## Original Article:

# Clinical Characteristics of Intravenous Pantoprazole Consumption in Cardiac Intensive Care Unit

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## ABSTRACT

**Background:** Proton Pump Inhibitors (PPIs) are the most common medicine for the treatment and prophylaxis of acid peptic conditions. The inappropriate use of the PPIs, mainly the intravenous form of pantoprazole may lead to excessive cost and unexpected adverse effects.

**Objectives:** The present study aimed to evaluate the use of intravenous pantoprazole in the International Heart Center in the north of Iran.

**Methods:** The current retrospective study was performed on 215 patients hospitalized in Fatemeh Zahra Hospital in Sari City, Iran. Patients' demographics, the type and doses of pantoprazole, and other relevant clinical data were recorded from their documentation. The appropriate use of pantoprazole was evaluated according to recommendations provided by Medscape 2020, and UpToDate 2020.

**Results:** Prescribing PPI was appropriate for 53.5% of the examined patients; however, the majority of intravenous prescription cases were inappropriate (76.7%). Oral PPIs could have been used in 93.5% of the cases; however, they received the parenteral form of pantoprazole. The main cause of pantoprazole prescription in the explored hospital was stress ulcer prophylaxis, with the median 4/18 days used, which internal specialists in most of the cases (45.6%) prescribed.

**Conclusion:** In the current study, administrating intravenous pantoprazole was inappropriate in most of the cases. As a result of this improper administration, the extensive cost is exposed to the healthcare system, i.e., likely to be unsafe for patients. Accordingly, risk and indication evaluation for the prescription of pantoprazole should be a priority in each patient. Finally, it seems necessary to determine a protocol for PPI prescription per hospital for the rational use of drugs.

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## Introduction

Drug Use Evaluation (DUE) studies are systematic methods of information gathering to consider drug-related problems, for optimizing drug use patterns in hospitals. DUEs are essential parts of rational medication use and help ensure the appropriate drug use [1, 2]. DUE studies are critical for medicine with a narrow therapeutic index, specific indications for expensive or widely prescribed drugs [3].

A serious complication developed after cardiac surgery or Coronary Artery Bypass Grafting (CABG) is a gastrointestinal disease, especially upper Gastrointestinal (GI) system bleeding; it is an infrequent but potentially lethal case, as these patients undergo anticoagulant therapy [4-7]. Numerous studies demonstrated the incidence and risk factors of upper GI bleeding for post-cardiac surgery [6-9]. The incidence of GI complications fallowed cardiac surgery was approximately 1%-5.5% [10, 11]. Furthermore, the frequency of the stress ulceration was reported to be approximately 0.35%-0.9%, as well as the mortality rate due to acute peptic ulcers after cardiac surgery ranged from 1% to 22% [12-17]. Therefore, it is reasonable to prescribe prophylactic treatment for upper GI diseases in these patients.

Pantoprazole is a Proton Pump Inhibitor (PPI) with oral and Intravenous (IV) dose forms. It seems that both doe forms present equal effects on reducing gastric acid secretion. An appropriate dose form is selected based on the patient's characteristics, such as the ability to take oral medication and hemodynamic status [18]. PPI selection is more important in critically ill patients. This is because an acid-secreting disorder or the prophylaxis of stress-related mucosal injury is more prevalent in these patients [18].

The inappropriate use of PPIs may increases risks, such as acute interstitial nephritis, infection, diarrhea, bone fracture, vitamin deficiencies, and hypomagnesemia [19]. In the cardiovascular setting, previous studies demonstrated that PPIs might increase cardiovascular risks in coronary artery disease patients and clopidogrel consumers [20]. In the general population, current evidence is insufficient to conclude the relationship between PPIs and MI [21]. Using PPIs might be a potential cause of hypomagnesemia; thus, it may aggravate arrhythmias and further complications [21].

According to the literature, the PPIs were indicated for erosive esophagitis, Gastroesophageal Reflux Disease (GERD), gastric ulcer associated with Nonsteroidal Anti-Inflammatory Drugs (NSAIDs), dyspepsia, H. pylori eradication, and Zollinger-Ellison (ZE) syndrome (Uptodate, Medscape). Pantoprazole is the only IV PPI existing in Iran; therefore, it was extensively used in hospitals. Adequate and acceptable IV pantoprazole conceptions result in decrease treatment cost, adverse effects related to injection and the incidence of nosocomial pneumonia, Spontaneous Bacterial Peritonitis (SBP), and Clostridium Difficile Infections (CDI) [18]. IV pantoprazole was among the most expensive and most commonly used drugs in our setting; other treatment options, such as oral pantoprazole and oral famotidine are significantly less costly. Thus, this study aimed to evaluate the prescription pattern of pantoprazole in a cardiac hospital to improve medication use.

## Materials and Methods

An observational retrospective study was conducted in the Intensive Care Units (ICUs) of Fatemeh Zahra Hospital in Sari City, Iran, from 2015-2016. This study investigated the medical records of admitted cardiac ICU patients receiving IV pantoprazole therapy.

In total, 215 medical records of admitted patients were studied concerning IV pantoprazole prescription. The inclusion criteria of the study were patients over the age of 18 years with IV pantoprazole prescription in cardiac critical settings. The exclusion criteria included patients under 18 years of age and without IV pantoprazole prescription.

The standard criteria for administering IV pantoprazole were determined from medical sources, including Lexi-Comp (based on the latest version of Uptodate software) and Medscape. The patients' demographic data (age, gender, clinical diagnosis, & concurrent disease) and drug usage (drug dose, duration, preparation, administration route, treatment indications, & concomitant medications) were recorded. The study evaluated IV pantoprazole prescription into two principal categories, i.e., "appropriate" and "inappropriate". It was classified as appropriate if it was confirmed to the medical recourse or inappropriate if it was not performed as per the medical recourse.

The obtained data were analyzed in SPSS using descriptive statistics, such as frequency and mean, as well as. two-way non-parametric Analysis of Variance (ANOVA). The significance level was set at $P<0.05$.

## Results

The total number of investigated documentation equaled 215. All data records were included for analysis. An overview of the clinical and demographic characteristics of the research participants is presented in Table 1.

Regarding the frequency of comorbidities in our study, most patients reported at least one co-morbidity with their cardiovascular disease; hypertension had the highest frequency, followed by diabetes mellitus. The concurrent diseases in patients receiving IV pantoprazole are presented in Table 2. The details of the physician's specialty who administered the IV pantoprazole among our study cases were as follows: internal specialist: 45.6%, gastroenterologist: 0.5%, cardiologist: 30.2%, and medical assistant: 23.7%. An overview of concomitant medications in patients receiving IV pantoprazole

**Table 1.** The clinical and demographic characteristics of the research participants

| Variables | | No.(%) |
|---|---|---|
| Gender | Female | 107(49.8) |
| | Male | 108(50.2) |
| Age (y) | 35-45 | 11(5.1) |
| | 46-55 | 23(10.7) |
| | 56-65 | 46(24.4) |
| | 66-75 | 87(40.5) |
| | >76 | 48(22.3) |
| Comorbidity | Hypertension | 19(8.8) |
| | Diabetes mellitus | 12(5.6) |
| | Others (dyslipidemia, stroke, COPD) | 5(2.3) |
| | Hypertension+diabetes mellitus+one of other comorbidity | 97(45.2) |
| | Without comorbidity | 82(38.1) |
| Renal or hepatic impairment | Yes | 50(23.0) |
| | No | 165(67.7) |
| Smoking | Yes | 60(27.9) |
| | No | 155(72.1) |
| Cause of prescription | Prevention | 195(91.0) |
| | Treatment | 20(9.0) |
| Patients GI condition | NPO | 14(6.5) |
| | PO | 201(93.5) |
| Cause of admission | CABG | 49(22.8) |
| | IHD | 160(74.4) |
| | Others (LHD & AVR) | 6(2.8) |
| History of drug allergy | Yes | 19(8.8) |
| | No | 196(91.2) |

**Table 2.** The preparation, route, and administration duration of pantoprazole

| Variable | | No.(%) |
|---|---|---|
| Initiation at admission | IV | 143(66.5) |
| | Oral | 72(33.5) |
| Dose, mg | 40 | 130(60.4) |
| | 80 | 85(39.6) |
| Preparation | Water | 2(1) |
| | Normal saline | 21(99) |
| Route of Administration | Bolus | 44(20.5) |
| | Infusion | 171(79.5) |
| Duration of use, day (Mean±SD) | 4.28±1.28 | |

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with their reported percentages is illustrated in Figure 1. Screening patients for the potential drug interactions demonstrated that 94 (43.7%) patients took medications, which may interact with pantoprazole. Clopidogrel, an adjunct to Aspirin had the highest frequency, compared to other drugs (86 out of 94 patients). However, only 3.7% of the examined patients required dose adjustment because of drug-drug interactions between pantoprazole and their medications.

In this study, IV pantoprazole was mostly being prescribed for patients with ischemic heart disease, and

**Table 3.** The frequency of appropriate administration per references for IV pantoprazole

| Variables | | References Recommendation | | Frequency |
|---|---|---|---|---|
| | | Medscape | UpToDate | |
| Indication, dose, duration | Dyspepsia | 40 mg once daily | Oral:20-40 mg once daily for 4 weeks | 53.5% for PPIs 23.3% for IV PPIs |
| | GERD | Oral:40 mg once daily for 8-16 weeks IV: 40 mg once daily for 7-10 days | Oral:40 mg once daily for 8 weeks IV: 40 mg once daily for 7-10 days | |
| | Zollinger Ellison syndrome | Oral:40 mg daily up to 240 mg IV:80 mg every 8-12hr up to 7 days | Oral:40 mg twice daily IV:80 mg twice daily up to 7 days | |
| | The prevention of rebleeding in peptic ulcer | - | IV: loading 80 mg, followed by 8 mg/hr or 40 mg every 12 hr for 72 hr Oral: 40 mg once daily for 4-8weeks | |
| | Helicobacter pylori eradication | - | Oral: 40-80 mg twice daily for 2 weeks | |
| | Prevention of NSAID induced ulcer | - | Oral:20-40 mg once daily | |
| | Peptic ulcer disease | Oral: 40 mg once daily for 2-4 weeks | - | |
| | Stress ulcer prophylaxis in critically ill patients | - | 40 mg once daily | |
| Laboratory test | Mg | Before starting and periodically | Before starting and periodically | 100% |
| | Vitamin B12 | - | Before starting and yearly | 50% |
| Drug interaction | Clopidogrel IRON Digoxin Ketoconazole Mycophenolate-mofetil | | | 100% |

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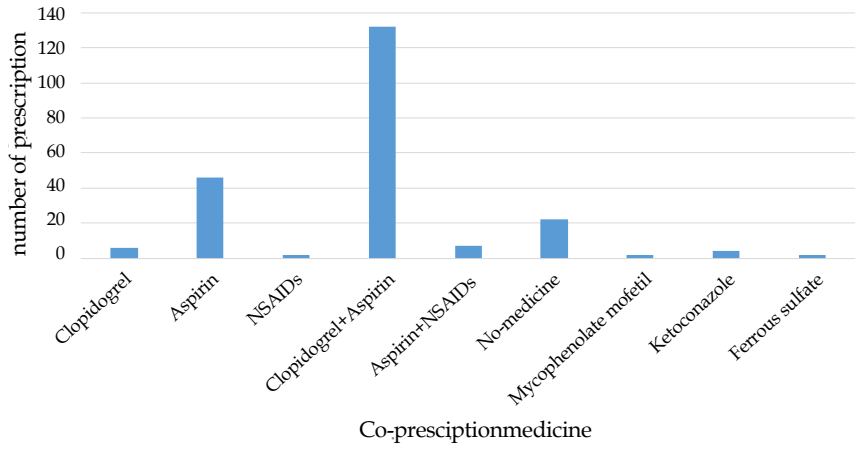


**Figure 1.** Co-prescription medicine with Pantoprazole

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CABG. The majority of the examined patients reported no liver or kidney problems. The main indication of IV pantoprazole was preventing stress ulcers. Although nearly all explored hospitalized patients (93.5%) were not NPO (nothing by mouth), they received IV pantoprazole. The details of the preparation and method of administrating pantoprazole are briefly outlined in Table 2. Pantoprazole was administered 40 mg once daily in 90% of the studied cases.

The Mean±SD duration of medicine use in the hospital was 4.28±1.28 days. Approximately, 50% of the pantoprazole prescription were considered acceptable as they fulfilled the clinical guidelines (Table 3). Most patients could tolerate the oral administration; thus, only 23.3% of the IV pantoprazole prescriptions were assumed appropriate.

## Discussion

Pantoprazole is the most commonly used PPI in ICUs and the only IV PPI in our settings. The current study evaluated the rational use of pantoprazole injections in cardiac ICUs. The obtained results revealed that the mean dose of pantoprazole use was 40 mg/day. Approximately, 53.5% of the pantoprazole cases were appropriately prescribed based on references. However, IV pantoprazole administration was inappropriate for most of the explored cases (76.7%). Furthermore, the collected data demonstrated that 60% of the patients who received 40 mg pantoprazole daily and 5.39% of the patients who took 80 mg pantoprazole daily had correct administration according to reliable sources. Consistent with our study, another investigation in the north of Iran found that 54% of the cases were rationally given PPIs; however, only 16% of the prescriptions were appropriate for the parenteral form of PPI [22]. One study in Yazd City, Iran found that the majority (63%) of IV pantoprazole administration cases were indicated irrationally [23]. Perwaiz et.al argued that 68.5% of their examined patients were inappropriately prescribed PPI beyond the recommendation of reliable sources [24]. Tze Chia et al. also found that 45.9% of PPI prescriptions in their study were appropriate as stated by the Food and Drug Administration (FDA) [25]. In line with our study, Kaplan et al. demonstrated that approximately 50% of the prescribed IV pan-

**Table 4.** The frequency of appropriate administration of IV pantoprazole in studies

| Reference | Indication for PPIs (%) | Appropriate IV Administration (%) | | Duration, Days (Mean) |
|---|---|---|---|---|
| 22 | 54 | 16 | | 17 |
| 23 | 60 | 37 | | 4 |
| 24 | 54.8 | 31.5 | | 4.5 |
| 26 | 50 | Upper GI bleeding | 50 | 9 |
| | | Non-upper GI bleedin | 33 | 14 |
| 30 | 58 | 11 | | 5 |

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toprazole cases were appropriate in high-risk and low-risk groups for Upper Gastrointestinal Bleeding (UGIB & non-UGIB). Moreover, 20% of patients in the UGIB group received correct doses; however, all prescriptions in non- UGIB were correct [26].

The UGIB group in the mentioned study was closer to those of ours. Some results slightly differed from our study, e.g. George et al. in the USA stated that 30% of PPI administrations were based on indication, i.e., conducted on geriatric ambulatory care centers [27]. Additionally, Gamelas et.al documented that 34.9% of patients in an internal medicine ward who were prescribed PPI at discharge, were indicated for receiving [28]. Another study at Malaysian Hospital presented that about 34% of the PPI prescriptions were appropriate, as per guidelines. Although, one-third of prescriptions had no clear reason in Elnaem et al.'s studies, only 19% of prescriptions were irrational per the references [29]. These data might be attributed to differences in settings and patients' conditions and comorbidities. Reviews indicated that the rate of rational use of pantoprazole varies from center to center; however, the rate of appropriate administration of IV PPI is to some extent similar worldwide (described briefly in Table 4).

Reviewing PPIs usage in different settings demonstrated that PPIs were generally prescribed for Stress Ulcer Prophylaxis (SUP) [28]. This is the most frequent indication in our study hospital. The Mean±SD duration of pantoprazole use in this study was measured as 4.28±1.28 days. The duration of pantoprazole treatment was consistent with the references in 95.9% for patients with 40 mg/day for SUP and 89.9% for 80 mg/day doses for treating the bleeding. In line with our survey, Moradi et al.'s results indicated that the SUP was the major cause of IV pantoprazole use after establishing their guideline; the mean duration in their study was approximately 4 days [30].

The main indication for PPI administration in Ahmadi et al.'s study was SUP; however, the duration of the administration was about 17 days [22]. The mean duration of pantoprazole consumption for SUP in Perwaiz's study was approximately 6 days [24]. SUP was the main reason for PPI administration with different mean durations in most studies; however, in Elnaem et al. and Sohrevardi et al.'s studies, gastritis due to concurrent medicines and abdominal pain was the mainspring for PPIs prescription, respectively [23, 29]. Pinto-Sanchez et al.'s systematic review data indicated that PPIs were the first-line treatment for functional dyspepsia due to H. pylori, followed by bleeding management [31].

Studies considered different criteria for evaluating PPI administration; thus, the appropriate prescription rate varied between investigations. However, the overall frequencies of appropriate PPI use never exceeded 50% [32-35]. Therefore, there is an insistent for improving the use of PPIs in the hospital setting. This was a retrospective study and without guidelines; however, some studies attempted to improve PPI's use. For example, Vazin et.al set checklists for PPIs prescription in their setting. Consequently, the results demonstrated that the total number of IV pantoprazole prescriptions and its relative cost significantly decreased (83.92%) through guidelines determined for pantoprazole prescription [36].

Moradi et al. designed protocols to correctly administer the drug. Accordingly, their study indicated that preparing the protocol reduced the extent of improper and inappropriate prescriptions, as well as the relevant costs. However, as protocol set time passed, the frequency of commitment made by physicians decreased, and less attention was given to the framework [30]. Kaplan et al. also signified decreased prescription of PPI after performing the PPI protocol [26]. Freedberg also addressed a 23% decrease in the prescription rate of PPIs after an electronic alert for IV PPI orders, i.e., associated with a significant reduction in costs [37].

Concerning the short duration of drug use in our study, no adverse effect was observed, or we could not attribute the adverse effect to the drug. In line with the previous case reports, there might be a relationship between PPI use and the incidence of acute hepatitis. However, hepatitis was developed after 4 weeks of PPI consumption, i.e., revealed as the transient elevation of the hepatic enzymes and returned to normal after discontinuing PPIs [38, 39]. The examined patient was monitored for hepatitis. There was no report of acute hepatitis or hepatic enzymes elevation in our study; it might be due to its short-term usage.

Based on these findings, the inappropriate use of pantoprazole was highlighted in most of the explored patients. Improper pantoprazole prescription is among the concerned issue, worldwide. The proper administration will result in quick recovery with lower costs; thus, informing these data to the medical staff may cause more appropriate IV pantoprazole prescription and dose optimization [23]. In addition, involving clinical pharmacists in drug prescribing may improve the quality of pharmacotherapy by decreasing medication errors and drug adverse effects. In conclusion, useful interventions may include regular medication reviews, electronic reminders before prescription, and continuing education for health professionals and consumers [33].

## Conclusion

The present study data suggested that pantoprazole prescription was required in approximately half of the explored patients; however, IV administration was in-

appropriate in most of the examined patients (76.7%), based on references. The main indication for pantoprazole was SUP in high-risk patients, since patients tolerate an oral product, there was no needed to prescribe injectable medication. Therefore, the individual assessment of the risks and indication for the prescription of pantoprazole should be a priority. Eventually, developing a protocol for PPIs prescribing was required per hospital.

The major limitation of this study was its retrospective nature; thus, any restrictions in documenting the patient's condition impacted the obtained results. Furthermore, this study observed patients who received only IV pantoprazole; therefore, different results may be obtained if all routes of pantoprazole administration are evaluated.

## Ethical Considerations

### Compliance with ethical guidelines

The participants were informed of the purpose of the research and its implementation stages. A written consent has been obtained from the subjects. They were also assured about the confidentiality of their information and were free to leave the study whenever they wished, and if desired, the research results would be available to them. The Helsinki Convention was also observed.

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### Authors' contributions

All authors equally contributed to preparing this article.

### Conflict of interest

The authors declared no conflict of interest.

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### References

[1] Hepler CD, Strand LM. Opportunities and responsibilities in pharmaceutical care. Am J Hosp Pharm. 1990; 47(3):533-43. [DOI:10.1093/ajhp/47.3.533] [PMID]

[2] Chomsky N. What is special about language? SBS Lecture Series: Noam Chomsky University of Arizona. 2012.

[3] Moore T, Bykov A, Savelli T, Zagorski A. Guidelines for implementing drug utilization review programs in hospitals. Arlington: Management Sciences for Health; 1997. https://pharmed.datapharma.ch/wp-content/uploads/dlm_uploads/2013/10/drug_utilization_reveiw_manual_MSH.pdf

[4] Zacharias A, Schwann TA, Parenteau GL, Riordan CJ, Durham SJ, Engoren M, et al. Predictors of gastrointestinal complications in cardiac surgery. Tex Heart Inst J. 2000; 27(2):93-9. [PMID]

[5] Byhahn C, Strouhal U, Martens S, Mierdl S, Kessler P, Westphal K. Incidence of gastrointestinal complications in cardiopulmonary bypass patients. World J Surg. 2001; 25(9):1140-4. [DOI:10.1007/BF03215861] [PMID]

[6] Hata M, Shiono M, Sekino H, Furukawa H, Sezai A, Iida M, et al. Prospective randomized trial for optimal prophylactic treatment of the upper gastrointestinal complications after open heart surgery. Circ J. 2005; 69(3):331-4. [DOI:10.1253/circj.69.331] [PMID]

[7] Aljarallah B, Wong W, Modry D, Fedorak R. Prevalence and outcome of upper gastrointestinal bleeding post-coronary artery bypass graft. nt J Health Sci (Qassim). 2008; 2(1):69-76. [PMID]

[8] Taylor PC, Loop FD, Hermann RE. Management of acute stress ulcer after cardiac surgery. Ann Surg. 1973; 178(1):1-5. [DOI:10.1097/00000658-197307000-00001] [PMID] [PMCID]

[9] Berkowitz D, Wagner BM, Uricchio JF. Acute peptic ulceration following cardiac surgery. Ann Intern Med. 1957; 46(6):1015-23. [DOI:10.7326/0003-4819-46-6-1015] [PMID]

[10] Ortoleva J, Bittner EA. Gastrointestinal complications and their management after adult cardiac surgery. In: Dabbagh A, Esmailian F, Aranki S, editors. Postoperative critical care for adult cardiac surgical patients. Berlin: Springer; 2018. p. 297-313. [DOI:10.1007/978-3-319-75747-6_9]

[11] Chaudhry R, Zaki J, Wegner R, Pednekar G, Tse A, Sheinbaum R, et al. Gastrointestinal complications after cardiac surgery: A nationwide population-based analysis of morbidity and mortality predictors. J Cardiothorac Vasc Anesth. 2017; 31(4):1268-74. [DOI:10.1053/j.jvca.2017.04.013] [PMID]

[12] van der Voort PH, Zandstra DF. Pathogenesis, risk factors, and incidence of upper gastrointestinal bleeding after cardiac surgery: Is specific prophylaxis in routine bypass procedures needed? J Cardiothorac Vasc Anesth. 2000; 14(3):293-9. [DOI:10.1053/cr.2000.5849] [PMID]

[13] Egleston CV, Wood AE, Gorey TF, McGovern EM. Gastrointestinal complications after cardiac surgery. Ann R Coll Surg Engl. 1993; 75(1):52-6. [PMID]

[14] Ait Houssa M, Selkane C, Moutaki Allah Y, Elbekkali Y, Amahzoune B, Wahid F, et al. [Upper digestive bleedings after cardiac surgery (French)]. Ann Cardiol Angeiol (Paris). 2007; 56(3):126-9. [PMID]

[15] Yoshida K, Matsumoto M, Sugita T, Nishizawa J, Matsuyama K, Tokuda Y, et al. Gastrointestinal complications in patients undergoing coronary artery bypass grafting. Ann Thorac Cardiovasc Surg. 2005; 11(1):25-8. [PMID]

[16] Behrens R, Hofbeck M, Singer H, Scharf J, Rupprecht T. Frequency of stress lesions of the upper gastrointestinal tract in paediatric patients after cardiac surgery: Effects of prophy-

laxis. Br Heart J. 1994; 72(2):186-9. [DOI:10.1136/hrt.72.2.186] [PMID] [PMCID]

[17] Houssa MA, Atmani N, Nya F, Abdou A, Moutakiallah Y, Bamous M, et al. Stress gastric ulcer after cardiac surgery: Pathogenesis risk factors and medical management. World J Cardiovasc Dis. 2013; 3(03):312-6. [DOI:10.4236/wjcd.2013.33049]

[18] Pang SH, Graham DY. A clinical guide to using intravenous proton-pump inhibitors in reflux and peptic ulcers. Therap Adv Gastroenterol. 2010; 3(1):11-22. [DOI:10.1177/1756283X09352095] [PMID] [PMCID]

[19] Yang YX, Metz DC. Safety of proton pump inhibitor exposure. Gastroenterology. 2010; 139(4):1115-27. [DOI:10.1053/j.gastro.2010.08.023] [PMID]

[20] Freedberg DE, Yang YX, Abrams JA. Proton pump inhibitors and myocardial infarction. Gastroenterology. 2015; 149(4):830-3. [DOI:10.1053/j.gastro.2015.08.002] [PMID]

[21] Zhu W, Hong K. Potential cardiovascular risks of proton pump inhibitors in the general population. Int Heart J. 2017; 58(2):163-6. [DOI:10.1536/ihj.16-208] [PMID]

[22] Ahmadi H, Ahangar N, Saghafi F, Ala S, Eslami G, Salehifar E. [Drug utilization evaluation of pantoprazole in a teaching hospital in North of Iran, 2016 (Persian)]. J Mazandaran Univ Med Sci. 2018; 28(162):69-76. http://jmums.mazums.ac.ir/article-1-9935-en.html

[23] Sohrevardi SM, Vahidi A, Mosadegh MH, Dehghani-Tafti A, Dadollahi A. 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(1-2):7-10. https://jpc.tums.ac.ir/index.php/jpc/article/view/88

[24] Perwaiz MK, Posner G, Hammoudeh F, Schmidt F, Neupane N, Enriquez D, et al. Inappropriate use of intravenous PPI for stress ulcer prophylaxis in an inner city community hospital. J Clin Med Res. 2010; 2(5):215-9. [PMID] [PMCID]

[25] Chia CT, Lim WP, Vu CK. Inappropriate use of proton pump inhibitors in a local setting. Singapore Med J. 2014; 55(7):363-6. [DOI:10.11622/smedj.2014087] [PMID] [PMCID]

[26] Kaplan GG, Bates D, McDonald D, Panaccione R, Romagnuolo J. Inappropriate use of intravenous pantoprazole: Extent of the problem and successful solutions. Clin Gastroenterol Hepatol. 2005; 3(12):1207-14. [DOI:10.1016/S1542-3565(05)00757-3] [PMID]

[27] George CJ, Korc B, Ross JS. Appropriate proton pump inhibitor use among older adults: A retrospective chart review. Am J Geriatr Pharmacother. 2008; 6(5):249-54. [DOI:10.1016/j.amjopharm.2008.12.001] [PMID]

[28] Gamelas V, Salvado V, Dias L. Prescription pattern of proton pump inhibitors at hospital admission and discharge. GE Port J Gastroenterol. 2019; 26(2):114-20. [DOI:10.1159/000488506] [PMID] [PMCID]

[29] Elnaem MH, Mohamed MHN, bin Nazar AH, binti Ibrahim RNK. Evaluation of proton pump inhibitors prescribing among non-critically Ill hospitalized patients in a Malaysian Tertiary Hospital. J Appl Pharm Sci. 2017; 7(12):077-83. https://www.researchgate.net/profile/Mohamed-Elnaem/publication/.pdf

[30] Moradi M, Raeesi S, Sepehri Z. Audit of IV pantoprazole: Pattern of administration and compliance with guideline in a teaching hospital. Springerplus. 2016; 5(1):1749. [DOI:10.1186/s40064-016-3428-2] [PMID] [PMCID]

[31] Pinto-Sanchez MI, Yuan Y, Bercik P, Moayyedi P. Proton pump inhibitors for functional dyspepsia. Cochrane Database Syst Rev. 2017; 3(3):CD011194. [DOI:10.1002/14651858.CD011194.pub2] [PMID] [PMCID]

[32] 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. [DOI:10.1016/j.ejim.2016.10.007] [PMID]

[33] Naunton M, Peterson G, Deeks L, Young H, Kosari S. We have had a gutful: The need for deprescribing proton pump inhibitors. J Clin Pharm Ther. 2018; 43(1):65-72. [DOI:10.1111/jcpt.12613] [PMID]

[34] Guda NM, Noonan M, Kreiner MJ, Partington S, Vakil N. Use of intravenous proton pump inhibitors in community practice: An explanation for the shortage? Am J Gastroenterol. 2004; 99(7):1233-7. [PMID]

[35] Molloy D, Molloy A, O'Loughlin C, Falconer M, Hennessy M. Inappropriate use of proton pump inhibitors.Ir J Med Sci. 2010; 179(1):73-5. [DOI:10.1007/s11845-009-0426-1] [PMID]

[36] Vazin A, Karimzadeh I, Karamikhah R, Oveisi Z, Mohseni S, Keykhaee M, et al. Clinical and economical impacts of guideline implementation by the pharmaceutical care unit for high cost medications in a referral teaching hospital. BMC Health Serv Res. 2018; 18(1):815. [DOI:10.1186/s12913-018-3627-3] [PMID] [PMCID]

[37] Freedberg DE, Salmasian H, Abrams JA, Green RA. Orders for intravenous proton pump inhibitors after implementation of an electronic alert. JAMA Intern Med. 2015; 175(3):452-4. [DOI:10.1001/jamainternmed.2014.6680] [PMID] [PMCID]

[38] Sandig C, Flechtenmacher C, Stremmel W, Eisenbach C. Pantoprazole induces severe acute hepatitis. Z Gastroenterol. 2011; 49(2):207-10. [DOI:10.1055/s-0029-1245613] [PMID]

[39] Koury SI, Stone CK, La Charité DD. Omeprazole and the development of acute hepatitis. Eur J Emerg Med. 1998; 5(4):467-9. [DOI:10.1097/00063110-199812000-00016] [PMID]