidelines and Chinese Medical Association therapeutic suggestions, we drafted the criteria for PIPU using an evidence-based method. The reference standards included therapeutic guidelines on SUP,[23] SUP in the postoperative period,[24] SUP in hospitalized patients not in intensive care units,[25] practice

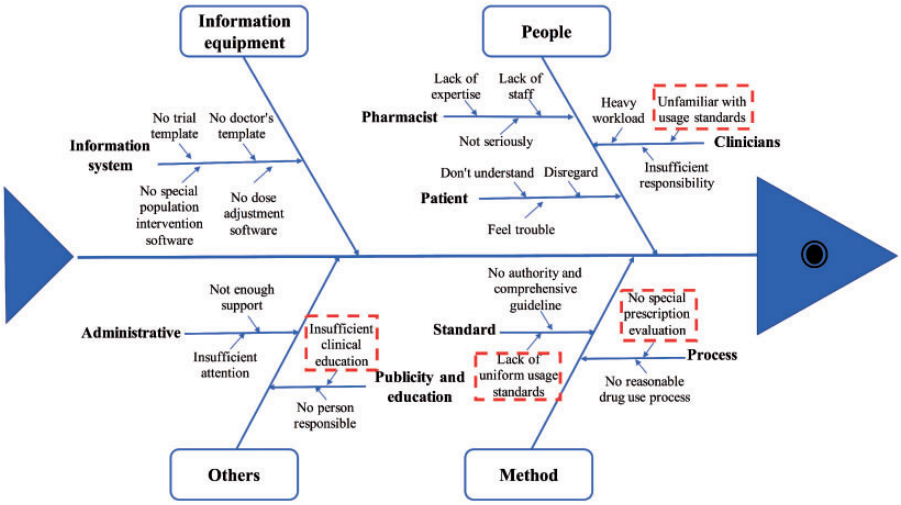

Figure 2. Fishbone diagram analysis of the main factors involved in high rates of irrational proton pump inhibitor use.

management guidelines for SUP,[26] prevention and treatment of general surgical stress-related mucosal disease,[27] expert recommendations for SUP,[28] prevention and treatment of stress-related mucosal disease,[29] and SUP.[30]

CPGT intervention. Inpatients were enrolled in the study during the pre-intervention (January to March 2017) and post-intervention (April to December 2017 and January to December 2018) periods, with 3 months defined as a stage. In each stage, CPGT-conducted interventions included: 1) evaluation of rational PIPU according to the established criteria; 2) data on inappropriate PIPU collected by pharmacists and communication with the prescribing doctor by E-mail or telephone for cases of irrational use; 3) revaluation and rechecking the case after feedback from doctors and modification of the prescription review system/criteria; 4) final statistical analysis performed by senior clinical pharmacists; 5) statistical results and review criteria submitted to the department of medical affairs and published online; 6) targeted continuous education provided by senior clinical pharmacists provide (Figure 1).

Check

Based on the established criteria, the same PE was conducted and compared before and after establishment of the PDCA cycle. The economic benefit was calculated using data provided by the information and statistics departments. The rate of rational PIPU was evaluated according to six aspects: indication, administration route, dosage and frequency, duration, drug selection, and medicine interactions.

Act

At each stage, statistical results and review criteria were submitted to the department of medical affairs and a reward-and-punishment mechanism was established. Additionally, aimed toward the problems found in the Check portion, the CPGT held meetings to discuss current issues that existed in the PE process and decided how to resolve them. The flowchart was

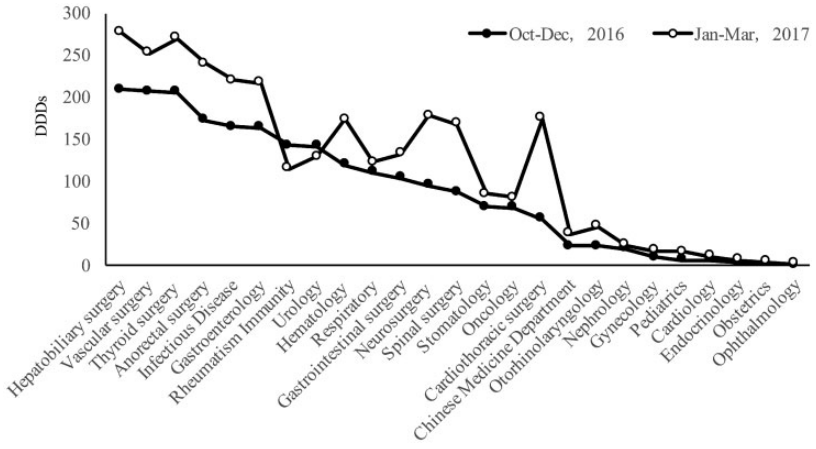

Figure 3. Utilization of injectable proton pump inhibitors for inpatients during October to December 2016 and January to March 2017.
DDDs, defined daily doses.

standardized for improvement and renewed every 3 months.

Results

Department selection

Based on the I-PPI DDDs from October 2016 to March 2017 before the PDCA cycle (Figure 3), we selected the 11 departments with the most frequent I-PPI use for "prophylaxis", including hepatobiliary surgery, vascular surgery, thyroid surgery, infectious diseases, anorectal surgery, urology, spinal surgery, neurosurgery, rheumatology, respiratory, and stomatology.

Patient characteristics

From January 2017 to December 2018, with 3 months defined as a stage, 814 patients received I-PPIs for prophylaxis in this study, including 98 patients during the pre-PDCA period (January to March 2017), 297 patients during first-round PDCA period (April to December 2017), and 419 in the second-round PDCA period (January to December 2018). General data for the eight stages are shown in Table 1. Among the 814 patients, most (56.63%) were men. There were no significant differences between the eight groups of patients with respect to demographics and clinical characteristics, such as sex, age, and length of hospital stay.

Practice and effects of adopting the PDCA cycle

Standards and objectives. According to the reference standards, we summarized major versus minor criteria for PIPU. After the CPGT held discussions and reached a consensus, the criteria for PIPU in the hospital were formulated (see Table 2). Among 98 patients in the pre-PDCA period, the rate of inappropriate PIPU was 53.06% (52/98). Inappropriate drug duration (18.4%, 18/98) was the most common reason for irrational use. The statistical results are shown in Figure 4. Based on the calculation, the target value of this project was a rate of rational PIPU of 85%.

Evaluation of clinical effects. After three stages of PE (April to December 2017, 3 months defined as a stage), the rate of irrational

Table 1. General characteristics of patients before and after establishment of PDCA cycle.

Characteristics	Before PDCA	After PDCA							*P*
	Phase I (n = 98)	Phase II (n = 99)	Phase III (n = 97)	Phase IV (n = 101)	Phase V (n = 105)	Phase VI (n = 103)	Phase VII (n = 106)	Phase VIII (n = 106)	
Male, n (%)	63 (64.28)	51 (51.52)	60 (61.86)	50 (49.50)	59 (56.19)	50 (48.54)	64 (60.38)	64 (60.95)	NS*
Age (years), mean ± SD	54.12 ± 17.58	56.55 ± 12.78	55.18 ± 12.52	54.06 ± 12.86	49.15 ± 19.38	50.61 ± 14.97	53.65 ± 17.72	52.57 ± 13.93	NS*
65–74, n (%)	19 (19.39)	18 (18.18)	15 (15.46)	13 (12.87)	12 (11.43)	13 (12.62)	17 (16.04)	11 (10.48)	
≥75, n (%)	8 (8.16)	7 (7.71)	8 (8.25)	7 (6,93)	6 (5.71)	5 (4.85)	6 (5.66)	5 (4.76)	
Length of stay (days), mean ± SD	14.52 ± 8.42	15.60 ± 10.31	13.64 ± 10.40	12.30 ± 7.83	12.11 ± 9.55	12.71 ± 9.01	12.53 ± 7.80	12.78 ± 8.11	NS*

Phase I: Jan–Mar, 2017; Phase II: Apr–Jun, 2017; Phase III: Jul–Sep, 2017; Phase IV: Oct–Dec, 2017; Phase V: Jan–Mar, 2018; Phase VI: Apr–Jun, 2018; Phase VII: Jul–Sep, 2018; Phase VIII: Oct–Dec, 2018.

*$P > 0.05$.

PDCA, Plan–Do–Check–Act; NS, not significant.

Table 2. Standard protocol for the use of prophylactic I-PPIs in hospitalized patients.

Major criteria	Minor criteria
① Respiratory failure (mechanical ventilation for more than 48 hours)	① ICU stay of >1 week
② Coagulation mechanism disorders (INR >1.5 or platelet $<50 \times 10^9$/L or APTT >2 times normal)	② Occult or overt bleeding for ≥3 days
③ Head injury (Glasgow Coma Score ≤10 or inability to obey simple commands) and spinal cord injury	③ High-dose corticosteroid therapy (>250 mg of hydrocortisone or equivalent daily)
④ Thermal injury involving >35% of body surface area	④ Long-term corticosteroid therapy (more than 1 month)
⑤ Multiple trauma with Injury Severity Score ≥16	⑤ Combination of non-steroidal anti-inflammatory drugs
⑥ Various difficult and complicated operations (according to surgical grades 3–4 in the "Surgical Classification Standards 2013 of the Ministry of Health" and the "Experts for the Prevention and Treatment of Stress Related Mucosal Diseases in China", and operation time >3 hours)	⑥ Combination of dual antiplatelet therapy
⑦ Hepatic failure	⑦ History of gastric ulceration or bleeding during the 1 year prior to admission
⑧ Shock or persistent hypotension	⑧ Acute renal failure
⑨ Sepsis	⑨ Indigestion or gastroesophageal reflux symptoms
⑩ Long-term fasting status (>7 days)	

Department	Evaluation basis	Dosage	Duration	Usage	Medicine interactions
ICU	Two major criteria or one major criteria and two minor criteria	Single dose/ QD or BID	Relief of major and minor criteria or patient can tolerate enteral nutrition	Reference drug instructions	Avoiding concurrent use of omeprazole and esomeprazole with clopidogrel
	One major criteria or two minor criteria	Single dose/QD			
Perioperative period	Hepatic or renal transplantation	Pre-operative: Single dose/QD	Pre-operative: 2–3 day		
	Long operation time (>3 hours) or excessive intraoperative bleeding (>1000 mL)	Postoperative: Single dose/ QD or BID	Post-operative: feeding basically meets daily needs (feeding half fluid) or can tolerate enteral nutrition, usually 5–7 days		
	Two major criteria or one major criteria and two minor criteria	Single dose/QD			
	One major criteria or two minor criteria				

(continued)

Table 2. Continued.

Department	Evaluation basis	Dosage	Duration	Usage	Medicine interactions
Drug related	Meets more than one major and minor criteria, and oral intolerance	Single dose/QD	Consistent with related drugs		
Chemotherapy related	Using intravenous antineoplastic agents with emetogenic potential	Single dose/QD	Before chemotherapy: the day or 1 day before or after chemotherapy: 2–3 days		
	Platelets $<50 \times 10^9$/L	Single dose/QD			
Disease related	Two major criteria or one major criteria and two minor criteria	Single dose/ QD or BID	Relief of major and minor criteria		
	One major criteria or two minor criteria	Single dose/QD			
Other	The doctor can submit relevant medical evidence through appeal and add it after discussion with CPGTs				

I-PPI, injectable proton pump inhibitors; ICU, intensive care unit; APTT, activated partial thromboplastin time; CPGT, clinical pharmacist-led guidance team.

PIPU decreased significantly (53.06% to 22.77%, $P < 0.001$). Obvious improvements were observed in inappropriate drug duration (18.37% to 0.99%, $P < 0.001$) and inappropriate administration route (10.20% to 2.97%, $P = 0.038$). The causes are compared in Table 3. However, the target value of this project was not reached, so we conducted a statistical analysis and began the second-round PDCA period. For another four stages of PE (January to December 2018, 3-month stage), obvious improvements were observed for no indications (6.93% to 0.95%, $P = 0.026$) and unnecessary drug replacement (3.96% to 0%, $P = 0.039$). The rate of irrational PIPU decreased from 22.77% to 8.57% ($P = 0.005$) (Table 4).

Economic benefit and I-PPI consumption analysis. As depicted in Table 5, the adoption of PDCA significantly decreased the average PIPU duration and average PIPU cost. Compared with before and after establishment of the first- and second-round PDCA cycles, the average PIPU duration (9.81 vs. 6.81 or 6.38 days, respectively; $P < 0.05$) and cost of total PIPU (USD 211.28 vs. USD 95.90 or USD 53.17, respectively; $P < 0.001$) were significantly decreased. Moreover, the cost of inappropriate PIPU per patient was also significantly reduced after two PDCA cycles (USD 76.70 vs. USD 14.21 and USD 2.25, respectively, $P < 0.001$). Furthermore, the DDDs of total and inappropriate PIPU per patient were significantly reduced after the first round of PDCA (147.42 ± 67.98 vs. 96.04 ± 78.69, 47.61 ± 15.37 vs. 12.60 ± 13.34, respectively; $P < 0.001$); these continued to decline after the second round of PDCA (96.04 ± 78.69 vs. 71.54 ± 49.86, $P = 0.008$, 12.60 ± 13.34 vs. 2.89 ± 3.73, respectively; $P < 0.001$). In brief, rational PIPU greatly decreased health care costs and reduced potential adverse effects.

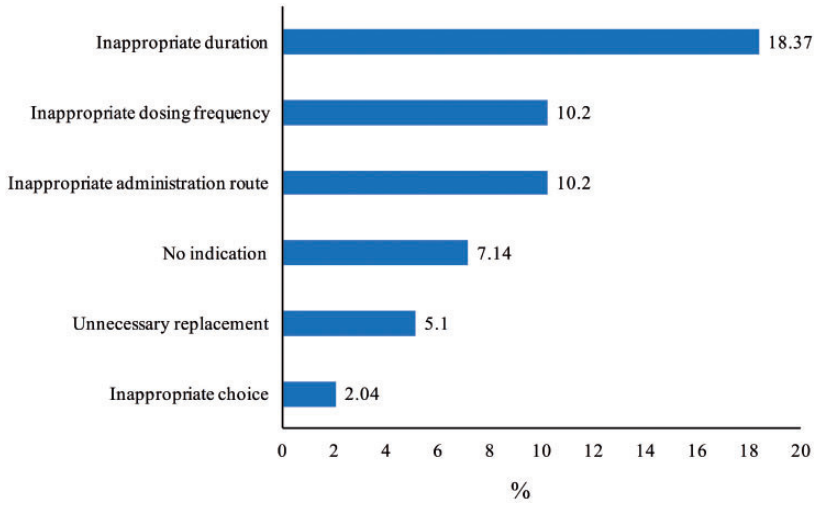

Figure 4. Reasons for irrational proton pump inhibitor use before Plan–Do–Check–Act cycles. PIPU: proton pump inhibitor use.

Continuous medical quality improvement. After the PDCA cycles, the effective intervention rate for inappropriate PIPU increased significantly, and irrational use decreased every 3 months (see Figure 5). In five stages of PE (April 2017 to June 2018), the rate of rational PIPU was 85.43%, reaching the target value of the project; this was maintained for the following 6 months. A much higher rate of rational PIPU was achieved after than before establishment of PDCA (46.94% of 98 patients during January to March 2017 vs. 91.43% of 106 patients during October to December 2018; $P < 0.001$). The target compliance rate was 107.56%.

Discussion

Our study showed that CPGT intervention could improve the rate of rational PIPU using two rounds of PDCA circulation, including optimization of prophylaxis duration, administration route and frequency, and use according to indications, among others. The incidence of irrational PIPU decreased from 53.06% to 8.57%. As the utilization of I-PPIs among inpatients was considerably higher than the WHO guidelines in developing countries,[31] a 44% reduction in the rate of irrational PIPU is clinically relevant and is critical for decreasing health care costs.

Several organizations have developed high-quality therapeutic guidelines and recommendations.[25–30] However, the implementation of these guidelines in routine clinical practice has been not effective. In analyzing the reasons for this, we found that the high utilization and expenditure of prophylactic I-PPIs was owing to inappropriate prescribing habits. Prophylactic I-PPIs should be given in the presence of high-risk factors. Once a patient is able to eat or can tolerate sufficient enteral nutrition and their clinical symptoms begin to improve, PPIs should be changed to oral formulations or gradually discontinued.[32,33] However, some clinicians have misconceptions including that oral PPIs are less effective than injectable formulations or that longer duration equals better efficacy. In our study, before establishment of the PDCA cycle, there were a total 38.77%

Table 3. Reasons for irrational PIPU before and after establishment of the first-round PDCA cycle.

	Before PDCA n (%)	PDCA-I n (%)			*P-value*		
	Phase I (n = 98)	Phase II (n = 99)	Phase III (n = 97)	Phase IV (n = 101)	P_1	P_2	P_3
Inappropriate duration	18 (18.37)	6 (6.06)	4 (4.12)	1 (0.99)	0.008	0.002	<0.001
Inappropriate administration route	10 (10.20)	5 (5.05)	2 (2.06)	3 (2.97)	0.173	0.018	0.038
Inappropriate dosing frequency	10 (10.20)	10 (10.10)	8 (8.24)	8 (7.92))	0.981	0.637	0.575
No indication	7 (7.14)	8 (8.08)	7 (7.22)	7 (6.93)	0.804	0.984	0.953
Unnecessary replacement	5 (5.10)	5 (5.05)	4 (4.12)	4 (3.96)	0.986	0.744	0.698
Inappropriate choice	2 (2.04)	2 (2.02)	1 (1.03)	0 (0)	0.991	0.567	0.149
Total irrational rate	52 (53.06)	36 (36.36)	27 (27.84)	23 (22.77)	0.018	<0.001	<0.001

P_1 indicates the *P*-value of phase II compared with phase I; P_2 is the *P*-value of phase III compared with phase I; P_3 is the *P*-value of phase IV compared with phase I.
Phase I: Jan–Mar, 2017; Phase II: Apr–Jun, 2017; Phase III: Jul–Sep, 2017; Phase IV: Oct–Dec, 2017.
PIPU, prophylactic injectable proton pump inhibitor use; PDCA, Plan–Do–Check–Act.

Table 4. Reasons for irrational PIPU before and after establishment of the second-round PDCA cycle.

	After PDCA-I n (%)	PDCA-II n (%)			*P-value*			
	Phase IV (n = 101)	Phase V (n = 105)	Phase VI (n = 103)	Phase VII (n = 106)	Phase VIII (n = 106)	P_1	P_2	P_3	P_4
Inappropriate dosing frequency	8 (7.92))	5 (4.76)	5 (4.85)	3 (2.83)	3 (2.86)	0.351	0.369	0.102	0.106
No indication	7 (6.93)	5 (4.76)	2 (1.94)	4 (3.77)	1 (0.95)	0.506	0.082	0.311	0.026
Unnecessary replacement	4 (3.96)	4 (3.81)	3 (2.91)	0 (0)	0 (0)	0.955	0.681	0.038	0.039
Inappropriate administration route	3 (2.97)	5 (4.76)	3 (2.91)	4 (3.77)	2 (1.90)	0.515	0.970	0.759	0.611
Inappropriate duration	1 (0.99)	1 (0.95)	1 (0.97)	1 (0.94)	1 (0.95)	0.977	0.988	0.972	0.977
Inappropriate choice	0 (0)	1 (0.95)	1 (0.97)	2 (1.88)	2 (1.90)	0.325	0.320	0.165	0.163
Total irrational rate	23 (22.77)	21 (20.00)	15 (14.57)	14 (13.21)	10 (8.57)	0.627	0.132	0.072	0.005

P_1 indicates the *P*-value of phase V compared with phase IV; P_2 is the *P*-value of phase VI compared with phase IV; P_3 is the *P*-value of phase VII compared with phase IV; P_4 indicates the *P*-value of phase VIII compared with phase IV.
Phase IV: Oct–Dec, 2017; Phase V: Jan–Mar, 2018; Phase VI: Apr–Jun, 2018; Phase VII: Jul–Sep, 2018; Phase VIII: Oct–Dec, 2018
PIPU, prophylactic injectable proton pump inhibitors use; PDCA, Plan–Do–Check–Act.

Table 5. Cost and consumption of PIPU before and after establishment of PDCA cycle.

	Before PDCA	After PDCA		*P*-value	
		PDCA-I	PDCA-II	P_1	P_2
Total rational rate of PIPU (%)	46.94	77.23	91.43	<0.001	<0.001
Duration of PIPU (days), mean ± SD	9.81 ± 7.73	6.81 ± 5.30	6.38 ± 4.91	0.016	<0.001
Cost of PIPU per patient (USD), mean ± SD	211.28 ± 162.33	95.90 ± 92.34	53.17 ± 22.32	<0.001	<0.001
Cost of inappropriate PIPU per patient (USD), mean ± SD	76.70 ± 59.78	14.21 ± 17.55	2.25 ± 3.86	<0.001	<0.001
DDDs of PIPU per patient, mean ± SD	147.42 ± 67.98	96.04 ± 78.69	71.54 ± 49.86	<0.001	<0.001
DDDs of inappropriate PIPU per patient, mean ± SD	47.61 ± 15.37	12.60 ± 13.34	2.89 ± 3.73	<0.001	<0.001

P_1 indicates the *P*-value of PDCA-I compared with Before PDCA; P_2 is the *P*-value of PDCA-II compared with Before PDCA.

PIPU, prophylactic injectable proton pump inhibitors use; PDCA, Plan–Do–Check–Act; DDDS, defined daily dose; SD, standard deviation.

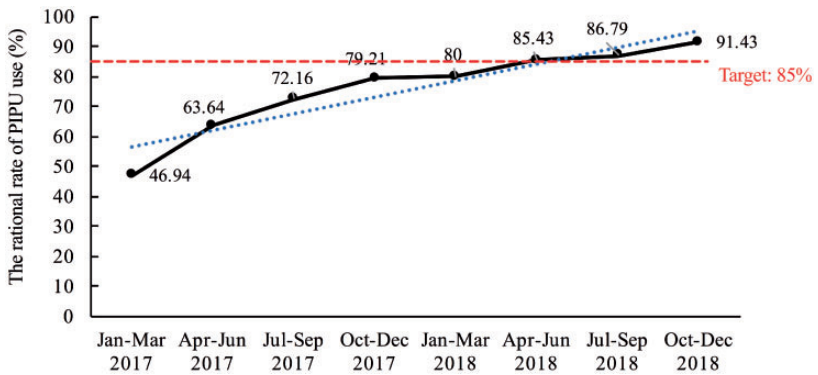

Figure 5. Rate of rational proton pump inhibitor use from 2017 to 2018, before and after establishment of the Plan–Do–Check–Act cycle.

cases of overdosage or excessive duration of I-PPI use for prophylaxis, among which 17.35% of cases were used until patient discharge. Furthermore, it has been reported that PIPU is not cost-effective, except in high-risk patients.[34] A survey revealed that some clinicians feel that PPIs are harmless and can be used by anyone.[35] Thus, clinicians prescribe I-PPIs in patients with low or no risk or no appropriate indications. The involvement of pharmacists may be promising, to help improve the above problems.

In this study, we demonstrated that the CPGT effectively improved the rate of rational PIPU by establishment of a PDCA cycle. The results of this work included economic benefits, with costs of total and inappropriate PIPU per patient significantly reduced. Furthermore, DDDs of total and inappropriate PIPU per patient were also effectively decreased. Most importantly, improvement

in the rate of rational PIPU continued for a long period after the CPGT intervention, indicating that the criteria of PIPU were successfully adopted by clinicians and well implemented in practice.

The main strengths of this study include PIPU standardization, application and implementation of a PDCA cycle, and effective pharmaceutical interventions. First, we developed criteria for PIPU using guidelines in a search of 10 databases and on the basis of consensus reached by a multidisciplinary CPGT. Detailed recommendations regarding indications, dose, frequency, and appropriate timing of PIPU were established in accordance with guidelines.[26–30] Second, we used PDCA circulation to ensure that the project was organized, systematic, and scientific. Standardization according to proven effective measures, to facilitate implementation and promotion, as well as other remaining issues, were automatically transferred to the next PDCA cycle for improvement. For example, clear improvement was observed in inappropriate duration and administration route of PPIs after the first-round PDCA cycle, and the rate of rational PIPU increased by 30%. However, some inappropriate indications and dosing frequencies remained, so these problems were transferred into the next PDCA cycle. After the second-round PDCA circulation, inappropriate indications and inappropriate dosing frequency were significantly reduced. Rational PIPU continued to improve, reaching our target value and maintaining it for more than 6 months. Third, we adopted effective pharmacological interventions, including review of medical records, feedback, and education outreach. The medication habits of clinicians were improved with educational outreach by the CPGT. The significant improvement in clinical and economic outcomes highlights the important role of a CPGT in promoting rational PIPU.

There are several limitations in this study. First, the data were collected from only one hospital. We only considered I-PPIs that were available at our hospital, although there are more than 300 brands of PPI available in China. Second, the results of this study are less convincing than those of a randomized controlled trial. Third, although rational PIPU increased significantly during the intervention phase, the sample size was small in this study. Additionally, the combination of clopidogrel and omeprazole or esomeprazole should be avoided;[36,37] several cases of inappropriate use were found before and after the PDCA cycles in our study. Therefore, larger sample sizes and further pharmacoeconomic analyses are warranted, to better quantify the outcomes. Prospective research is required to analyze the impact of clinical pharmacist involvement in enhancing the appropriate use of medications.

Conclusion

Rational PIPU can be appropriately achieved by CPGT intervention using the PDCA method, to attain beneficial clinical and economic outcomes. Nevertheless, inappropriate drug use cannot be completely avoided, so room for improvement remains. We hope that clinical pharmacists will actively participate in promoting rational drug use to yield optimal cost-effectiveness for patients. PDCA circulation can be effectively implemented to improve quality of care in numerous medical fields.

Acknowledgements

This study was supported by the First Affiliated Hospital of ZheJiang University. Yun Hong and Yuefeng Rao contributed to manuscript preparation and conceived and designed the study. Ziqi Ye and Zhe Gao contributed to the methods and data collection. Yun Hong wrote the manuscript.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was supported by the Zhejiang Provincial Natural Science Foundation of China (YY20H300002) and the Medical and Health Science and Technology Project of Zhejiang Province (2018KY402).

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