

Physicians' Compliance With Order Entry Forms for Intravenous Pantoprazole in a Tertiary Care Hospital

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Abstract- The widespread inappropriate use of intravenous (IV) pantoprazole, due to its high cost, is a substantial issue. To improve its rational use, an order entry form (OEF) based on the institutional guideline, was implemented. Physicians were required to fill an OEF upon administration of IV pantoprazole. We aimed to evaluate the compliance of physicians as well as the accuracy of filled OEFs six months after the implementation. The study was conducted in a tertiary care teaching hospital in Tehran. Chart review was performed for all patients with an IV pantoprazole order. IV pantoprazole OEFs received by the hospital pharmacy for these patients were evaluated in terms of quantity and quality (e.g., completeness, accuracy of filled items, etc.). Only for 270 (62%) patients, OEFs were received by the hospital pharmacy. Indications were specified in 199 (73.5%) forms, and their agreement with the forms filled by the researcher was 37.8%. The most frequent indication specified in OEFs was stress ulcer prophylaxis (40.7%). IV pantoprazole administration was rational only in 15.9% of cases. The emergency ward had the highest frequency of orders (57.9%), while having the lowest fill rate (56.7%) among the wards with the highest number of orders. The disagreement between the researcher and the OEFs regarding the need for IV medication was 39.5%. This study demonstrated that the compliance of physicians with the accurate completion of OEFs was suboptimal. It seems that for long-lasting changes in IV pantoprazole utilization patterns, barriers should be determined, and additional methods such as ongoing educational seminars or feedback might be needed along with OEF.

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Introduction

Following the introduction of proton pump inhibitors (PPI) in the 1980s (1), the treatment of acid-related disorders considerably improved (2). Although the histamine type 2 receptor antagonists (H2RA) were effective in decreasing symptoms and ameliorating mucosal lesions, PPI replaced them due to advantages such as better efficacy, longer duration of action, basal and postprandial acid suppression, and lack of tolerance to their effects (3).

The growing consumption of PPI deserves specific

attention concerning the appropriateness of indications, lengths of use, adverse drug reactions, and costs imposed on both the healthcare system and patients (4). Inappropriate use of PPI occurs in hospitals as well as outpatient settings (2). Previous studies were conducted to evaluate PPI utilization and assess the adherence to guidelines for their use (5-7). Inappropriate PPI use, specifically in intravenous (IV) dosage form, has occurred in 25-75% of cases (8). Prevention of gastric ulcers in low-risk populations, as well as stress ulcer prophylaxis (SUP) in non-ICU patients were reported to be the most frequent inappropriate uses (3).

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The irrational use of PPI is more profound, considering recent evidence that raised doubts about their previously known rational uses. A systematic review showed that in critically ill patients receiving enteral feeding, PPI does not decrease GI bleeding (9). Another study reported that administration of pantoprazole was not associated with a significant difference in 90-day mortality or other clinical events when compared with a placebo in critically ill patients at risk of GI bleeding (10).

Pantoprazole is the only IV PPI available in Iran, and when it comes to inappropriate IV PPI utilization, Iran is not exception (11). This is worth attention since IV pantoprazole was reported to be among the medications that constituted the highest drug costs in hospitals (12). Additionally, studies revealed that IV pantoprazole can be replaced by oral dosage forms in most of the indications (13,14), and this could cause a remarkable decrease in healthcare costs (15,16).

Different strategies were developed to improve the rational use of medications (17-19). Interventions that were examined to improve PPI appropriate use in studies were educational (20), along with a web-based quality improvement tool (21), appropriate use guidelines (12), designing a clinical decision support system (22), and multifaceted interventions (23). Most of the mentioned studies were conducted during a short period following the intervention, and evaluation of the effects over a longer period was limited. Meanwhile, conducting audits is an inseparable part of the assessment of the interventions since it can provide data regarding how long the effect of an intervention, lasts.

Designing and implementing an order entry form (OEF) or medication request form is another intervention to improve the rational use of drugs. In these printed or computerized forms, the indication is specified by the provider at the time of prescribing a particular medication. These forms can be restrictive, and the hospital pharmacy does not dispense the medication if the specified indication is not acceptable (24). However, one limitation of these restrictive forms can be the inaccuracy of the declared indication, which can be detected by evaluating the patient's profile and condition (24).

Based on a previous investigation (unpublished data), we noticed that the inappropriate use of IV pantoprazole in a tertiary care teaching hospital affiliated with the Tehran University of Medical Sciences (TUMS) was high. Therefore, considering interventions to optimize IV pantoprazole use in this hospital seemed crucial. Consequently, multifaceted interventions, including appropriate use guidelines, health care education, and the design of an OEF were implemented to improve the

appropriate use of IV pantoprazole in parallel with other medications with similar irrational utilization issues in the hospital (25).

The challenges regarding the implementing OEF in a tertiary care teaching hospital for a medication with widespread inappropriate use need to be elucidated. In this study, we aimed to assess the compliance of physicians with filling OEFs for IV pantoprazole. Furthermore, the quality and accuracy of filled OEFs were evaluated by investigation of the patients' clinical conditions.

Materials and Methods

Study setting

This study was conducted from 3rd April to 21st May 2016 in Shariati hospital, a tertiary care teaching hospital, affiliated with TUMS in Tehran, Iran. The study was approved by the ethics committee of TUMS.

Interventions and implementation of OEFs

One year before the initiation of the current study, sequential interventions, including institutional guideline and educational sessions, were implemented to improve the appropriate use of IV pantoprazole in the hospital. This was a part of a comprehensive hospital-wide project to optimize rational use of medications. The guideline was developed using recent evidence-based literature, revised after considering comments received from hospital attending professors and approved by the hospital's drug and therapeutic committee. The educational sessions were planned to include the attending physicians and medical residents of various wards. A clinical pharmacist lectured about the rational use of IV pantoprazole and the institutional guidelines in the sessions.

Six months after the abovementioned interventions, an OEF for IV pantoprazole was designed and introduced to the wards. The form comprised the following items:

- 1) The patient's demographics
- 2) The name of the inpatient ward
- 3) The rational indications for prescribing IV pantoprazole (Table 1)
- 4) The name stamp and signature of the prescriber.

The appropriate indications and conditions for IV pantoprazole were included in the OEF to be chosen by the prescribers. The indication items in the form were determined by clinical pharmacists based on the previously developed appropriate use guideline for rational IV pantoprazole in the hospital.

Table 1. Indications for IV pantoprazole in the order entry forms

Indications for administration of IV pantoprazole	
1.	Stress ulcer prophylaxis in critically ill patients (one of the list A conditions OR ≥ 2 list B conditions AND at least 1 of the list C conditions)
A.	One of the following conditions:
-	Coagulopathy defined as platelet count < 50000 per microliter or INR>1.5
-	Mechanical ventilation for >48 hours
-	History of peptic ulcer disease or GI bleeding in the past year
-	Trauma with injury severity score ≥ 16
-	Traumatic brain injury or severe spinal cord injury
-	Severe burn >35% of BSA
B.	Two or more of the following conditions:
-	Severe sepsis or septic shock
-	ICU stay for more than a week
-	Occult GI bleeding for ≥ 6 days
-	Receiving one of the following medications: glucocorticoids (250 mg hydrocortisone or equivalent doses of other agents), NSAIDs, ASA, anticoagulants, fibrinolytics
-	Renal failure
-	Hepatic failure
-	Solid organ transplantation
C.	One of the following conditions:
-	NPO or intolerance to gavage
-	Contraindication or intolerance of IV ranitidine
2.	Upper GI bleeding (non-variceal)
3.	Zollinger-Ellison syndrome in NPO patients or intolerant to gavage
4.	Erosive esophagitis related to GERD in NPO patients or intolerant to gavage
5.	Gastric outlet obstructions

INR: international normalized ratio, GI: gastrointestinal, BSA: Body surface area, ICU: Intensive care unit, NSAID: Non-steroidal anti-inflammatory drugs, NPO: Nil per os (nothing by mouth), GERD: Gastroesophageal reflux disease

Table 2. Characteristics of physicians who filled medication administration forms

Characteristics	N	%
Medical Specialty of physicians	Emergency medicine	28.0
	Internal medicine	25.0
	Cardiology	17.8
	Surgery	13.6
	Oncology	7.6
	Others	8.0
Educational level of physicians	Medical resident†	90.5
	Specialist	1.9
	Fellow‡	3.0
	Subspecialist	4.6

†Post graduate medical student, ‡ Medical subspecialty assistant

Table 3. Quantity and quality of filling OEFs in the wards

Wards	Orders, n (%)†	OEFs, n (%)			Rational orders with OEF ‡* n (%)
		Number (fill rate) ‡	with indication specified¥	with physician's name stamp¥	
Emergency	252 (57.9)	143 (56.7)	105 (73.4)	140 (97.9)	38 (26.6)
Hematology and BMT	73 (16.8)	48 (65.8)	35 (72.9)	47 (97.9)	2 (4.2)
ICU	40 (9.2)	26 (65)	21 (80.8)	25 (96.1)	0 (0)
Surgery	17 (3.9)	13 (76.5)	8 (61.5)	13 (100)	0 (0)
Endocrinology	13 (3)	12 (92.3)	7 (58.3)	12 (100)	2 (16.7)
Other wards	40 (9.2)	28 (70.0)	23 (82.1)	27 (96.4)	1 (3.6)
Total	435 (100)	270 (62.1)	199 (73.7)	264 (97.8)	43 (15.9)

BMT: bone marrow transplantation, ICU: intensive care unit, OEF: order entry form

†Percentage is calculated based on the total of 435 orders, ‡Percentage is calculated based on the total orders in the ward, ¥ Percentage is calculated based on the total number of OEFs in the ward, * Refers to the orders with filled OEF that were found to be rational. OEFs were not necessarily documented a rational order

Physicians' compliance with order entry form

Physicians were asked to fill out, sign, and name stamp the OEF upon ordering the first dose of IV pantoprazole for each patient. The physicians were allowed to write down indications other than those mentioned in the OEF. The wards were also required to hand over the completed forms to the hospital pharmacy. The completion of the OEF was announced to be mandatory for dispensing the medication by the pharmacy. However, access to the medication was not limited by the hospital pharmacy in cases for whom the OEF was not complete, specifically at the time of the initiation of the current study.

Patients' assessments

During the study period, the medical charts of the patients with IV pantoprazole orders were evaluated by a trained pharmacist. Patients for whom IV pantoprazole was initiated, were detected daily, by using the hospital information system. The researcher collected data on patient demographics, clinical diagnosis, and indication for use of IV pantoprazole following a manual chart review. Other necessary data to assess whether the substitution of IV pantoprazole with an oral dosage form or IV ranitidine was possible or not were also recorded.

Compliance of physicians with filling OEFs

In the context of the current study, we defined compliance as the concordance of the physicians with the policies of the hospital in prescribing IV pantoprazole consisting of filling an OEF completely, and accurately for each patient.

-Fill rate calculation

The fill rate was calculated by dividing the number of OEFs by the total number of orders in a ward and reported as a percentage. Additionally, filling different parts of the OEFs such as the indication for the administration were reported separately.

-Completion of OEFs

All the OEFs received by the hospital pharmacy were evaluated by the researcher in terms of completeness (specifying indication, having the physician's name stamp, and signature, necessity of IV pantoprazole, and possibility of IV ranitidine substitution).

-Accuracy of OEFs

To evaluate the accuracy of the OEFs, the agreement between the researcher and the OEFs completed by physicians on following items were considered.

-Indication

The agreement between the researcher's assigned indication and the selected indication in the OEF were evaluated. In cases with more than one indication in the OEF, agreement on one indication was acceptable.

-Necessity of IV pantoprazole

This agreement was evaluated in patients with SUP, Zollinger-Ellison syndrome, and erosive esophagitis related to GERD, etc., per the researcher and the physicians. These indications were selected, as shown in Table 1, since for cases other than GI bleeding and gastric outlet obstruction (GOO), oral dosage of pantoprazole could be administered to patients with PO or gavage tolerance. Therefore, it was presumed that only in cases of NPO or gavage intolerance would physicians order an IV dosage form. The evaluation was not limited only to the OEFs with the same indications in both sources.

-Possibility of IV ranitidine substitution

This was evaluated in patients who received pantoprazole for SUP. The substitution deemed to be impossible in patients with a history of PPI use before admission and a contraindication or intolerance to ranitidine.

Evaluation of the rational use of IV pantoprazole

Prescribing IV pantoprazole was assumed to be rational (optimal) if there was consistency between the OEF and the researcher's chart review regarding the specified indication, the need for an IV dosage form, and the possibility of ranitidine substitution.

Statistical analysis

For describing quantitative variables mean (SD) and for categorical data frequency (%) were reported. Data analysis was performed using Microsoft Excel (2013).

Results

Patients

During the study period a total of 435 patients received IV pantoprazole. Mean (SD) age of patients was 52.71 (20.92) years and 263 (60.5%) patients were men. The medication was ordered for patients in 12 wards in the study hospital.

OEFs

Overall, for 270 (62.1%) of 435 patients with IV pantoprazole order, OEF was received by the hospital

pharmacy from the wards. The mean (SD) age of patients with IV pantoprazole OEF was 51.76 (19.93) years, and 40.7% (n=110) of them were female. Table 2 shows the frequency of filled OEFs by different physicians' specialties and educational levels as specified in the forms. Among the physicians who filled the OEFs, emergency medicine specialists were the most frequent (28%), and oncologists were the least (7.6%).

Compliance of physicians with filling OEFs

-Completion of OEFs

Among the received OEFs, 264 (97.8%) and 158 (58.5%) forms had a physician's name stamp, and signature, respectively. Only in 199 (73.7%) forms, the indication was specified. In terms of educational level and specialty, post-graduate medical students (medical residents) and emergency medicine specialty, name-stamped 63 (88.7%) and 19 (26.8%) forms, respectively. Among OEFs in which no indication was specified, 38 (53.5%) forms were received from the emergency ward.

-Fill rate of OEFs

We also investigated the fill rate. Although in the urology ward OEF was filled for all the patients and the lowest fill rate belonged to the CCU ward with 33.3%, the number of medication orders were very small in these wards (2 and 3 orders, respectively). In Table 3, the wards

with the highest number of IV pantoprazole orders, the number of OEFs, and their fill rate are shown. Among the wards with high IV pantoprazole orders, the highest and lowest OEF fill rates belonged to the endocrinology (92.3%) and the emergency ward (56.7%), respectively.

Accuracy of OEFs

-Indication

The leading indication in the received OEFs was SUP, as documented in 110 (40.7%) OEFs. However, when all patients for whom SUP was assigned as an indication (either alone or along with other indications) were considered, we found this indication was selected in 142 (52.6%) forms. Among them, only 18 (12.7%) patients were in the ICU wards.

Based on the researcher's investigation of patients with OEF, the most frequent indication for IV pantoprazole was SUP in 115 (42.6%) patients (Figure 1). The second most prevalent indication was upper GI bleeding in 34 (12.6%) patients. There was just one patient with more than one indication to receive the medication. However, for a considerable number of patients, none of the indications listed in the institutional guideline could be assigned. Figure 2 shows the proportion of filled OEFs for each indication based on the researcher's investigation.

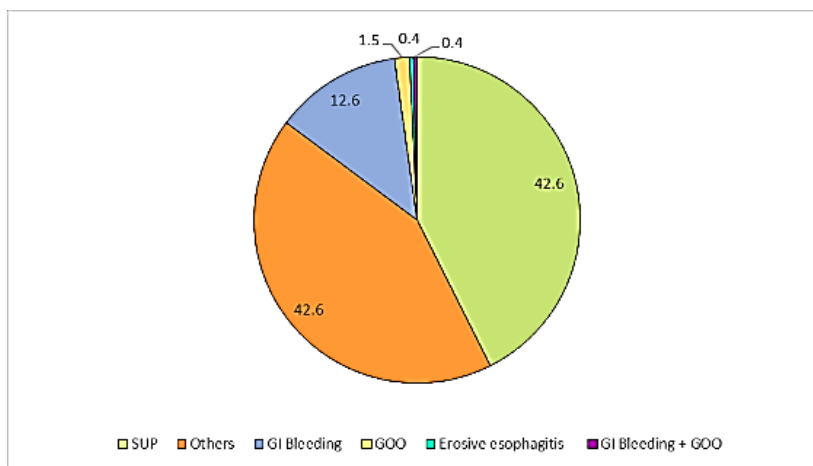


Figure 1. Researcher's specified indications for IV pantoprazole in patients with order entry form

Numbers represents percentages of each indication

SUP: stress ulcer prophylaxis, GOO: gastric outlet obstruction, GI: gastrointestinal

Other indication here refers to the patients without indication for IV pantoprazole based on the hospital guideline

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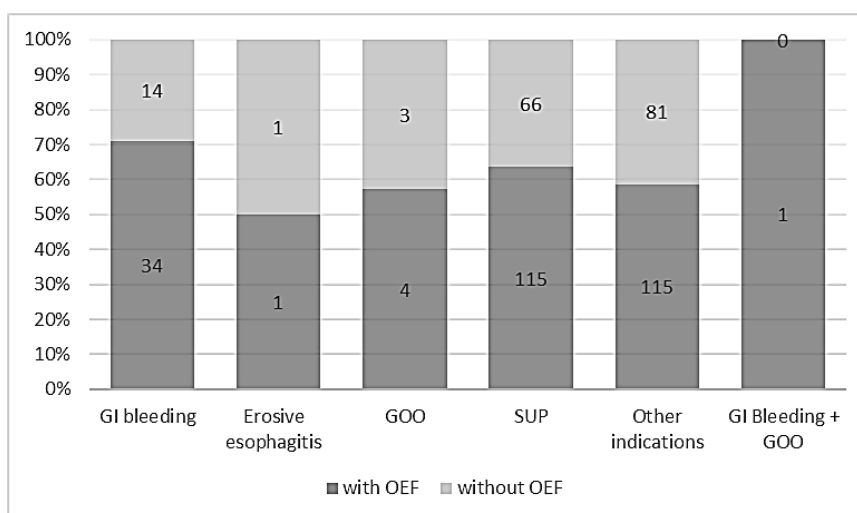


Figure 2. Indications for IV pantoprazole in the study patients based on the researcher's investigation

Numbers shown in the figure represents the number of patients who received IV pantoprazole.

SUP: stress ulcer prophylaxis, GOO: gastric outlet obstruction, GI: gastrointestinal, OEF: order entry form

Agreements between the researcher's assigned indications and selected indications in OEFs are shown in Table 4. Only for 102 (37.8%) patients there was an agreement on specified indication between the two mentioned sources. OEFs with more than one indication along with SUP, had the highest concordance.

-Necessity of IV pantoprazole

We found that in 39.5% of patients, the necessity of IV medication as judged by the researcher and physicians was not compatible. The percentage of patients who could not receive oral dosage forms was lower based on the researcher's investigation vs. the OEFs (19.3% vs. 52.6%), as shown in Table 5. The agreement between two sources regarding the need for IV dosage form in patients with SUP (per the indication specified in the OEF as well as the researcher) was noted in 31 (54.4%) patients.

-Possibility of ranitidine substitution

In patients who received IV pantoprazole for SUP (based on the indication assigned in OEF and by the researcher), the agreement between the researcher and OEFs regarding the possibility of IV ranitidine administration was observed in 86% (49) of cases.

Rational use of IV pantoprazole

When the medical charts of patients with OEFs were reviewed, we found that only for 43 (15.9%) patients was the administration of pantoprazole rational, based on the institutional guideline. It included 26.6% of orders in the emergency ward which ranked this ward first in terms of appropriate use and comprised 88.4% of all rational orders. None of the orders of patients with OEF in the ICU and the surgery ward showed rational use of IV pantoprazole.

Table 4. Agreements between the researcher's assigned indications and selected indications in OEFs

Indications	Based on OEF n (%)	Agreement between researcher and OEF n (%)
Stress ulcer prophylaxis	110 (40.7)	57(51.8)
GI bleeding	44 (16.3)	16(36.4)
1> indication	36 (13.3)	25(69.4)
Other indications*	9 (3.3)	4(44.4)

Other indications in OEF consisted of inefficiency of oral pantoprazole (n=6), Zollinger-Ellison syndrome, gastric outlet obstruction and SUP in renal insufficiency each in one patient
GI: Gastrointestinal, OEF: order entry form

Table 5. Potential for substitution of IV pantoprazole with its oral dosage form or IV ranitidine

Potential substitution	for	Description	Based on OEFs n (%)		Based on the researcher's investigation n (%)		Agreement n (%)
			No	Yes	No	Yes	
Oral dosage form		indications for which IV pantoprazole was not mandatory in PO patients [†]	60 (52.6)	54 (47.4)	22 (19.3)	92 (80.7)	69 (60.5)
IV ranitidine for SUP		Indication per the researcher [‡]	6 (5.2)	109 (94.8)	12 (10.4)	103 (89.6)	101 (87.8)
		Indication per the OEF [¥]	5 (4.5)	105 (95.5)	11 (10)	99 (90)	98 (89)

IV: intravenous, OEF: order entry form, PO: per os (per oral/orally), SUP: stress ulcer prophylaxis

[†] Based on both OEF and the researcher, [‡] regardless of the indication specified in OEF, [¥] regardless of the indication specified by the researcher

Discussion

Our results revealed insufficient physicians' compliance with IV pantoprazole OEF implementation in the study hospital. During the study period, for 38% of patients, OEF was not sent to the hospital pharmacy. Unexpectedly, neither the pre-defined indications nor any other indications were specified in 26.3% of the OEFs. Although 97.8% of forms had a physician's name stamp, 41.5% of them lacked the physician's signature.

Insufficient physicians' compliance with OEF might be attributed to the following issues. The time elapsed from implementing the intervention to the evaluation performed in this study (six months) could be one of the main reasons.

It was previously shown that the effects of interventions targeting PPI decreased over time. Thompson et al. found that the implementation of a guideline for de-prescribing PPI in a long-term care home in Canada decreased utilization during the first six months. However, this effect was dampened, resulting in a non-significant change at the end of the study (26). Similar findings were reported in a study in Iran, in which the positive effects of a guideline for the rational use of IV pantoprazole and adherence to it, decreased over time (12).

Studies have shown that improvements and long-lasting changes in physicians' practice might not occur following introducing an intervention in the hospital. Successful implementation of interventions requires overcoming barriers in the context in which they are used and considering methods to facilitate their effective integration into practice (27). Moreover, continuous and consistent interventions might be necessary to achieve steady improvements in rational medication use. A study in Thailand showed implementation of antimicrobial order forms, reviewing them, and giving feedback to the prescribers, endorsed by the executive committee of the hospital decreased the costs of three costly antibiotics

(imipenem, vancomycin, and ciprofloxacin) over three years. However, the cessation of the endorsement and the review and feedback resulted in a dramatic increase in medication costs during the following year (28).

We observed indications were not accurately documented in the forms. For 36 (13.3%) patients, physicians selected more than one indication in OEFs. Although the agreement of these indications between the manual chart review and the OEF was 69.4%, this agreement was substantially overestimated. This might be resulted primarily from considering concordance for even one indication. The selection of two or more indications by the physicians eventually increased the chance of agreement on one indication. If the exact indications specified in OEFs were considered, none of those cases would be classified in this category.

The agreement of indications between the two sources was only 37.8%, which was quite low. In nearly half of the cases of SUP (based on OEFs), the researcher and physicians were not in agreement regarding the indication. SUP was responsible for the largest proportion of indications for IV pantoprazole in this study. For other indications, the agreement was even less. It was a finding shared by earlier studies as well. In a hospital in the US, a computerized physician order entry system was designed to improve the appropriate use of three medications (lansoprazole, IVIG, and factor VIIa) frequently prescribed off-label. Patients' profiles were randomly reviewed to assess the accuracy of the selected indications. The result showed that the agreement between the selected indications by the physicians and the patient profile review was 29%, 49%, and 63% for factor VIIa, IVIG, and lansoprazole, respectively (22).

Although no restriction was considered in dispensing IV pantoprazole from the hospital pharmacy for orders without an OEF, it was previously shown that physicians tended to select appropriate indications in the OEFs to bypass supposed drug dispensing limitations (24). This might be a reason for disagreement between the

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researcher's and physicians' assigned indications. Furthermore, it is possible that some of the OEFs were filled by nurses, who were not completely aware of the indications for IV pantoprazole, using the name stamps the physicians.

According to the researcher's evaluation, administration of an oral dosage form was possible in 80.7% of patients, whereas this was declared to be 47.4% in OEFs. In other words, physicians tended to administer IV dosage forms for indications that could be managed PO, while patients were able to receive the medication orally or via gavage. Considering several known advantages of PO administration, including the cost (29), the use of IV pantoprazole in such cases was inappropriate. Additionally, following successful therapeutic endoscopy in a bleeding peptic ulcer with high risk for re-bleeding, no significant difference has been reported between patients who received high-dose IV vs. PO pantoprazole in terms of surgery, hospital stay, volume of blood transfusion, or mortality (30). A meta-analysis also revealed that using PO instead of IV PPI was not associated with higher re-bleeding rates, the need for surgery, repeat endoscopies, or blood transfusions (13).

We noted that for patients who received IV pantoprazole for SUP, in more than 87% of cases, there was an agreement between the researcher and the physicians that substitution of IV ranitidine could be considered. This shows that a substantial proportion of IV pantoprazole administration and consequent costs, could have been restrained.

More than half of the IV pantoprazole orders were from the emergency ward in the study hospital. However, this ward had the lowest OEF fill rate (56.7%) in comparison with the wards with the highest number of IV pantoprazole orders. Additionally, among the OEFs without a specified indication, 53.5% belonged to this ward. On the other hand, the highest percentage of orders with appropriate use of IV pantoprazole were from this ward (26.6%), which constituted 88.4% of total cases with rational orders. In other words, despite the low fill rate and low quality of OEFs regarding specifying indications, the appropriateness of IV pantoprazole use was higher in this ward compared with other wards with a high number of orders.

This study suffers from some limitations. One of them resulted from the teaching nature of the hospital. In our study, 90.5% of OEFs were filled by medical residents. In a teaching hospital, new medical residents who attend the hospital and replace the previously oriented individuals might not be properly aware of the implemented guidelines and OEFs. Another limitation

was poor documentation of the patients' charts. Although the prospective nature of the study design helped us to complete the required data from different sources, some patients' charts lacked clinical details regarding patients, medical situations, clinical disease progression, or indication. Poor documentation might have led to a different judgment made by the researcher about the indication for IV pantoprazole from the intention of the physician in this regard. Moreover, the hospital pharmacy had limitations in assigning pharmacists to follow up and send feedback to the physicians regarding the OEFs, which could have endorsed the process substantially. Additionally, there was a lack of data regarding the compliance of the physicians with the OEFs at the time of initiation of the intervention to compare with the current results.

The compliance of physicians with the OEF, designed to improve the rational use of IV pantoprazole six months after its implementation, was suboptimal. The fill rate as well as the quality of the filled OEFs in terms of accuracy of indication, specification, and appropriate use were not adequate. Continuous endorsements by educational interventions for the new medical team members might be necessary. Moreover, considering feedback or applying restrictions to the dispensing of the medication for inappropriate orders could be helpful. Further research is needed to determine the reasons for non-compliance with the implemented intervention as the point of physicians' view.

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References

1. Eslami L, Nasseri-Moghaddam S. Meta-analyses: does long-term PPI use increase the risk of gastric premalignant lesions? *Arch Iran Med* 2013;16:449-58.
2. Lanas A. We are using too many PPIs, and we need to stop: a European perspective. *Am J Gastroenterol*. 2016;111:1085-6.
3. Savarino V, Dulbecco P, de Bortoli N, Ottonello A, Savarino E. The appropriate use of proton pump inhibitors (PPIs): need for a reappraisal. *Eur J Intern Med* 2017;37:19-24.

4. Lin D, Eke C, Cai C, Thrift AP, Shukla R. Decreasing overall and inappropriate Proton Pump Inhibitor use: perspective from a large safety-net healthcare system. *Clin Gastroenterol Hepatol* 2020;18:763-6. e762.
5. Santos YAPD, Younes-Ibrahim MS, Crozatti LL, Raglione D, Cardozo Junior LCM, Besen BAMP, et al. Adherence to a stress ulcer prophylaxis protocol by critically ill patients: a prospective cohort study. *Rev Bras Ter Intensiva* 2020;32:37-42.
6. Rafinazari N, Abbasi S, Farsaei S, Mansourian M, Adibi P. Adherence to stress-related mucosal damage prophylaxis guideline in patients admitted to the intensive care unit. *J Res Pharm Pract* 2016;5:186-92.
7. Foroughinia F, Madhooshi M. Attachment to stress ulcer prophylaxis guideline in the neurology wards of two teaching and non-teaching hospitals: A retrospective survey in Iran. *J Res Pharm Pract* 2016;5:138-41.
8. Lai PS, Wong YY, Low YC, Lau HL, Chin KF, Mahadeva S. Unexplained abdominal pain as a driver for inappropriate therapeutics: an audit on the use of intravenous proton pump inhibitors. *PeerJ* 2014;2:e451.
9. Huang HB, Jiang W, Wang CY, Qin HY, Du B. Stress ulcer prophylaxis in intensive care unit patients receiving enteral nutrition: a systematic review and meta-analysis. *Crit Care* 2018;22:20.
10. Krag M, Marker S, Perner A, Wetterslev J, Wise MP, Scheffold JC, et al. Pantoprazole in Patients at Risk for Gastrointestinal Bleeding in the ICU. *N Engl J Med* 2018;379:2199-2208.
11. Sohrevardi SM, Vahidi A, Mosadegh MH, Dehghani-Tafti A, Dadollahi A, et al. Evaluation of Prescriptions and Use of Intravenous Pantoprazole in General Wards and Intensive Care Unit of Shahid Sadoughi Hospital in Yazd. *J Pharm Care* 2016;3:7-10.
12. Moradi M, Raeesi S, Sepehri Z. Audit of IV pantoprazole: pattern of administration and compliance with guideline in a teaching hospital. *Springerplus* 2016;5:1749.
13. Tringali A, Manta R, Sica M, Bassotti G, Marmo R, Mutignani M. Comparing intravenous and oral proton pump inhibitor therapy for bleeding peptic ulcers following endoscopic management: a systematic review and meta-analysis. *Br J Clin Pharmacol* 2017;83:1619-35.
14. Bajaj JS, Dua KS, Hanson K, Presberg K. Prospective, randomized trial comparing effect of oral versus intravenous pantoprazole on rebleeding after nonvariceal upper gastrointestinal bleeding: a pilot study. *Dig Dis Sci* 2007;52:2190-4.
15. Foroutan N, Fahimi F, Dabin Y, Foroutan A, Habibi M, Salamzadeh J. Budget Impact Analysis of Using Omeprazole Immediate-Release Oral Suspension in Replace of Intravenous Pantoprazole in Critically Ill Patients. *J Popul Ther Clin Pharmacol* 2015;22:e292-302.
16. Lau BD, Pinto BL, Thiemann DR, Lehmann CU. Budget impact analysis of conversion from intravenous to oral medication when clinically eligible for oral intake. *Clin Ther* 2011;33:1792-6.
17. Hogerzeil HV. Promoting rational prescribing: an international perspective. *Br J Clin Pharmacol* 1995;39:1-6.
18. Laing R, Hogerzeil H, Ross-Degnan D. Ten recommendations to improve use of medicines in developing countries. *Health Policy Plan* 2001;16:13-20.
19. Taghizadeh-Ghehi M. Professional Interventions to Improve Rational Prescribing and Drug Utilization: Role of Pharmacists. *J Pharm Care* 2018;6:37-8.
20. Walker MJ, Crews NR, El-Halabi M, Fayad NF. Educational Intervention Improves Proton Pump Inhibitor Stewardship in Outpatient Gastroenterology Clinics. *Gastroenterology Res* 2019;12:305-11.
21. McDonald EG, Jones J, Green L, Jayaraman D, Lee TC. Reduction of inappropriate exit prescriptions for proton pump inhibitors: A before- after study using education paired with a web- based quality- improvement tool. *J Hosp Med* 2015;10:281-6.
22. Walton SM, Galanter W, Rosencranz H, Meltzer D, Stafford RS, Tiryaki F, et al. A trial of inpatient indication based prescribing during computerized order entry with medications commonly used off-label. *Appl Clin Inform* 2011;2:94-103.
23. Del Giorno R, Ceschi A, Pironi M, Zasa A, Greco A, Gabutti L. Multifaceted intervention to curb in-hospital over-prescription of proton pump inhibitors: A longitudinal multicenter quasi-experimental before-and-after study. *Eur J Intern Med* 2018;50:52-9.
24. Salmasian H. Identifying and reducing inappropriate use of medications using Electronic Health Records [dissertation]. New York: Columbia University.; 2015.
25. Laki B, Taghizadeh- Ghehi M, Assarian M, Heidari K, Torkamandi H, Javadi MR, et al. Effect of hospital- wide interventions to optimize albumin use in a tertiary hospital. *J Clin Pharm Ther* 2017;42:704-9.
26. Thompson W, Hogel M, Li Y, Thavorn K, O'Donnell D, McCarthy L, et al. Effect of a proton pump inhibitor deprescribing guideline on drug usage and costs in long-term care. *J Am Med Dir Assoc* 2016;17:673.e1-4.
27. Søndergaard J, Hansen DG, Rowett D. Interventions that influence prescribing decisions and drug utilization. *Drug Utilization Research: Methods and Applications*. UK: Wiley-Blackwell; 2016.
28. Sirinavin S, Suvanakoot P, Sathapatayavongs B, Malatham K. Effect of antibiotic order form guiding national use of expensive drugs on cost containment. *Southeast Asian J*

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Trop Med Public Health 1998;29:636-42.

29. Cyriac JM, James E. Switch over from intravenous to oral therapy: A concise overview. *J Pharmacol Pharmacother* 2014;5:83-7.
30. Valizadeh Toosi M, Elahi Vahed AR, Iradj Maleki I, Bari Z. Comparison of Oral versus Intravenous Proton Pump Inhibitors in Preventing Re-bleeding from Peptic Ulcer after Successful Endoscopic Therapy. *Middle East J Dig Dis* 2018;10:236-41.