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BRIEF ARTICLE

Clinical and cost impact of intravenous proton pump inhibitor use in non-ICU patients

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Abstract

AIM: To assess the appropriateness of the indication and route of administration of proton-pump-inhibitors (PPIs) and their associated cost impact.

METHODS: Data collection was performed prospectively during a 6-mo period on 340 patients who received omeprazole intravenously during their hospital stay in non-intensive care floors. Updated guidelines were used to assess the appropriateness of the indication and route of administration.

RESULTS: Complete data collection was available for 286 patients which were used to assess intravenous (IV) PPIs utilization. Around 88% of patients were receiving PPIs for claimed stress ulcer prophylaxis (SUP) indication; of which, only 17% met the guideline criteria for SUP indication, 14% met the criteria for non-steroidal-anti-inflammatory drugs-induced ulcer prophylaxis, while the remaining 69% were identified as having an unjustified indication for PPI use. The initiation of IV PPIs was appropriate in 55% of patients. Half of these patients were candidates for switching to the oral dosage form during their hospitalization, while only 36.7% of these patients were actually switched. The inappropriate initiation of PPIs *via* the IV route was more likely to take place on the medical floor than the surgical floor (53% *vs* 36%, $P = 0.003$). The cost analysis associated with the appropriateness of the indication for PPI use as well as the route of administration of PPI revealed a possible saving of up to $17732.5 and $14571, respectively.

CONCLUSION: This study highlights the over-utilization of IV PPIs in non-intensive care unit patients. Restriction of IV PPI use for justified indications and route of administration is recommended.

Key words: Cost saving; Lebanon; Non-intensive care unit patients; Omeprazole; Over-utilization; Proton-pump-inhibitors; Stress ulcer prophylaxis

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INTRODUCTION

Proton-pump-inhibitors (PPIs) are the most effective agents for reducing gastric acid secretion and are commonly used in a variety of gastrointestinal (GI) related disorders[1]. The dramatic increase in PPI prescribing patterns over the past several years has raised concerns

relating to their appropriate utilization and associated cost[2,3]. Many health care centers have raised concerns related to the inappropriate use of the intravenous (IV) route of administration and unsuitable indications and to a lesser extent incorrect doses and length of therapy. Furthermore, many patients are being inappropriately discharged on PPIs which could potentially increase treatment costs, and the risk of pneumonia and *Clostridium difficile* associated disease[4]. Part of the over-utilization of IV PPIs can be explained by their safety profile and the tendency of physicians to manage ill in-patients aggressively[5]. Approved indications for IV PPIs are limited to erosive esophagitis in patients unable to tolerate oral medications and patients with pathologic hypersecretory state including Zollinger-Ellison syndrome[6]. Oral PPIs are associated with several advantages compared to the IV formulation including lower cost, reduced utilization of hospital resources, and fewer IV related complications. Guda *et al*[6] in 2004 reporting on the use of IV PPIs in two hospital settings observed that 56% of patients receiving IV PPIs had inappropriate indications and the majority of these claimed to have stress ulcer prophylaxis (SUP) indications. Prophylaxis against stress ulcer is not routinely recommended in general medicine patients[4]. Inappropriate dosing of IV PPIs has attributed to a 292% increase in the cost related to these medications and hence has resulted in an additional expenditure of $7766 for 64 patients[7]. There is a need to assess the prescribing pattern of IV PPIs in the Middle East and Arab countries. In response to the inadequate literature available in the aforementioned region, a drug use evaluation was conducted to assess the appropriateness of the indication and route of administration of PPIs and their associated cost impact in a university hospital in Lebanon.

MATERIALS AND METHODS

Data collection was performed prospectively from October 15, 2008 to April 15, 2009 on 340 adult patients who received a PPI after being admitted to the medical or surgical floors of a 200 beds university hospital in the Beirut area that attracts patients from all over the country. Patients were identified from the pharmacy computer system prior to and during the dispensing process. Data collection forms were filled for 340 patients, out of which 286 were determined to be complete and accurate. The form included data on patient demographics, medical problems, list of medications used, pertinent laboratory data, and criteria for PPI IV indication, dose, frequency, duration, and indication for switching to oral formulation. Assessment of the appropriateness of IV PPI use was then performed based on the American Society of Health-System Pharmacists guidelines[8] and the Eastern Association for the Surgery of Trauma for SUP[9], non-steroidal-anti-inflammatory drugs (NSAIDs)-induced ulcer prophylaxis[10], and criteria for IV to *po* conversion[11].

Patients assessed for PPI indication were divided into two groups, one group of patients using the drug for treatment indication and another group using the drug for claimed SUP indication. The claimed SUP indication group was then sub-classified into (1) meeting criteria for SUP indication; (2) meeting criteria for NSAIDs-induced ulcer prophylaxis; and (3) unjustified prophylactic use.

Another analysis, focusing on the route of administration, divided patients into two groups, one group representing those with appropriate initial IV use and the other group representing inappropriate initial IV use.

Cost analysis was performed comparing the cost associated with appropriate initial IV PPI with that of inappropriate initial IV PPI use. The cost included 100 mL solution bag, 5 mL syringe, drug vial, IV line and related materials. Cost analysis was performed on the unnecessary duration of IV use, in cases where oral PPI was used instead of IV and inappropriate utilization. It was assumed that switching from IV to PO was done 1 d earlier in the group of appropriate IV users and prior to initial dispensing in the group of inappropriate IV users.

Table 1 Patient characteristics (n = 286)

	n (%)
Age, yr (median ± IQR)	64 ± 30
Weight, kg (median ± IQR)	72 ± 23
Creatinine clearance, mL/min (median ± IQR)	71.5 ± 57.6
Age ⩾ 65 yr	143 (51)
Male	149 (52)
Medical floor	146 (51)
Surgical floor	140 (49)
Dose 40 mg omeprazole	272 (95)
Frequency as once daily	251 (88)
Medications	
Heparins	133 (47)
NSAIDs	74 (26)
Corticosteroids	74 (26)
Aspirin (100 mg)	42 (15)
Clopidogrel	15 (5)
Acenocoumarol	10 (4)

IQR: Interquartile range; NSAIDs: Non-steroidal-anti-inflammatory drugs.

Statistical analysis

Statistical analysis was performed using SPSS software. Data were entered into the computer and frequencies, percentages, means, and standard deviations were calculated. Differences in percentages were assessed using the χ^2 test, and differences in means were assessed using the student t test. P-values were assessed at the 5% level.

RESULTS

Patient characteristics

The study included a similar number of males and females. Half of the patients were 65 years or older, and most of them were receiving omeprazole 40 mg IV once daily. The number of patients from the medical floor and the surgical floor was equal (Table 1).

The reasons for hospital admission were various and included surgery, pain, infection, cancer treatment, dyspnea, trauma or fracture.

Table 2 Justification of PPI indications

	n (%)
Out of the total sample (*n* = 286)	
Treatment indications	35 (12)
Claimed as using PPI for SUP indication	251 (88)
Classification of patients claimed as using PPI for SUP indication (*n* = 251)	
Meeting criteria for SUP indication	43 (17)
Meeting criteria for NSAIDs-induced prophylaxis	35 (14)
Age ⩾ 65 yr + NSAIDs	12 (5)
NSAIDS + antithrombotics	23 (9)
NSAIDS + corticosteroids	17 (7)
Unjustified prophylactic use	173 (69)
Age ⩾ 65 yr	81 (32)
Age ⩾ 65 yr + LMWH	55 (22)
Age ⩾ 65 yr + antiplatelets	60 (24)
Age ⩾ 65 yr + corticosteroids	25 (10)
Others	90 (36)

PPI: Proton-pump-inhibitor; SUP: Stress ulcer prophylaxis.

Table 3 Correlation of initial IV administration with indication and eligibility for oral conversion *n* (%)

	Appropriate initial IV use	Inappropriate initial IV use	*P* value
Total IV use (*n* = 286)	158 (55)	128 (45)	
Switched	58 (37)	49 (38)	0.785
Candidate for Switch	82 (52)	127 (99)	< 0.001
Indication			
Treatment (35)	22 (14)	13 (10)	0.556
SUP justified (43)	26 (17)	17 (13)	0.556
NSAIDs-induced (justified) (35)	17 (11)	18 (14)	0.556
Other unjustified prophylaxis (173)	93 (59)	80 (63)	0.556
Frequency as once daily	138 (87)	113 (88)	0.81
Dose 40 mg	152 (96)	120 (95)	0.491
Medical floor	68 (47)	78 (53)	0.003
Surgical floor	90 (64)	50 (36)	0.003
Duration of IV use (median ± IQR)	4.0 ± 4.0	4.0 ± 4.0	0.422

IV: Intravenous.

The most common criteria for using the IV route of administration were an order for nothing by mouth (*n* = 95, 33.2%), unable to swallow (*n* = 18, 6.3%), severe nausea and vomiting (*n* = 17, 5.9%), acute GI bleeding (*n* = 12, 4.2%), and others (*n* = 15, 5.2%) such as gastric obstruction, ileus, severe diarrhea, and malabsorption. Many patients were on antithrombotics, NSAIDs and corticosteroids during hospitalization (Table 1). Other medications included antibiotics (*n* = 205, 71.7%), analgesics (*n* = 171, 59%), metoclopramide (*n* = 98, 34.3%), antihypertensive drugs (*n* = 101, 35.3%) and insulin (*n* = 32, 11.2%).

Justification of PPI use

The use of IV PPIs was assessed in 286 patients. The indication for claimed SUP was used in 88% of patients, of which only 17% met the guideline criteria for SUP indication, 14% met the criteria for NSAIDs-induced ulcer prophylaxis while the majority (69%) were receiving PPI for an unjustified indication. These indications for PPI treatment were peptic ulcer (4.5%), GERD (1.4%), and stress ulcer treatment (2.4%). Stratification of the unjustified prophylactic use was correlated with age ⩾ 65 years and whether or not the patient was receiving antithrombotics or corticosteroid therapy (Table 2). Antithrombotics mainly consisted of low molecular-weight heparins.

Table 4 Cost analysis for inappropriate route of administration and indication

	Appropriate initial IV PPI use	Inappropriate initial IV PPI use
Candidate for switch	*n* = 82	*n* = 128
Cost of 40 mg IV PPI daily dose that could be avoided	$1681	$13 120
Cost of 40 mg PPI oral daily dose (if used instead of IV)	$184	$1434
Cost that could be avoided with the oral use	$1497	$11 686
Total cost that could be avoided with IV to po conversion	$13 183	
Cost that could be avoided from Unjustified prophylactic use of IV PPI (*n* = 173)	$17 732.5	

Appropriateness of initial iv use and eligibility for oral conversion

Only about 50% of patients who were initiated on PPIs *via* the IV route were deemed appropriate, of which half were candidates for switching to the oral form during their hospitalization. Only one third of the latter were switched to the oral form. The inappropriate initiation of PPIs *via* the IV route was more likely to take place on the medical floor compared with the surgical floor (53% *vs* 36%, *P* = 0.003).

Regardless of the type of indication, the rate of inappropriate initiation of PPIs *via* the IV route was similar to the rate of appropriate initiation (*P* = 0.556). The likelihood of switching patients to the oral form was independent of the appropriateness of initial IV use (36.7% *vs* 38.3%, *P* = 0.785) (Table 3). Most patients received a 40 mg IV dose once daily for a period of approximately 5 d.

Cost analysis

The cost analysis was based on the mean of 5-d of IV administration which could be avoided in the group with inappropriate IV use, and the assumption that switching could be done at least 1 d earlier in the group with appropriate IV use.

If PPIs were used for the appropriate indication and by the correct route of administration in the 286 patients assessed during the 6-mo period, at least $17 732.5 and $13 183, could have been saved, respectively (Table 4).

DISCUSSION

The high prescribing pattern of IV PPIs has been dem-

onstrated in this study. The majority of patients were identified as using IV PPIs for claimed SUP indication with a relatively small percentage of patients (17%) meeting the criteria for SUP, which is expected since only non-intensive care unit (ICU) patients were included in the trial. The inappropriateness of use was encountered more on the medical floor compared with the surgical floor. This highlights the need for a clinical pharmacist in that area. Among other patients claimed to be treated for SUP, 14% met the criteria for other indications such as prophylaxis of NSAIDs-induced ulcer. This left a large number of patients using PPIs for unjustified indications. Thus, to minimize over-utilization of PPIs for SUP, prescribers should specify the indication and the reason for the PPI on the medication orders, which would then facilitate medical order screening by the dispensing pharmacist. Around 36% of the patients who claimed to receive IV PPIs for SUP had no risk factors or any known justification for PPI use. It seems that age $\geqslant$ 65 years old was used as a criterion for PPI use; however, these patients had several medical illnesses and were on multiple drug regimens that may have increased the risk of adverse effects. A retrospective review of the medical charts of elderly patients revealed that around 30% of geriatric patients with a prescription for a PPI from a geriatric ambulatory care practice within an urban academic medical center had no documented indication[12].

These findings highlight the role of the clinical pharmacist in the selection of appropriate candidates for switching.

The cost burden associated with inappropriate IV PPI use should be minimized. An annual projection of cost could reflect a saving of $26 366 and $35 465 with the appropriate route of administration and indication, respectively. It is important to note that this cost saving was underestimated since the cost of health care staff time was not included in the calculations and the delay in switching was assumed to be only 1 d. This highlighted the crucial role of a clinical pharmacist to review orders for proper indications, route of administration, and appropriate timing for switching.

The results of this study are comparable with several trials in the USA and UK that discussed the inappropriate use of IV PPIs in several institutions[7,13-15]. SUP was the most commonly encountered claimed indication for IV PPIs. A 14-mo observational study assessing the use of IV PPIs in non-ICU patients revealed that 22% of patients were receiving the drug according to their established indications. SUP was the presumed indication in 70% of patients receiving IV PPIs, of which only 13% were considered appropriate[7]. These findings were also supported by Qadeer *et al*[16] who addressed the concern of SUP in non-ICU patients, stating that such an intervention is often unnecessary and not recommended.

With regard to the limitations of this study, the study was observational and conducted in a single academic medical center. In addition, there are no current established guidelines for the appropriate use of IV PPIs in the hospital to evaluate their actual use. Moreover, we assumed that patients with no clear documented indication for PPI use received the drug for SUP. An additional step could have been to investigate the seniority and/or the specialty of the physicians over-prescribing IV PPIs.

As for the strengths of this study, the number of patients involved was adequate (n = 286) over a sufficient period of time (6 mo). Non-ICU adult patients were selected because these patients may be more prone to inappropriate SUP treatment. Patients were monitored and followed during their hospital stay until discharge, PPI discontinuation or switching to oral PPI. In addition, there are limited data on the utilization pattern of an IV PPI in an institutional setting.

This study highlights the over-utilization of PPIs *via* the IV route of administration and for a claimed SUP indication in non-ICU patients, which results in increased cost to the patients, institution and payers.

Improving the prescribing patterns requires the Hospital Pharmacy and Therapeutics Committee to establish guidelines with input from gastroenterologists on the proper indications for IV PPIs, criteria for switching, dosing, and duration of therapy. Implementation of these guidelines requires multidisciplinary involvement and education of health care professionals concerning appropriate use of this class of medication. Other approaches include creating an IV order template, pharmacists reviewing orders before dispensing to patients, and automatic switching to an H2 blocker if a PPI was ordered for SUP until more robust trials on PPI become available[17,18].

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COMMENTS

Background

Proton pump inhibitors (PPIs) are the most effective agents for treating acid related gastrointestinal (GI) disorders. The utilization of intravenous (IV) formulations of PPIs has dramatically increased in health care institutions for inappropriate indications, route of administration and length of treatment. This is associated with an increased cost burden, increased risk of IV related infections, and utilization of hospital resources.

Research frontiers

Utilization of IV PPIs in a hospital setting in a Middle East country was evaluated and compared to data from European and USA hospitals. The evaluation was carried out in non-intensive care units where patients do not meet the indication and/or route of administration criteria for IV PPIs, especially those receiving the drug for stress ulcer prophylaxis (SUP) where little or no evidence supports their use.

Innovations and breakthroughs

Reports of the over-utilization of IV PPIs have been published in different international journals mainly involving European and American hospital settings. Available literature from the Middle East (especially prospective in nature) addressing this overuse pattern in non-intensive care units and emphasizing the role of a clinical and hospital pharmacist in health care systems is inadequate. In addition, a detailed cost analysis projection was performed for inappropriate indications and route of administration of PPIs.

Applications

The study highlights the essential role of the clinical pharmacist in defining candidates for IV PPIs, especially for SUP, and fosters the role of the Pharmacy and Therapeutics Committee in implementing restriction guidelines for IV PPIs in patients who are not candidates for oral treatment or when the IV route shows better efficacy. A multifaceted approach is needed to improve the prescribing pattern which would involve education of health care professions regarding the appropriate prescribing pattern of IV PPIs.

Terminology

Proton pump inhibitors are the most effective anti-secretory agents which inhibit the final step in gastric acid secretion and are used to treat several GI related disorders. Stress ulcers also called stress mucosal related disease is a form of hemorrhagic gastritis that occurs in patients after major stressful events such as trauma, surgery, or severe head injury.

Peer review

The paper is well written. The observations are comparable to those made in Europe, USA, and Asia, as acknowledged by the authors in Discussion. The appropriateness of the statistics applied to analyze the data obtained may be debated, but the use of non-parametric tests is considered preferable in this type of studies.

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