Original Article

Compliance with Guidelines for Stress Ulcer Prophylaxis in Surgical and Orthopedic Units at Ramathibodi Hospital

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Objective: Evaluate the appropriateness of proton-pump inhibitors [PPIs] use for stress-related mucosal disease [SRMD] prophylaxis in surgical and orthopedics units.

Materials and Methods: A retrospective chart review study was conducted among patients admitted to the surgical and orthopedic units and received PPIs during their hospitalization at Ramathibodi Hospital between August 30, 2016 and January 18, 2017. Demographic data, medical history, and pertinent laboratory tests were obtained from medical records. Available practice guidelines and related clinical studies were utilized as references for assessing appropriateness of PPIs use. Prescribing PPIs not according to the guideline is marked as inappropriate or improper.

Results: Of the 105 patients included in the present study, 58 patients (55.24%) were started on PPIs without indication as stated in the guideline. Twenty-four patients (22.86%) were continued on PPIs during hospitalization while their risk factors for SRMD was resolved. Twelve patients (11.43%) received PPIs dose inconsistent with the guideline, particularly too-high dose. Upon discharge, 37 patients (35.24%) continued to receive PPIs without proper indication.

Conclusion: Improper use of PPI was common in surgical and orthopedics units. Monitoring for PPIs use is required to ensure appropriate SRMD prophylaxis.

Keywords: Proton pump inhibitors, Stress, Ulcer, Prophylaxis, Acid-suppression

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Stress ulcer or stress-related mucosal disease [SRMD] is a condition that stressful event induces superficial lesions of the mucosal layer of the stomach, especially in the acid producing areas such as corpus and fundus[1]. SRMD may induce clinically important bleeding associated with several undesirable outcomes including prolonged hospital stay or increased mortality risk, particularly in critically ill patients[2,3]. Therefore, an evidence-based therapeutic guideline by the American Society of Hospital Pharmacy [ASHP] was published to guide clinician on appropriate use of acid suppressive agent to prevent SRMD in 1999[1]. Proton-pump inhibitors [PPIs] has been a commonly used agent for SRMD prophylaxis due to its superior efficacy data in reducing incidence of SRMD or clinically important bleeding when compared to histamine-2 receptor antagonists [H2RAs] or sucralfate[4,5]. However, even with the available guideline, inappropriate use of PPIs has been observed in several practice settings and several countries[6,7]. Therefore, a comprehensive evaluation on compliance to the evidence-based guideline for SRMD prophylaxis in Thailand is necessary to guide hospital policy on using PPIs.

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Material and Method

Study design and population

The present study was retrospectively conducted by reviewing medical records of the randomly-selected eligible patients who were adult patients (18 years or older) admitted in either surgical or orthopedics units at Ramathibodi Hospital between August 30, 2016 and January 18, 2017, and received an order for PPIs for

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SRMD prophylaxis. Patients who had been taking PPI prior to the index hospital admission or, were being admitted for the management of gastrointestinal [GI] bleeding or GI ulcer were excluded from the study.

Study outcome and data collection

The primary outcome of this study was appropriateness of PPIs use during hospitalization and upon discharge. Demographic data including age, sex, ward type, type of surgery or procedure, medical history, history of alcohol use, type of PPI used, an event of GI bleeding (melena stool or coffee ground emesis), discharge medication list, and pertinent laboratory parameters such as activated partial thromboplastin time [aPTT], international normalized ratio [INR], platelets, renal or liver function tests were obtained from medical records. Data collection was performed for every day of hospitalization of the eligible patients to allow a comprehensive evaluation for appropriateness of PPIs use throughout the process of hospital care, including initiation and discontinuation of PPIs, and discharge prescription for PPIs.

Criteria for appropriate PPIs use

For meaningful clinical application of the study results, we categorized appropriateness of PPIs use into three subgroups, 1) appropriate PPIs initiation, 2) appropriate PPIs discontinuation, and 3) appropriate PPIs prescription upon discharge. Criteria for appropriate PPIs use was developed by using the ASHP guideline as a main reference[1], along with the addition of significant risk factors associated with SRMD that have been studied or described in well-designed studies or clinical protocol that had been implemented in actual practice[3,8-10]. An order for PPIs was considered appropriate when the patient had at least one of mechanical ventilation, nasogastric [NG] or nasojujenal [NJ] tube insertion, hypotensive episode, liver failure with coagulopathy (INR >1.5, platelet $<50x10^3/\mu L$, or aPTT >2 times of baseline value), acute renal failure, sepsis, history of GI bleeding within one year prior to admission, administration of at least 250 mg per day of hydrocortisone or equivalent, Glasgow Coma Scale [GCS] of less than 10 points, thermal injury involving greater than 35% of body surface area, or post-operative transplantation (*de novo*).

In addition to the indications for starting PPIs, we also evaluated appropriateness of PPIs dosing. Appropriate PPIs dosing in the present study was defined as the PPIs dose that had been used in well-designed clinical studies, had efficacy to maintain gastric pH greater than 4 over 24-hour period, or described in systematic review, including lansoprazole 30 mg orally (or via NG/NJ tubes) as a loading dose [LD], followed by 15 to 30 mg daily, omeprazole 40 mg orally (or via NG/NJ tubes) as an LD, followed by 20 to 40 mg daily or omeprazole 40 mg intravenously [IV] followed by continuous infusion with the rate of 4 to 8 mg per hour, and pantoprazole 40 mg orally as an LD, followed by 20 to 40 mg daily[10-12].

Statistical analysis

Descriptive statistic was used to described data and outcomes of the present study. All computation was performed using SPSS Statistics version 18.0 (SPSS Inc., Chicago).

Ethical considerations

The present study was approved by the Committee on Human Rights Related to Research Involving Human Subjects, Faculty of Medicine Ramathibodi Hospital, Mahidol University. Protocol Number: ID 08-59-64 (MURA2016/550).

Results

One hundred five patients were randomly enrolled during the study period. Patient characteristics are shown in Table 1. In brief, majority of the patients were admitted in the surgical unit (93 patients, 88.57%) with similar proportion of male and female. Average age of the patients was 59 years. Three major reasons for admission were for GI tract surgery (57.14%) and cardiovascular surgery (20%) and orthopedic surgery (11.43%). Omeprazole was the most common agent used for SRMD prophylaxis (96%), followed by pantoprazole (3.8%) and lansoprazole (1.9%), respectively. Of note, some patient was switched between PPIs during their hospitalization. Each patient was studied for an average of 5.85, thus, 614 days for the study.

Upon PPIs initiation, inappropriate order was found in 58 patients (55.24%), of these, forty-nine patients were in surgical unit, and nine patients in orthopedic unit. Among 105 patients started on PPIs, regardless of whether the order was appropriate, 24 patients (22.86%) continued to receive PPIs when their risk factor(s) for SRMD disappeared during hospital stay. In terms of dosing, 12 patients (11.43%) received inappropriate PPIs dose, particularly a twice-daily dosing regimen. Further detail on inappropriate PPIs use for each unit is shown in Table 2.

At discharge, there were unnecessary prescriptions for PPIs in 37 patients (35.24%) due to the absence of

Table 1. Patient characteristics

Patient characteristics	All patients (n = 105)	Surgical unit (n = 93)	Orthopedic unit (n = 12)
Age (years), mean ± SD	59.08±15.08	58.88±14.70	60.67±18.43
Female, n (%)	58 (55.23)	51 (54.84)	7 (58.33)
Body mass index, mean ± SD	23.63±4.03	23.59±4.04	23.89±4.11
Comorbidities, n (%)			
Hypertension	45 (42.86)	42 (45.16)	3 (25.00)
Type 2 diabetes	18 (17.14)	16 (17.20)	2 (16.67)
Chronic kidney disease	10 (9.52)	10 (10.75)	0 (0.00)
Chronic liver disease	7 (6.67)	7 (7.53)	0 (0.00)
Peripheral arterial disease	7 (6.67)	7 (7.53)	0 (0.00)
Asthma	5 (4.76)	3 (3.22)	2 (16.67)
Cerebrovascular diseases	4 (3.81)	4 (4.30)	0 (0.00)
Dyspepsia/GERD	3 (2.86)	3 (3.22)	0 (0.00)
COPD	3 (2.86)	3 (3.22)	0 (0.00)
Previous GI bleeding (<1 year prior)	3 (2.86)	3 (3.22)	0 (0.00)
History of alcohol use, n (%)	21 (20.00)	20 (21.50)	1 (8.33)

GERD = gastroesophageal reflux disease; COPD = chronic obstructive pulmonary disease; GI = gastrointestinal

Table 2. Inappropriate proton-pump inhibitor use during hospitalization

Inappropriate events	All patients (n = 105)	Surgical unit (n = 93)	Orthopedic unit (n = 12)
Initiation, n (%)	58 (55.24)	49 (52.69)*	9 (75.00)*
Discontinuation, n (%)	24 (22.86)	23 (24.73)*	1 (8.33)*
Dosing, n (%)	12 (11.43)	9 (9.68)*	3 (25.00)*

* Percentage calculated using the number of patient in such unit as a denominator

SRMD risk factors, thirty-three patients were in surgical unit and four patients in orthopedic unit.

In addition, during the study period we also found four patients (3.8%) experiencing GI bleeding while taking PPIs. One patient in surgical unit experienced melena. Coffee ground emesis was found in two patients and one patient in surgical and orthopedic units, respectively.

Discussion

The result of this study confirmed that inappropriate use of PPIs in surgical and orthopedic units is common. Approximately half of the patients enrolled in this study received PPIs for SRMD prophylaxis without an indication stated in the guidelines, which we consider this practice as inappropriate. The rate of inappropriate PPIs initiation in the present study is twice as high as several other studies conducted in non-intensive care unit [non-ICU] settings in other countries. For example, the studies by Nardino et al and Parente et al reported the rate of inappropriate PPI use were 20% and 25%, respectively[13,14]. However, this rate is slightly lower than the previous study by Sirivunnabood and Barameerungsikul[15], conducted in Thai patients in the non-ICU settings, which the overall rates of inappropriate PPIs use was 65.1%. It is worth to note that the evidence supporting the use of acid suppressive agents for SRMD prophylaxis were mostly from the studies in ICU setting, therefore the benefit of using acid suppressive agent in non-ICU setting is still uncertain, especially when the clinical benefit such as reduction in significant GI bleeding has not been proven by any randomized controlled trial in non-ICU patients. Data from previous and the present studies suggest that monitoring for indication of PPIs for SRMD prophylaxis is warranted. Implementation of interprofessional collaboration among physicians, nurses, and pharmacists may reduce this PPIs overuse problem[16,17].

Another interesting result found in the present study was a significant number of patients (22.86%) who were started on PPIs did not have their PPIs discontinued when the risk factor for SRMD was resolved during hospitalization. To our best knowledge, we did not find any study specifically addressing this issue before. This is also an important problem for the hospital care process that we may put the patient at higher risk of experiencing possible short-term adverse events associated with PPIs use such as pneumonia, or *Clostridium difficile* infection unnecessarily[18]. Awareness for monitoring the valid of PPIs order during hospitalization of the patients should be raised.

We found a lower rate of unnecessary PPIs prescription at discharge (35.24%) when compared to other studies conducted in several regions of the world. The rates of inappropriate PPIs prescription at discharge in those studies were close to or above 50%, ranging from 48.9% to 68.8%[19-21]. A study in

Thai patients has not been conducted prior to the present study. This problem can lead to a life-time PPIs use posing a significant risk associated with long-term use of PPIs, such as bone fracture, hypomagnesemia, low vitamin B12 serum level, iron deficiency anemia, and acute interstitial nephritis[22].

Furthermore, GI bleeding was observed in 4% of patients taking PPIs during the study period. This number was in between the GI bleeding rate, ranging from 0 to 6%, among patients taking PPIs for SRMD prophylaxis previously reported in the literature[23,24].

To our knowledge, this is the first comprehensive study evaluating appropriateness of PPIs use throughout the entire hospitalization and at discharge. Criteria for evaluation of appropriate PPIs used were developed by combining the data from reliable clinical practice guideline and well-designed clinical studies. Due to the nature of retrospective study, recall bias might have occurred. In addition, due to small number of the patients in orthopedic unit enrolled, the rate of inappropriate PPIs use in the present study could have been overestimated.

Conclusion

Inappropriate use of PPIs is commonly observed throughout the entire hospitalization of the patients admitted in surgical and orthopedic units. Collaborative approach to monitoring for indication of PPIs for SRMD prophylaxis should be implemented to minimize this problem.

What is already known on this topic?

Inappropriate initiation and discharge prescription of PPIs for SRMD prophylaxis is commonly observed in both ICU and non-ICU settings.

What this study adds?

This study also revealed that significant number of patients were not discontinued on their PPIs when their risk factor for SRMD was resolved during hospitalization, suggesting that attention to proper indication for PPIs use for SRMD prophylaxis must be paid in every patient throughout the course of PPIs use.

Potential conflicts of interest

None.

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การปฏิบัติตามแนวทางการใช้ยาป้องกันการเกิดแผลในกระเพาะอาหารในผู้ป่วยแผนกศัลยกรรม และแผนกออร์โธปิดิกส์ โรงพยาบาลรามาธิบดี

ศุภทัต ชุมนุมวัฒน์, พิชญา ดิลกพัฒนมงคล, ธนพิพัฒน์ วิริยานนท์, ธิติวุฒิ ศรีชลวัฒนา, นันทพร เล็กพิทยา, ปพน สง่าสูงส่ง, ปรีดา สัมฤทธิ์ประดิษฐ์

วัตถุประสงค์: เพื่อศึกษาความเหมาะสมของการใช้ยากลุ่ม proton pump inhibitors [PPIs] ในผู้ป่วยแผนกศัลยกรรม และแผนกออร์โธปิดิกส์

วัสดุและวิธีการ: การศึกษานี้ดำเนินการโดยการเก็บข้อมูล เช่น ข้อมูลพื้นฐานและค่าทางห้องปฏิบัติการที่เกี่ยวข้อง ย้อนหลังจากเวชระเบียนผู้ป่วยที่รักษาตัวในแผนกศัลยกรรมและแผนกออร์โธปิดิกส์ โรงพยาบาลรามาธิบดี โดยมี ระยะเวลาเก็บข้อมูลตั้งแต่วันที่ 30 สิงหาคม พ.ศ. 2559 ถึง 18 มกราคม พ.ศ. 2560 ซึ่งความเหมาะสมการสั่งใช้ยากลุ่ม PPIs จะถูกประเมินโดยเกณฑ์ที่ปรับปรุงจากแนวทางการใช้ยา PPIs ในการป้องกันภาวะ stress-related mucosal disease [SRMD] โดยอาศัยข้อมูลจากการศึกษาทางคลินิกที่มีคุณภาพดีร่วมด้วย

ผลการศึกษา: จากกลุ่มตัวอย่างจำนวน 105 ราย พบการเริ่มใช้ยากลุ่ม PPIs อย่างไม่เหมาะสม (ไม่มีข้อบ่งใช้) ในผู้ป่วย 58 ราย (ร้อยละ 55.24) นอกจากนี้ยังพบว่ายากลุ่ม PPIs ไม่ถูกหยุดแม้ว่าจะไม่มีข้อบ่งใช้ยาแล้วในผู้ป่วย 24 ราย (ร้อยละ 22.86) และจากกลุ่มตัวอย่างที่ได้รับ PPIs ทั้งหมด จะพบว่ามีผู้ป่วย 12 ราย ที่ได้รับขนาดยาที่ไม่ถูกต้อง และเมื่อพิจารณาจากรายการยาก่อนกลับบ้านของผู้ป่วยจะพบว่ามีการจ่ายยากลุ่ม PPIs อย่างไม่เหมาะสมในผู้ป่วย 37 ราย (ร้อยละ 35.24)

สรุป: การใช้ยากลุ่ม PPIs อย่างไม่เหมาะสมเป็นปัญหาที่พบได้บ่อยและเกิดขึ้นได้ตลอดช่วงเวลาของการรักษาพยาบาล ในแผนกศัลยกรรมและแผนกออร์โธปิดิกส์ ดังนั้นความร่วมมือระหว่างสาขาวิชาชีพในการติดตามความเหมาะสมของ การใช้ยากลุ่ม PPIs อย่างสม่ำเสมอจึงเป็นสิ่งที่จำเป็น เพื่อลดปัญหาเหล่านี้ให้น้อยลง