Original Article

# A Study on Drug Utilization Review of Pantoprazole in a Tertiary Care Hospital, Bangalore, India

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## Abstract

Objective: The goal of the research is to conduct a retrospective study on drug utilization review of Pantoprazole in the various department. Methodology: Drug utilization review of Pantoprazole in a tertiary care hospital is a retrospective study conducted for the period of 6 months. The data collected are subjected for various drug-drug interaction and ADR by using, primary (Micromedex), secondary and tertiary resources which are available in clinical pharmacy department. Result: Out of 150 prescriptions prescribed with pantoprazole 102 prescriptions were prescribed along with NSAIDS and 90 prescriptions were prescribed along with antibiotics. The majority (78.7%) of the patients were endorsed with pantoprazole. By NICE rules, fitting utilization of PPIs was found in 64% where as it was unseemly to use in 36% of cases. A large portion of the potential medication sedate associations were moderate. Characterized every day dose(DDD)/100 bed day of PPIs was seen as 0.929. Rabeprazole (20 mg, tablet) demonstrated most extreme rate value variety of 672.32% while pantoprazole (40mg, infusion) indicated a base rate value variety of 18.72%. Conclusion: Prevalence shows pantoprazole was prescribed more for male and age group of 60-70years with the significant risk factor of smoker (18%) and alcoholic (9.3%). Among 150 Prescriptions 22.67% prescriptions were irrationally prescribed. PPIs should be used only when there is documented evidence and when their use is clinically justified so that the appropriate prescription of PPIs will decrease the social insurance weight of the patient.

**Keywords:** *pantoprazole, PPIs, Drug Utilization Review, NICE guidelines*

## Introduction

The World Health Organization (WHO) defines drug utilization research (DUR) as "the promoting, dissemination, remedy and utilization of medications in a general public, with uncommon accentuation on the subsequent medicinal, social and financial results" [1]. The extreme objective of DUR is to assess whether the medication treatment is normal or not which may give experiences into the different parts of endorsing examples, for example, recurrence, measurements, term of treatment, sign quality, determinants and result of medication use. DUR is utilized as a potential device in the assessment in the medicinal services frameworks just as a ground-breaking exploratory instrument to clarify the job of medications in the general public. PPIs are one among the most ordinarily endorsed class of prescriptions in both outpatient and inpatient medicines. These prescriptions are utilized for enduring concealment of gastric corrosive by hindering the hydrogen-potassium adenosine triphosphates catalyst framework, which makes the stomach acidic, and it is found in the cells that line the stomach. [2]

Pantoprazole is a proton ceremony inhibitor (PPIs) with both oral and intravenous (IV) measurements structures. Consequences of various examinations indicated that in spite of increasingly fast beginning of activity in IV pantoprazole, both measurements structures (oral and intravenous) can decrease gastric acid emission to a similar degree. The choice to choose a suitable measurements structure relies upon a few elements, for example, patient's capacity to take oral prescription, patient's hemodynamic status just as intestinal porousness and absorptive limit. These elements frequently ought to be considered particularly in fundamentally sick patients when pantoprazole is demonstrated for either treating a corrosive discharging issue or prophylaxis of stress related mucosal damage.

These are effective acid-suppressive drugs that inhibit the final pathway for acid secretion in the parietal cell. All PPIs are substituted benzomidazole derivate and they function as

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pro-drugs and accumulate in the acid space of the parietal cell where they are converted to active sulphenamides by an acid catalyzed reaction. By covalent binding, the sulphenamides inhibit the proton pump (H+/K+ATPase) irreversibly, resulting in a marked inhibition of both basal and stimulated gastric acid secretion. Proton pump inhibitors only bind to active proton pumps. Therefore, only activated parietal cells will be inhibited, and resting parietal cell will escape inhibition. The ability of the parietal cell to secrete acid is restored when a new proton pump is converted from its inactive status in the tubulovesicle to the active form resulting in its location on the canalicular surface. As PPIs are best when the parietal cell is animated to discharge corrosive postprandial the planning of the portion is significant. [3, 4]

Pantoprazole is used primarily by CYP2C19 and to minor degrees by CYPs 3A4, 2D6 and 2C9. In vivo drug-drug communication contemplates with CYP2C19 substrates (diazepam [also a CYP3A4 substrate] what's more, phenytoin [also a CYP3A4 inducer]), nifedipine (a CYP3A4 substrate), metoprolol (a CYP2D6 substrate), diclofenac (a CYP2C9 substrate) and theophylline (a CYP1A2 substrate) in sound subjects, the pharmacokinetics of pantoprazole were definitely not essentially modified. It is, in this manner, expected that different medications utilized by CYPs 2C19, 3A4, 2D6, 2C9 and 1A2 would not fundamentally influence the pharmacokinetics of pantoprazole. In vivo examinations additionally, recommend that pantoprazole doesn't altogether influence the energy of different medications (cisapride, theophylline, diazepam [and its dynamic metabolite, dimethyl diazepam], warfarin, metoprolol, carbamazepine and oral contraceptives) utilized by CYPs 2C19, 3A4, 2C9, 2D6 and 1A2. In this manner, it is normal that pantoprazole would not altogether influence the pharmacokinetics of different medications used by these isozymes. Measurements alteration of such drugs isn't fundamental when they are co-managed with pantoprazole. In other in vivo examinations, ethanol, glyburide, antipyrine, and caffeine had no clinically important cooperation's with pantoprazole. [5, 6]

## Materials and Methods

This study was carried out in tertiary care hospital, Bengaluru which is a 300 bedded secondary care hospital. In order to record necessary data from the sources mentioned above, a self-designed Case Record Form was designed based on the data required for the study, which includes patient demography, family history, social history, medication history, clinical parameters like blood pressure and blood sugar levels, antihypertensive therapy and adjunct therapy. Study was conducted in 150 patients. for inclusion criteria Patients receiving pantoprazole drug treatment for Peptic ulcer, gastritis, GERD, and also Patient receiving prophylactic pantoprazole therapy during NSAID, antibiotics, steroids, etc.

Eligible patients were enrolled based on inclusion and exclusion criteria. Structured data collection was used for collecting the details. This form mainly contains demographic details, social habits, current medication, past medical and medication history, laboratory investigations, and other relevant data needed for present study were collected from patient's progress records, treatment chart, and laboratory reports.

The data collected are subjected for various drug-drug interaction and ADR by using, primary (Micromedex), secondary and tertiary resources which are available in clinical pharmacy department. The collected information was documented and subjected for assessment using suitable statistical method. Data were analyzed using descriptive statistics. Continuous data were expressed as mean ± S.D., and the nominal data were expressed as percentages. Analysis of the data was carried out by using Statistical Package for Social Science (SPSS) 16.0 for windows.

## Result and Discusion

Drug utilization review of Pantoprazole in the various departments was done by retrospective study on 150 cases. The results of our study suggest that Among 150 cases examined in tertiary care hospital Pantoprazole was prescribed more in Male 104 (69.33 %) in comparison with female 46 (31. 67%).Accompanying major age group having Pantoprazole is 60- 70 years i.e. 22.6 % and 40-50 yrs. i.e. 20%. Our study shows that around 18% of patients had smoking habits and 9.33% have alcoholic behavior which can be determined as well established risk factor of various disease and 72.67% were nonsmokers and non-alcoholics under PPIs therapy.

Pantoprazole was mostly prescribed in General medicine 29.33% followed by Cardiology department 24% for the various indication. Among them Pantoprazole was mostly prescribed to prevent drug induced ulcer 87.9% and for peptic ulcer 5.17%. Table 1

**Table 1:** Use of Pantoprazole in Various Departments

| Departments | NO: of Patients | Percentage % |
|---|---|---|
| **Gastroenterology** | 10 | 6.67% |
| **Cardiology** | 36 | 24% |
| **Urology** | 14 | 9.33% |
| **Nephrology** | 20 | 13.33% |
| **Integrated Liver Care Units** | 10 | 6.67% |
| **General Medicine** | 44 | 29.33% |
| **Orthopedics** | 2 | 1.34% |
| **Neurology** | 6 | 4% |
| **Pulmonology** | 8 | 5.33% |

Among 150 prescriptions 137 (91.33%) prescriptions were prescribed with 40mg and 13(8.67%) were prescribed with 20mg. Among prescribed Pantoprazole 76% prescription were prescribed once a day while 24% of prescriptions were prescribed twice a day.

On our study 77.33% prescription were rationally prescribed whereas 22.67% prescription were irrationally prescribed. Irrational prescriptions were mostly found on those prescriptions where pantoprazole was prescribed without any indication or any disease condition.

Major route of drug administration was intravenous route 90 (60%) and remaining 60(40%) were prescribed in oral form. Among the 90 IV prescriptions 20(22.2%) were switched to oral therapy after patient being stable and 70(77.77%) were continued as I.V therapy. Out of 150 prescriptions prescribed with pantoprazole 102 prescriptions were prescribed along with NSAIDS and 90 prescriptions were prescribed along with antibiotics. Table 2

**Table 2:** Concurrent drugs prescribed

| S.N | DRUG | NO. of Prescription |
|---|---|---|
| 1 | Antibiotics | 90 |
| 2 | Nsaids | 102 |
| 3 | Antiemetic | 60 |
| 4 | Antidiabetic | 24 |
| 5 | Diuretics | 44 |
| 6 | Antihypertensive | 43 |
| 7 | Vitamins | 20 |
| 8 | Statins | 29 |
| 9 | Corticosteriods | 16 |
| 10 | Anticonvulsants | 26 |
| 11 | Antianginal | 8 |
| 12 | Anti-Allergic | 16 |
| 13 | Antiplatelet | 24 |
| 14 | Antiasthmatic | 24 |
| 15 | Thyroid Drug | 9 |
| 16 | Anticoagulants | 35 |
| 17 | Antacids | 22 |
| 18 | Iron Products | 6 |
| 19 | Antimalarial | 4 |
| 20 | Insulin | 16 |

**Table 3:** Frequency and outcomes of potential drug-drug interactions

| PDDIs involving PPIs | Outcomes of interaction | Number (N =150) | Percentage (%) |
|---|---|---|---|
| **Atorvastatin Pantoprazole** | Increased blood levels of atorvastatin | 31 | 20 |
| **Propranolol +Pantoprazole** | Increased propranolol exposure | 22 | 12.7 |
| **Torsemide +Pantoprazole** | Hypomagnesemia | 16 | 8.7 |
| **Furosemide +Pantoprazole** | Hypomagnesemia | 16 | 10 |
| **Fluconazole +Pantoprazole** | Increased plasma concentration | 2 | 1.3 |
| **Clopidogrel +pantoprazole** | Increased effectiveness of clopidogrel | 9 | 6 |
| **Cefpodoxime +Pantoprazole** | Increased blood levels of cefpodoxime | 3 | 2 |
| **Rifampin +Pantoprazole** | Increased blood levels of rifampin | 7 | 4.7 |
| **Ferrous fumarate +Pantoprazole** | Increased absorption of iron | 9 | 6 |
| **Metolazone +Pantoprazole** | Hypomagnesemia | 1 | 0.7 |
| **Digoxin +Pantoprazole** | Increased effects of digoxin | 2 | 1.3 |
| **Aspirin +Pantoprazole** | - | 13 | 15.3 |
| **Cilostazol +Pantoprazole** | Increased cilastazole exposure | 2 | 1.3 |
| **Budesonide +Pantoprazole** | Decreased effects of budesonide | 4 | 1.3 |
| **Theophylline +Pantoprazole** | Increased effect of theophylline | 9 | 6 |
| **Cyanocobalamin +Pantoprazole** | - | 4 | 2.7 |

Majority of drug-drug interactions was caused by atorvastatin + pantoprazole 31 (20%), followed by propranolol + pantoprazole 22 (12.7%). The frequency and outcomes of the potential drug-drug interactions involving PPIs are summarized in Table 3.

**Table 4:** Utilization of PPIs in the general medicine ward

| Drugs | Total cost (INR) | % of the total drug cost | No. of prescriptions encountered (N=174) | % of prescriptions | The average cost per prescription (INR) |
|---|---|---|---|---|---|
| **Pantoprazole tablet** | 5743.98 | 40.9 | 105 | 60.3 | 54.7 |
| **Pantoprazole injection** | 5434.2 | 38.8 | 32 | 18.4 | 169.81 |
| **Fixed dose combinations** | 1,146.455 | 8.2 | 15 | 8.7 | 76.43 |

The highest average cost per prescription was found for pantoprazole injection (INR 169.81).

**Table 5:** Price variation of different brands of PPIs

| Drug | Dosage form | Dose (mg) | Number of brands | Minimum cost (INR) | Maximum cost (INR) | Percentage price variation |
|---|---|---|---|---|---|---|
| **Pantoprazole** | Tablet | 20 | 4 | 3.5 | 6.1 | 74.28 |
| | Injection | 40 | 8 | 5.292 | 10.3 | 94.63 |
| **Omeprazole** | Tablet | 10 | 2 | 2 | 2.825 | 82.5 |
| **Pantoprazole + Domperidone** | Tablet | 40/30 | 9 | 7.63 | 15.325 | 100.85 |

These results were contrary to the study conducted by Kolasani and Divyashanthi et al., (2016) and Patel, D et al., (2009) where pantoprazole (40mg; EC tablet) showed the highest price variation (500.75%) while omeprazole (40 mg; Injection) showed the least price variation (2.15%) because in this study price variation was done for different brands of PPIs available in the Indian market [7, 8]. Wide variation in the prices of the different brands of PPIs was seen, which will increase the economic burden of the patients [1]. Hence, importance should be given for the prescription of the generic drugs.

In this study, anti-infective were mostly commonly prescribed concurrent medications (22.5%) which showed similar results to the studies conducted by Nousheen et al., (2014); Airee et al., (2016) [2, 9]. According to the severity classification of drug-drug interactions, the study showed 87% moderate, 10% minor, and 3% major interactions. The results were comparable with those observed in the Airee et al., (2016) study. Major interactions were caused by rabeprazole + clopidogrel, which increased the risk of thrombosis and pantoprazole + cilastazol, which increased the cilastazol exposure [9].

## Conclusion

The appropriate indications for pantoprazole based on our approved administration guideline were as follows: IV pantoprazole was viewed as characteristic when patient was NPO (nothing per oral) and showed with in any event one of the accompanying conditions: Erosive esophagitis related with gastrointestinal reflux illness (GERD). Pathologic hyper discharge related with Zollinger–Ellison disorder. Upper gastrointestinal dying (UGIB) and avoidance of re-draining Stress ulcer prophylaxis (SUP). In patients who could endure oral medicine and the individuals who are applicant of PPI treatment

Prevalence shows pantoprazole was prescribed more for male and age group of 60-70years with the significant risk factor of smoker (18%) and alcoholic (9.3%). Our study revealed that Pantoprazole was mostly prescribed to prevent drug induced ulcer and for peptic ulcer. Major route of drug administration was Intravenous route (60%). Among 150 Prescriptions 22.67% prescriptions were irrationally prescribed.

This study showed a wide price variation of PPI brands. Hence there is a need to decrease the variation in the prices, thereby reducing the economic burden on the patients. Finally, this study concludes that the pharmacists and the other medical professionals should work together for the rational use of PPIs by making interventions like the educational programs and institutional specific guidelines should be developed and implemented to reduce the usage of PPIs in the inpatients.

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