

Inappropriate usage of intravenous proton pump inhibitors and associated factors in a high complexity hospital in Brazil

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ABSTRACT – Background – Intravenous (IV) use of proton pump inhibitors (PPIs) is advised only in cases of suspected upper gastrointestinal bleeding (UGIB) or impossibility of receiving oral medication, although there has been a persistent practice of their inappropriate use in health institutions. **Objective** – The purpose of our study was to measure the inappropriate use of IV PPIs in a high complexity hospital in Brazil and to estimate its costs. **Methods** – Retrospective study of 333 patients who received IV omeprazole between July and December of 2018 in a high complexity hospital in Brazil. **Results** – IV omeprazole was found to be appropriately prescribed in only 23.4% patient reports. This medication was administered mainly in cases of suspected UGIB (19.1%) and stress ulcer prophylaxis in patients with high risk of UGIB unable to receive medication orally (18.7%). It was observed a statistically significant association between adequate prescription and stress ulcer prophylaxis in patients with high risk of UGIB unable to receive medication orally; patient *nil per os* with valid indication for PPIs usage; prescription by intensive care unit doctors; prescription by emergency room doctors; intensive care unit admission; evolution to death; sepsis; and traumatic brain injury ($P < 0.05$). On the other hand, inadequate prescription had a statistically significant association with surgical ward prescription and non-evolution to death ($P < 0.05$). The estimated cost of the vials prescribed inadequately was US\$1696. **Conclusion** – There was a high number of inappropriate IV omeprazole prescriptions in the studied hospital, entailing greater costs to the institution and unnecessary risks.

HEADINGS – Proton pump inhibitors. Peptic ulcer. Gastrointestinal hemorrhage. Inappropriate prescribing. Off-label use. Endoscopy. Medical overuse.

INTRODUCTION

The most efficient medications for gastric acid suppression nowadays are proton pump inhibitors (PPIs), available in the Market since 1989 with the launch of omeprazole⁽¹⁾. These pharmaceutical drugs inhibit H⁺, K⁺-ATPase of gastric parietal cells, causing an increase in stomach pH⁽²⁾.

The main clinical indications approved by the Food and Drug Administration for the administration of this class of medication are treatment for erosive esophagitis and its maintenance; treatment of gastro esophageal reflux; reduction of risk of gastric ulcer associated to non-steroid anti-inflammatory drug (NSAID); *Helicobacter pylori* eradication; hyper secretive pathological conditions, such as Zollinger-Ellison syndrome; and duodenal ulcer treatment and its maintenance⁽³⁾.

However, the intravenous (IV) preparations, according to recent studies, are reserved for cases of patients with: gastric hyper secretion associated with neoplastic conditions and Zollinger-Ellison unable to receive medication orally; severe cases of non-variceal upper gastrointestinal bleeding (UGIB); gastrointestinal hemorrhage with risk of recurrent continuous bleeding; and in stress peptic ulcer prophylaxis in high risk patients on the intensive care unit (ICU) without access to enteral feeding or unable to receive orally, *nil per os* (NPO)^(4,5). According to the Brazilian National Health

Surveillance Agency (ANVISA), intravenous sodium omeprazole is indicated when the usage of the pharmaceutical form of pills is not possible. Sodium omeprazole is to be used to treat: gastric or duodenal peptic ulcer; reflux esophagitis; Zollinger-Ellison syndrome; and prophylaxis for aspiration of gastric content during general anesthesia in high risk patients⁽⁶⁾.

The adequate use of IV PPIs in patients with suspected non-variceal UGIB, according to current international guidelines, consists on the implementation of an initial bolus of 80 mg and, subsequently, an infusion of 8 mg/h for 72 hours, executing a new treatment for 72 hours if recurrence of bleeding^(7,8). However, in a systematic review and meta-analysis conducted by Sachar, Vaidya and Laine, it was observed that the utilization of PPIs intermittently, with an initial bolus of 80 mg followed by 40 mg every 12 hours presented similar outcomes to the continuous infusion of 8 mg/h⁽⁹⁾. In patients unable to receive oral drugs, the IV dosage should be individualized in accordance to the specific indication^(10,11).

The inappropriate use of IV PPIs has been observed in various studies, especially in cases without the suspicion of UGIB^(4,11-14). There are, however, studies demonstrating that oral preparations of PPIs have similar efficacy to IV preparations in cases of bleeding ulcers suggesting that it seems to be no need for such an excessive IV administration in hospitals resulting undoubtedly to higher institutional costs⁽¹⁵⁻¹⁷⁾.

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There is little data regarding the usage of IV PPIs in Brazil and Latin America. This present study had, therefore, the objective of evaluating the indications, posologies, duration of treatment and cost of IV omeprazole prescriptions, the only IV PPI available in the studied institution.

METHODS

This present study was approved by the Ethics and Research with Human Beings Committee from the *Universidade do Extremo Sul Catarinense* (3.084.465) and from the Hospital São José Criciúma (3.145.505).

This study was held in a high complexity hospital in the Southern region of the state of Santa Catarina, Brazil, estimating that in six months about a thousand patients receive IV omeprazole in this institution and the minimum sample calculation was of 291 patient records. Three hundred thirty three patient records of patients who received IV omeprazole were assessed retrospectively in the period of July to December of 2018. Patients with age inferior to 18 years were excluded.

An instrument for data collection was used, evaluating sex, age, race and comorbidities of the patient; which was the indication for initiating treatment with IV omeprazole; what were the reasons for its use when there was no suspected UGIB; if the patient was subjected to upper digestive endoscopic exam (UDE) or surgical procedure in case of suspected upper gastrointestinal bleeding and reasons for non-subjection of the patient; UDE findings, if performed; surgical procedure findings, if performed; IV omeprazole's posology; duration of treatment; service responsible for prescribing the medication; admission in the intensive care unit during hospital stay; prescription by emergency room doctor; if there was evolution to death during hospital stay; if there was IV omeprazole suspension in 48 hours when initiated by inadequate reason; total number of vials of this pharmaceutical drug utilized during hospital stay; number of vials utilized inadequately; cost involved with the use of this medication; if the indication of use was adequate; if the dosage was adequate; if the duration of treatment was adequate and if the prescription of IV omeprazole was entirely correct.

The indications considered as adequate for the administration of this IV drug were upper gastrointestinal bleeding or its suspicion before a confirmatory procedure, like endoscopy or surgery; stress ulcer prophylaxis in patients with high risk of upper gastrointestinal bleeding and unable to receive medication orally; and patient in NPO with valid indication for oral PPI. Of the patients with suspected non-variceal UGIB, were considered with appropriate indication those presenting peptic ulcer disease with stigmata of high risk of rebleeding in the endoscopic or surgical report according to Forrest classification: Forrest IA (spurting hemorrhage), IB (oozing hemorrhage), IIA (visible vessel) or IIB (adherent clot), in addition to erosive disease of the esophagogastric mucous membrane with active bleeding, tumoral lesion with active bleeding, or while awaiting for confirmatory procedure. If the patients did not match the formerly cited situations, it was also considered an adequate indication those patients who had the medication suspended in up to 48h after the result of the endoscopy. Of the patients unable to receive enteral diet, those in NPO or intolerant to oral medication with valid indication for PPIs were considered with adequate indication, or those that were receiving prophylaxis for stress ulcer because of high risk of upper gastrointestinal bleeding.

For stress ulcer prophylaxis, we considered as critically ill patients with high risk for upper gastrointestinal bleeding those with at least one of the following criteria: hemorrhagic diathesis – platelet count <50.000 by mm^3 , an International Normalized Ratio (INR) >1.5 or an activated partial thromboplastin time (aPTT) >2 the control value; mechanical ventilation >48 hours; history of gastrointestinal ulcer or gastrointestinal bleeding in the last year; traumatic brain injury; traumatic spinal cord injury; burn; or at least two of the following findings: sepsis; period of intensive care unit stay superior to one week; gastrointestinal bleeding for six or more days; glucocorticoid therapy (superior to 250 mg of hydrocortisone or equivalent); or use of NSAID or antiplatelet agents⁽⁵⁾.

Posology was considered adequate when, in the case the patient had UGIB suspicion, a bolus of 80 mg followed by continuous infusion of 8 mg/h for 72 hours or bolus of 80 mg followed by 40 mg every 12 hours for 72 hours was instituted. If the usage was due to stress ulcer prophylaxis in patients with high risk of UGIB unable to receive it orally or in patients in NPO with valid indication for oral PPI, it was considered adequate the use of 40 mg of intravenous omeprazole once a day.

Regarding the duration of treatment, all the patients who did not present any indication for intravenous omeprazole use and those with UGIB suspicion who did not suspend the medication in up to 48 hours after the absence of valid indication or absence of stigmata of peptic ulcer with high risk of rebleeding in the diagnostic procedure results were considered inadequate.

In cases where the indication was considered inadequate, dosage and duration of treatment were also considered inadequate. Only when indication, dosage and duration of treatment were adequate, the prescription was considered entirely adequate.

The collected data was analyzed with the help of the software IBM Statistical Package for the Social Sciences (SPSS) version 21.0. The quantitative variables were expressed by median and interquartile amplitude or minimum and maximum value when these did not present normal distribution and by mean and standard deviation when these did present with normal distribution. Qualitative variables were expressed by frequency and percentage.

For the calculation of the number of inadequately prescribed vials and the cost of these to the hospital, we multiplied the number of days of inadequate prescription by the number of vials used in the period. The hospital onus was calculated by multiplying the total number of inadequate vials by the cost of each vial in the time of the study.

The statistical tests were made with a significance level $\alpha = 0.05$ and, therefore, 95% confidence interval. The data distribution in relation to normality was evaluated by application of the Kolmogorov-Smirnov test. The investigation of association between qualitative variables was made by application of the Pearson's chi-square test, Fisher's exact test and the likelihood ratio test, followed by residual analysis when statistical significance was observed.

RESULTS

Of the 333 patients analyzed, 13 were excluded due to age inferior to 18 years, with a subsequent sample of 320 patients. The studied population was composed mainly by men (54.4%), whites (93.4%) with a mean age of approximately 60 years (± 16.29). The comorbidities most commonly found in these patients are described in TABLE 1.

TABLE 1. Demographic data and comorbidities of patients using intravenous omeprazole.

	Mean ±SD, n (%) n=320
Age (years)	59.92±16.29
Sex	
Male	174 (54.4)
Female	146 (45.6)
Race	
White	298 (93.4)
Black	11 (3.4)
Brown	9 (2.8)
Indigenous	1 (0.3)
Not specified	1
Comorbidities	
Systemic arterial hypertension	125 (39.1)
Pneumonia	81 (25.3)
Diabetes Mellitus	76 (23.8)
Malignant neoplasia	62 (19.4)
Acute coronary syndrome	45 (14.1)
Sepsis	44 (13.8)
Cerebrovascular accident	28 (8.8)
COPD	20 (6.3)
Congestive heart failure	15 (4.7)
Chronic hepatopathy	15 (4.7)
Traumatic brain injury	12 (3.8)
UTI	10 (3.1)
Gallstones	9 (2.8)
Chronic kidney disease	9 (2.8)
Other	95 (29.7)

SD: standard deviation; COPD: chronic obstructive pulmonary disease; UTI: urinary tract infection.

The suspicion of presence of UGIB was the most frequent indication for initiating the use of IV omeprazole, occurring in 19.1% of the cases. The median of duration of treatment was of 4.00 days, with an interquartile amplitude of 2.00–8.00, and periods of duration varying from 1 to 61 days were found (TABLE 2).

The largest part of the prescriptions was made by doctors of the ICU (39.7%) and the prescription was initiated by emergency room doctors in only 10.3% of the cases. Half of the patients were admitted to the ICU during hospital stay and 69 (21.6%) patients evolved to death (TABLE 3).

Regarding the group of patients with UGIB suspicion, 34.4% did not undergo any procedure for confirmation of presence of upper gastrointestinal bleeding. The endoscopic report of patients who did undergo UDE showed normal or unspecific findings in most cases (31.6%). Regarding the 28 (73.6%) patients who did not have confirmed high risk of bleeding, 9 (32.2%) remained utilizing the IV omeprazole for more than 48 hours after receiving the UDE report (TABLE 4).

The indication for use of IV omeprazole was considered adequate in only 41.6% of cases. Regarding posology, the following findings were observed in reference to the group with UGIB suspicion: 15 (24.6%) in use of initial bolus of 80 mg followed by

TABLE 2. Indications for initiating intravenous omeprazole usage and duration of treatment.

	n (%), Median (minimum – maximum) n=320
Adequate indications	
Upper gastrointestinal bleeding suspicion	61 (19.1)
Stress ulcer prophylaxis in patient with high risk of UGIB unable to receive orally	60 (18.7)
Patient in NPO with valid PPI indication	12 (3.7)
Inadequate indications	
PUD prophylaxis after surgical procedure	58 (18.1)
Stress ulcer prophylaxis in patients with low risk of UGIB	40 (12.5)
Abdominal pain	23 (7.2)
Absence of clear indication	19 (5.9)
Stress ulcer prophylaxis and high risk of UGIB with possibility of oral administration	12 (3.7)
Anticoagulants/ platelet antiaggregant/ anti-inflammatories usage	11 (3.4)
Abdominal pain associated with vomiting	8 (2.5)
Other	16 (5.0)
Duration of treatment (days)	4.00 (1–61)

UGIB: upper gastrointestinal bleeding; PUD: peptic ulcer disease; NPO: nil per os; PPI: proton pump inhibitor.

TABLE 3. Sectors involved in prescribing intravenous omeprazole and evolution to death.

	n (%) n=320
Prescribing sector	
ICU	127 (39.7)
General medicine	81 (25.3)
Surgery	56 (17.5)
Oncology	18 (5.6)
Gastroenterology	16 (5.0)
Cardiology	8 (2.5)
Pneumology	5 (1.6)
Other	9 (2.8)
Prescription by ER doctor	
Yes	33 (10.3)
No	287 (89.7)
Admission in the ICU during hospital stay	
Yes	160 (50.0)
No	160 (50.0)
Evolution to death	
Yes	69 (21.6)
No	251 (78.4)

ICU: intensive care unit; ER: emergency room.

TABLE 4. Performance of procedures for confirmation of bleeding in patients using intravenous omeprazole with suspicion of upper gastrointestinal bleeding.

	n (%)
	n=61
Procedure	
UDE	38 (62.3)
Surgery	2 (3.3)
Gastric or duodenal perforated ulcer	2 (100.0)
Not performed	21 (34.4)
Reason for not performing any procedure (n=21)	
Critically ill patient	6 (28.6)
Recent UDE	4 (19.0)
Unnecessary UDE or patient too well for procedure	4 (19.0)
Not informed	7 (33.4)
UDE results (n=38)	
Normal or unspecific findings	12 (31.6)
Peptic ulcer disease with stigmata of low risk of rebleeding (Forrest IIC or III)	10 (26.3)
Peptic ulcer disease with stigmata of high risk of rebleeding (Forrest IA, IB, IIA or IIB)	8 (21.1)
Gastro-esophageal varicose veins	3 (7.9)
Esophagogastric mucous membrane erosive disease without active bleeding	2 (5.3)
Esophagogastric mucous membrane erosive disease with active bleeding	1 (2.6)
Tumoral lesion with active bleeding	1 (2.6)
Gastric angiodysplasia without signs of recent bleeding	1 (2.6)
Medication suspended in up to 48h in case of absence of indication for maintenance of intravenous omeprazole (n=28)	
Yes	19 (67.8)
No	9 (32.2)

UDE: upper digestive endoscopy.

40 mg every 12 hours and 8 (13.1%) in use of bolus of 80 mg on IV omeprazole followed by continuous infusion of 8 mg/h for 72 hours. In regard to the group of patients with stress ulcer prophylaxis and high risk of gastrointestinal bleeding unable to receive medication orally or in NPO with valid indications for PPI usage, 70 (97.2%) used 40 mg of IV omeprazole once a day. In any other case, the posology was considered inadequate.

Considering that when the indication was considered inadequate, dosage and duration were also considered inadequate, only 93 (29.1%) patients were in use of correct doses and only 101 (31.6%) patients presented adequate duration of treatment. Prescription was entirely adequate in only 23.4% of analyzed prescriptions (TABLE 5). Comparing the group with UGIB suspicion and the one that initiated IV omeprazole for other reasons, prescription was entirely adequate in 31.1% and 21.6% of cases, respectively, thus having no statistically significant difference ($P=0.114$) (TABLE 6).

The median of the number of vials utilized per patient was 6.00, with variations from 1–74 phials per patient and interquartile amplitude of 2.50–11.00. The median for the number of inadequate vials per patient was 3.00, with variations from 0–60 inadequate vials per patient and interquartile amplitude of 0.00–7.00. It was

TABLE 5. Evaluation of prescriptions of patients who used intravenous omeprazole.

	n (%)
	n=320
Adequate indication	
Yes	133 (41.6)
No	187 (58.4)
Adequate dosage*	
Yes	93 (29.1)
No	227 (70.9)
Adequate duration*	
Yes	101 (31.6)
No	219 (68.4)
Entirely adequate prescription	
Yes	75 (23.4)
No	245 (76.6)

*When the indication was considered inadequate, dosage and duration were also considered inadequate. Source: Research data, 2019.

TABLE 6. Factors associated with adequate and inadequate prescription of intravenous omeprazole.

	n (%)		P-value
	Adequate prescription	Inadequate prescription	
Adequate indications	n=74	n=180	
Suspected upper gastrointestinal bleeding	19 (31.1)	42 (68.9)	<0.001 [†]
Stress ulcer prophylaxis in patient with high risk of UGIB unable to receive orally	44 (73.3) ^a	16 (26.7)	
Patient in NPO and valid indication for PPI usage	11 (91.7) ^a	1 (8.3)	
Prescribing sector	n=75	n=223	
ICU	44 (34.6) ^a	83 (65.4)	0.010 [†]
General medicine	18 (22.2)	63 (77.8)	
Surgery	7 (12.5)	49 (87.5) ^a	
Prescription by ER doctor	n=75	n=245	
Yes	15 (45.5) ^a	18 (54.5)	0.002 [‡]
No	60 (20.9)	227 (79.1) ^a	
ICU admission	n=75	n=245	
Yes	50 (31.3) ^a	110 (68.8)	0.001 [‡]
No	25 (15.6)	135 (34.4) ^a	
Evolution to death	n=75	n=245	
Yes	31 (44.9) ^a	38 (55.1)	<0.001 [‡]
No	44 (17.5)	207 (82.5) ^a	
Sepsis			
Yes	23 (54.5) ^a	20 (45.5)	<0.001 [‡]
No	51 (18.5)	225 (81.5) ^a	
Traumatic brain injury			
Yes	8 (66.7) ^a	4 (33.3)	0.001 [†]
No	67 (21.8)	241 (78.2) ^a	

UGIB: upper gastrointestinal bleeding; NPO: nil per os; PPI: proton pump inhibitor; ICU: intensive care unit; ER: emergency room. [†]Value obtained after applying the Likelihood Ratio test; [‡]Value obtained after applying the Pearson qui-square test. ^aStatistically significant value after residual analysis.

utilized a total of 2853 vials in these 320 patients and, of these, 1696 were considered inadequate. Considering the approximate value of each vial is US\$1.00, it is estimated a cost of US\$1696.00 spent with inadequate use of IV omeprazole prescribed for these patients, and a total of US\$2853.00 with the total of utilized vials evaluated in this study. As it was collected about a third of the number of patient reports of those who used IV omeprazole in six months in the studied hospital, it is estimated a cost of about US\$5088.00 with the administration of inadequate vials and a cost of US\$8559.00 with the total of vials of IV omeprazole administered in a period of one semester.

It was observed a statistically significant association between adequate prescription and the following factors: stress ulcer prophylaxis in patients with high risk of UGIB unable to receive medication orally; patient in NPO with valid indication for PPI usage; ICU doctor prescription; evolution to death; sepsis; and traumatic brain injury ($P < 0.05$). Inadequate prescription, however, had a statistically significant association with prescription by the surgical ward and non-evolution to death ($P < 0.05$) (TABLE 6).

DISCUSSION

This study was conducted in a high complexity hospital evaluating the usage of IV omeprazole during a period of six months. It was verified that the prescription was inadequate in 76.6% of cases, a higher rate than those observed in studies conducted in other countries^(4,11-14).

In the study by Lai et al., in 76.4% of the cases an unexplained abdominal pain was the reason for initiating the use of IV PPIs and, in these cases, 68.9% had UGIB suspicion⁽¹⁴⁾. In this present study, the most frequent reason for initiating the use of IV omeprazole was UGIB suspicion, however this occurred in only 19.1% of cases. Other studies demonstrated that most patients receiving IV PPIs, did it for stress ulcer prophylaxis, data that is compatible with this study, in which it was administered IV omeprazole in 53% of the patients for prophylaxis of peptic ulcer disease, if we add the patients in high and low risk^(4,13).

Former studies observed that most of the doctors responsible for IV PPI prescription were part of the surgical ward^(11,14), a data that differs from this present study, in which most of the prescribing doctors were from the ICU (39.7%) and from the clinical ward (25.3%). In this study, it was also observed that half of the patients had an ICU stay. It is possible that patients who were evaluated at the studied institution had a larger admission in this sector in light of being a tertiary hospital, with cases of higher gravity, which could be better evaluated in posterior studies with a larger number of patients.

On a study made in England, IV PPI prescriptions were found to be inadequate in 75.4% of cases, and most of these patients receiving this medication inadequately had no suspicion of UGIB⁽¹¹⁾. In this present study there was a larger percentage of patients in use of IV omeprazole inadequately in the group without UGIB suspicion. There was no statistically significant difference, however, between the group with UGIB suspicion and the group that initiated IV omeprazole for other reasons.

In a Canadian study that evaluated IV PPI prescriptions in cases of UGIB suspicion, it was found that 68% of the patients underwent an UDE. Of those that underwent endoscopic procedure, 86.2% had no stigmata for high risk of rebleeding and, of these, 56.9% remained in use of the medication despite the low

risk of rebleeding⁽¹⁸⁾. In regard to the present study, 73.6% of the patients who underwent UDE did not have high risk of rebleeding, a similar finding to the one observed in the Canadian study, but only 32.3% of these remained utilizing IV omeprazole 48 hours after the procedure.

In this study, the adequate prescription was associated with stress ulcer prophylaxis in patients with high risk of UGIB unable to receive oral medication; patient in NPO with valid indication for PPI usage; prescription by ICU doctor; prescription by emergency room doctor; ICU admission; evolution to death; sepsis; and traumatic brain injury. The inadequate prescription was associated to surgical ward prescription and non-evolution to death. It is important to highlight that traumatic brain injury and sepsis combined to long stay in ICU were considered adequate indications for stress ulcer prophylaxis in patients with high risk of UGIB unable to receive oral medication. Since all these factors are associated with greater severity and were more prevalent in patients with adequate prescription, we believe they contributed to the association between adequate prescription and evolution to death. The factors associated with adequate and inadequate prescriptions are relevant in facilitating the identification and correction of inadequate practices in health institutions.

This study presented limitations regarding sample. Although the minimum sample was matched, the total number of patient records in use of IV omeprazole in the studied period was not analyzed due to little time available for data collection, and also this being a retrospective study. It is important to point out, however, that there is not sufficient data in literature about how the administration of IV PPIs is carried out in Brazil and Latin America. Thus, this article is still relevant so that greater information regarding the hospital practices in the studied region is obtained.

Knowing that IV PPIs entail a high cost to institutions, a few models were already proposed, suggesting that the administration of these IV medications in every case of suspected UGIB probably is not a cost-effective approach, and also most of the patients treated for UGIB are not hemodynamically unstable^(11,19). Although UGIB suspicion still being a formal indication for the use of IV PPIs, a few studies already demonstrated that patients who tolerate oral medication can receive this class of medication this way, which is effective even in cases of bleeding peptic ulcers, entailing a smaller cost than the usage of IV vials⁽¹⁵⁻¹⁷⁾.

Some therapeutic strategies aiming to minimize IV PPI prescription errors have been shown in literature. In a study conducted by Kaplan et al., it was observed that, initially, only 50% of the patients receiving IV pantoprazole had adequate indication. A multidisciplinary intervention involving medical education; computerized dosage model; pharmaceutical intervention when a patient without suspected UGIB and with tolerance for oral medication received IV PPI and recommendation of a consult with a gastroenterologist when a continuous infusion of these medications was applied. After this intervention, there was a significant reduction of inadequate prescriptions in the groups with UGIB suspicion (26%) and without UGIB suspicion (41%)⁽¹²⁾.

In the study conducted by Lai et al., every fourth IV PPI prescription received by the pharmaceutical sector was traced against the guidelines from that hospital. PPIs were incorrectly prescribed in 52.8% of cases and interventions were more effective when made by senior doctors (100%), followed by clinical pharmacists (50%)⁽¹⁴⁾.

Despite PPIs being considered one of the safest pharmaceuti-

cal classes, there are potential side effects with chronic use of these medications and gastric suppression in the long term⁽²⁰⁾. These drugs present few interactions with other drugs. The most notable would be caused by the inhibition of the P450 2C19 cytochrome, especially by omeprazole, leading to a reduction of clopidogrel conversion in its active metabolite, enlarging the risk of cardiovascular diseases in patients who use both medications simultaneously⁽²¹⁾. Other drugs which may also be affected by inhibiting the P450 2C19 cytochrome are diazepam, phenytoin and warfarin, while dexlansoprazole and lansoprazole may induce theophylline metabolism by the P450 1A2 cytochrome⁽²²⁾.

The most important side effects related to the usage of these drugs are rebound gastric hypersecretion; hypergastrinemia; hypomagnesemia; reduction of calcium, iron and vitamin B12 absorption; greater risk of bone fracture; enteric infections, with diarrhea by *Clostridium difficile* the most significant within those; the possibility of spontaneous bacterial peritonitis in cirrhotic patients; community acquired pneumonia; nephrotoxicity and possible augmented risk of dementia and myopathies. There is an inverse relation between gastric acidity and plasmatic levels of gastrin, justifying the hypergastrinemia in chronic users of PPIs. The rise in serum levels of gastrin has the potential to cause cellular hyperplasia in enterochromaffin-like cells, which caused discussions about the possibility of greater development of gastric neoplasia in these patients. There isn't, however, clear evidence that the prolonged use of these drugs predisposes the occurrence of cancers. The appearance of polyps on the gastric fundus region, on the other hand, is common in patients with

hypergastrinemia, and they don't seem to have any potential for malignant transformation⁽²³⁾.

In conclusion, this study demonstrated an elevated number of inadequate IV omeprazole prescriptions in the studied hospital, a common problem in many other health institutions in the world, entailing a greater cost associated with the unnecessary administration of vials of this medication. These results prompt the implementation of multidisciplinary intervention strategies and medical education in order to minimize prescription errors, reducing costs and risks involved with IV PPI usage.

Authors' contribution

Bischoff LM and Faraco LSM: conception and design; analysis and interpretation of the data; drafting of the article; critical revision of the article for important intellectual content. Machado LV, Bialecki AVS and Almeida GM: analysis and interpretation of the data; critical revision of the article for important intellectual content. Becker SCC: conception and design; analysis and interpretation of the data; critical revision of the article for important intellectual content; final approval of the article.

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Bischoff LM, Faraco LSM, Machado LV, Bialecki AVS, Almeida GM, Becker SCC. Uso inapropriado de inibidores de bomba de prótons intravenosos e fatores associados em um hospital de alta complexidade no Brasil. *Arq Gastroenterol.* 2021;58(1):32-8.

RESUMO – Contexto – Atualmente, o uso intravenoso (IV) dos inibidores de bomba de prótons (IBPs) é indicado em poucas situações, como em casos de hemorragia digestiva alta ou impossibilidade de recebê-los via oral. Há diversos estudos mostrando o uso excessivo desse fármaco, na forma intravenosa, desnecessariamente e acarretando altos custos aos hospitais. **Objetivo** – Avaliar as indicações, posologias, duração do tratamento e custos das prescrições de omeprazol intravenoso. **Métodos** – Estudo retrospectivo de 333 pacientes que receberam omeprazol intravenoso entre julho e dezembro de 2018 em um hospital de alta complexidade no Brasil. **Resultados** – A prescrição de omeprazol intravenoso foi considerada totalmente adequada em apenas 23,4% das prescrições analisadas. O medicamento foi administrado principalmente em casos de suspeita de hemorragia digestiva alta (HDA) (19,1%) e profilaxia de úlcera de estresse em paciente com alto risco de HDA impossibilitado de receber via oral (18,7%). Foi observada associação estatisticamente significativa entre prescrição adequada e profilaxia de úlcera de estresse em paciente com alto risco de HDA impossibilitado de receber medicamento via oral; paciente em *nil per os* com indicação válida de IBPs; prescrição por médico da UTI; prescrição por médico do pronto atendimento; admissão na UTI; evolução a óbito; sepse; e traumatismo cranioencefálico ($P < 0,05$). Já a prescrição inadequada teve associação estatisticamente significativa com prescrição por setor cirúrgico e a não evolução a óbito ($P < 0,05$). O custo estimado do total de ampolas prescritas inadequadamente foi de US\$1696,00. **Conclusão** – Houve um elevado número de prescrições de omeprazol intravenoso inadequadas no hospital estudado, acarretando um custo elevado para a instituição.

DESCRITORES – Inibidores da bomba de prótons. Úlcera péptica. Hemorragia gastrointestinal. Prescrição inadequada. Uso off-label. Endoscopia. Sobremedicalização.

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