Drug Utilization Evaluation of Intravenous Pantoprazole with Focus on Appropriateness, Route Switching, and Economic Impact in a Pediatric Tertiary Hospital

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Abstract

Background: Proton pump inhibitors (PPIs), including intravenous (IV) pantoprazole, are frequently prescribed in hospital settings. Although effective, IV formulations are often used inappropriately, leading to unnecessary risks and increased financial burden. Data on IV pantoprazole use in pediatric populations remain limited.

Methods: This study was designed as a retrospective, descriptive, cross-sectional Drug Utilization Evaluation (DUE) conducted in a tertiary pediatric teaching hospital. All inpatients aged ≥3 months who received at least one dose of IV pantoprazole during hospitalization were included. Prescribing appropriateness was evaluated according to international guidelines with respect to indication, dose, route, and duration. Opportunities for intravenous-to-oral (IV-to-PO) conversion and direct medication costs were also assessed.

Results: A total of 260 pediatric patients were analyzed. Overall, 42% of IV pantoprazole prescriptions were classified as appropriate, reflecting the composite appropriateness score across all evaluated domains (indication, dose, route, and duration). The majority of prescribing errors were related to unjustified indications and prolonged duration of therapy. Nearly 81% of eligible patients did not undergo IV-to-PO conversion. Dosing deviations were uncommon. Economic analysis showed that 76.6% of total pantoprazole expenditures were attributable to inappropriate use, corresponding to approximately 1.57 billion Iranian Rials (IRR) [≈8,300 United States dollars (USD)]. The Internal Medicine II ward accounted for the highest absolute excess cost, while the Surgery ward demonstrated 92.3% inappropriate prescribing.

Conclusion: PInappropriate use of IV pantoprazole is prevalent among pediatric inpatients, primarily driven by unjustified indications and missed opportunities for IV-to-PO conversion. These practices impose substantial economic costs and raise safety concerns. Implementation of pharmacist-led DUE and stewardship interventions may improve prescribing practices, reduce unnecessary expenditures, and enhance the quality of pediatric patient care.

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Introduction

Rational medication use is a fundamental principle of pharmaceutical care and hospital pharmacy practice (1). In contrast, inappropriate prescribing can increase healthcare costs, compromise the quality of care, and raise the incidence of adverse drug events (ADEs) (2, 3). To promote optimal pharmacotherapy, health systems implement

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Drug Utilization Evaluation (DUE) programs, which are structured and ongoing assessments of prescribing quality and medication use (4, 5). When applied in hospital settings, DUE programs enable clinical pharmacists to evaluate the indication, dose, route, and duration of drug therapy and to provide feedback to prescribers, thereby improving patient outcomes and preventing medication-related problems (4). Such interventions have been shown to enhance therapeutic effectiveness, reduce preventable adverse reactions, and limit unnecessary pharmaceutical expenditures (2, 6).

Proton pump inhibitors (PPIs) exemplify the challenges associated with ensuring rational drug use in hospital practice. PPIs are among the most widely prescribed acid-suppressive medications worldwide and are valued for their high efficacy and short-term safety in the management of acid-related disorders (7). Nevertheless, numerous studies have documented substantial overuse and inappropriate prescribing of PPIs across diverse healthcare settings (8). A recent systematic review and meta-analysis estimated that up to 60% of PPI prescriptions worldwide lack a valid clinical indication (9). Despite the availability of effective oral formulations, the intravenous (IV) form of pantoprazole, a commonly used PPI, is frequently prescribed without clear clinical justification (5).

Common examples of inappropriate use include unwarranted administration of IV pantoprazole for stress ulcer prophylaxis (SUP) in non–critically ill patients or its routine use as gastroprotection in low-risk cases (10, 11). Studies from various countries consistently report high rates of inappropriate IV PPI utilization. For example, an audit conducted in a tertiary hospital in the Middle East found that only approximately 32% of IV PPI prescriptions were appropriate, with the remainder deemed unnecessary; inappropriate IV PPI use in that center resulted in excess costs of about $156,000 over a period of a few weeks (12). Similarly, a Brazilian hospital reported that only 23.4% of IV PPI (omeprazole) prescriptions met appropriate-use criteria, and the unnecessary use of vials led to avoidable institutional costs (13). Such misuse not only imposes a substantial financial burden on healthcare systems but also exposes patients to unwarranted risks and adverse effects (12).

Although the high prevalence of inappropriate PPI use has been well documented internationally (8,12), data on IV pantoprazole prescribing patterns in Iran remain limited. This knowledge gap is particularly evident in pediatric hospital settings. Patterns of PPI use in children may differ from those in adults because of distinct indications and risk profiles, yet relatively few studies have specifically evaluated PPI utilization in pediatric populations (7). Moreover, limited information is available regarding the extent to which IV pantoprazole prescribing in Iranian teaching hospitals adheres to evidence-based guidelines and approved indications, and the associated economic consequences of irrational use remain unclear. In resource-limited healthcare systems, assessment of the financial impact of inappropriate medication use is especially important (1). Notably, a single-center study conducted in Iran in an adult population reported that 96.5% of administered IV pantoprazole vials were inconsistent with guideline-based indications, resulting in approximately $17,822 in excess costs to the healthcare system (5). Comparable evaluations in pediatric populations are lacking, underscoring the need for targeted DUE studies in this group.

In light of these gaps, the present study was designed using a DUE approach to investigate the utilization patterns of IV pantoprazole in a specialized pediatric hospital. Specifically, the study aimed to determine the proportion of rational (appropriate) versus irrational (inappropriate) IV pantoprazole prescriptions; to evaluate indications for use, dosing, route of administration, and duration of therapy in comparison with accepted clinical guidelines; to identify opportunities for substituting IV therapy with oral pantoprazole when clinically feasible; and to estimate the direct costs attributable to inappropriate use. By addressing these objectives, the study seeks to generate evidence that can inform improvements in hospital prescribing policies, strengthen clinical pharmacy services, and ultimately reduce unnecessary healthcare expenditures associated with PPI overuse.

Methods

Study Design and Setting

This investigation was designed as a retrospective, descriptive, cross-sectional DUE study. It was conducted in a tertiary pediatric teaching hospital that serves as a referral center for a wide range of pediatric subspecialties. Given its high admission rate of complex cases and frequent use of IV pantoprazole, this setting provided an appropriate environment for evaluating prescribing patterns and assessing the rationality of IV pantoprazole use in hospitalized children. The study was carried out over one year, from April 2021 to April 2022, and included all hospitalized pediatric patients who received at least one dose of IV pantoprazole during their admission. The study protocol was reviewed and approved by the Institutional Review Board (IRB) under approval code IR.GUMS.REC.1400.605. All methods were performed in accordance with relevant national and institutional ethical guidelines and regulations. Because the study involved retrospective data collection from medical records and routine clinical documentation without any intervention, the requirement for informed consent was formally waived by the IRB.

Eligibility Criteria

All pediatric patients aged ≥3 months who received at least one intravenous dose of pantoprazole during hospitalization were eligible for inclusion. Patients admitted to medical,

surgical, infectious disease, hematology, intensive care, and emergency wards were considered. Exclusion criteria included hospitalizations with incomplete clinical or medication records that precluded assessment of prescribing appropriateness, as well as patients discharged within 24 hours of the first pantoprazole dose, in accordance with prior studies (14,15). These criteria ensured adequate evaluation of indication, dosing, route of administration, and duration of therapy within the DUE framework. A census sampling approach was applied, whereby all eligible cases during the one-year study period were included, yielding a final sample size of 260 patients.

Data Sources and Variables

Data was extracted from patients' medical records, medication charts, and clinical documentation during hospitalization. Collected variables included demographic characteristics (age and sex), ward of admission, primary diagnosis, underlying comorbidities, and length of hospital stay. Information related to pantoprazole therapy comprised the indication for use, ability to tolerate oral intake, prescribed dose and dosing frequency, route of administration, duration of treatment, and the total number of vials used. Concomitant medications were also recorded to identify potential factors influencing prescribing patterns. These variables enabled a comprehensive assessment of prescribing appropriateness across all DUE domains. All pantoprazole prescriptions were independently reviewed through a two-step process by a pediatric gastroenterologist and a clinical pharmacist. Any discrepancies were resolved by consensus to ensure accurate adjudication of prescribing appropriateness based on predefined criteria.

Appropriateness Criteria and Outcomes

In this DUE, pantoprazole prescriptions were classified as appropriate when the indication, dose, route of administration, and duration of therapy were consistent with internationally accepted clinical guidelines for PPI use, including the Medscape pantoprazole profile (16) and the Izaak Walton Killam (IWK) Pediatric Drug Dosing Guidelines (17). Prescriptions were considered inappropriate if they lacked a valid clinical indication, exceeded or fell below recommended dosing ranges, were administered via an unjustified route (IV rather than oral when oral intake was feasible), or were continued beyond guideline-supported durations. The appropriateness of intravenous-to-oral (IV-to-PO) conversion was assessed in patients who were hemodynamically stable, able to tolerate oral intake, free from persistent vomiting, and without contraindications to oral medications. Dosing errors were identified when the prescribed daily dose exceeded or was below the recommended pediatric range, whereas duration errors were defined as treatment continued beyond the guideline-recommended period for the specified indication. The detailed criteria used to determine appropriateness are summarized in Table 1 to allow concise reporting in the main text.

Table 1. Criteria for evaluating appropriateness of intravenous pantoprazole prescriptions

Domain	Appropriate Use Criteria	Inappropriate Use Criteria	Reference
Indication	- Active esophagitis with a history of Gastroesophageal Reflux Disease, or other approved disease states according to the FDA label for pediatric patients ≥3 months. - In patients with documented conditions such as peptic ulcer disease, Zollinger-Ellison syndrome, or post-surgical situations where IV administration is necessary for a quick therapeutic effect. -Stress ulcer prophylaxis only in critically ill/high-risk patients (PICU).	- Prescribing without a documented disease state or for conditions where oral therapy would be equally effective. - Routine prophylaxis without indication, especially in cases where oral administration is feasible, is not appropriate. - Stress ulcer prophylaxis in non–critically ill pediatric patients.	(16,18)
Dosing	- Based on the patient's age and weight, as recommended by the FDA: - 0.8 mg/kg once daily for infants aged 3 months to <1 year. - 10-20 mg once daily for children aged 1-16 years, based on body weight. - Doses should not exceed 40 mg daily unless treating hypersecretory conditions (Zollinger-Ellison syndrome).	- Doses exceeding the FDA-recommended upper limit for pediatric patients (40 mg daily). - Doses lower than the minimum recommended dose for a given age/weight group. - Subtherapeutic dosing that does not meet the patient's clinical needs.	(19)

Table 1. Continued

Domain	Appropriate Use Criteria	Inappropriate Use Criteria	Reference
Route	- IV pantoprazole should only be administered when the patient cannot tolerate oral intake, such as in cases of severe nausea/vomiting, swallowing difficulties, or during emergency surgery. - Switch to oral pantoprazole when the patient is stable and can tolerate oral medication. - IV use should be short-term and for therapeutic benefit only.	- IV pantoprazole is continued despite the patient being eligible for oral therapy. - No contraindication to oral medication exists, yet the patient remains on IV therapy unnecessarily. - IV pantoprazole is continued when the oral route is feasible and safe.	(16,17)
Treatment Duration	- Should be limited to the approved period per indication, such as up to 7 days for GERD with erosive esophagitis or until the patient can tolerate oral intake. - Duration of therapy should not exceed clinical necessity and should follow evidence-based guidelines.	- Continuing IV therapy beyond the approved treatment period for specific indications (e.g., more than 7 days for GERD with erosive esophagitis). - Continuing IV therapy beyond the point when the patient can switch to oral therapy.	(16,18)
Switch to Oral Feasibility	- Daily reassessment should be done to consider switching to oral pantoprazole when the patient is hemodynamically stable, able to tolerate oral intake, has no active vomiting, and has no contraindications to oral medications (such as swallowing disorders or severe malabsorption).	- Inappropriate use is when oral therapy is delayed despite the patient meeting criteria for oral intake. - Lack of daily reassessment or failure to switch to oral therapy when all criteria are met.	(19)

IV: Intravenous, GERD: Gastroesophageal Reflux Disease, FDA: Food and Drug Administration, PICU: Pediatric Intensive Care Unit, IV-to-oral: Intravenous-to-oral.

The primary outcome was the proportion of IV pantoprazole prescriptions classified as appropriate versus inappropriate. Appropriateness was defined by the presence of a valid clinical indication, correct dosing, a justified route of administration, and a treatment duration consistent with guideline recommendations (16, 18). Secondary outcomes included: (1) Dosing errors, defined as prescriptions exceeding or falling below the recommended pediatric dosing range of 0.8 - 1 mg/kg/day (maximum 40 mg), as specified in pediatric pharmacotherapy references (19); (2) duration errors, defined as continuation of IV therapy beyond the recommended treatment period or despite the patient's ability to tolerate oral intake (16, 18); (3) opportunities for IV-to-PO conversion, assessed in hemodynamically stable patients without persistent vomiting or contraindications to oral therapy (19); and (4) estimation of direct hospital costs attributable to inappropriate prescribing, calculated based on the cost of IV pantoprazole vials and projected savings associated with conversion to oral therapy (15).

Cost Analysis

The economic evaluation was conducted from the hospital perspective over the index admission period. Direct medication costs were calculated using institutional purchase prices for the years 2021 - 2022. For intravenous pantoprazole (40 mg per vial), the unit cost was 175,112 Iranian Rials from April to September 2021 and 224,200 Iranian Rials from October 2021 to April 2022; identical prices were applied for products manufactured by Dana Pharmaceutical Co. and Afa Chemi Pharmaceutical Co. For oral pantoprazole tablets (40 mg; Kharazmi Pharmaceutical Co.), the unit cost was 9,530 Iranian Rials from April to September 2021 and 10,900 Iranian Rials from October 2021 to April 2022. For each patient, the total number of IV vials administered was multiplied by the corresponding unit cost to estimate total intravenous expenditure. Oral substitution scenarios were modelled, assuming a standard daily dose of 40 mg oral pantoprazole. Excess cost was defined as the difference between the actual IV expenditures incurred for inappropriate prescriptions and the projected costs that would have been incurred if oral therapy had been used when clinically appropriate. For international comparability, costs were converted to United States dollars (USD) using an average exchange rate for 2021–2022 of 1 USD ≈ 125,000 Iranian Rials. This approach is consistent with methodologies used in previous DUE studies assessing the financial burden of inappropriate PPI use (14,15).

Statistical Analysis

Data were analyzed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were summarized as mean ± standard deviation (SD) or median (interquartile range), as appropriate, and categorical variables were presented as frequencies and percentages.

The normality of continuous variables was assessed using the Shapiro-Wilk test. Comparisons of continuous variables between appropriate and inappropriate prescriptions were performed using the independent-samples t-test or the Mann-Whitney U test, depending on data distribution. Categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate, based on expected cell counts. Proportions were reported with 95% confidence intervals (CIs), which were calculated using Wilson's score method for selected outcomes, including rates of missed IV-to-PO conversion across hospital wards. Cost data were analyzed descriptively and reported in both Iranian Rials (IRR) and USD. Avoidable costs associated with inappropriate IV use and missed IV-to-PO conversion opportunities were calculated accordingly.

R statistical software version 4.3.1 (R Foundation for Statistical Computing, Vienna, Austria) was used exclusively for calculating confidence intervals and generating summary statistics that were not directly available in SPSS. A P-value of < 0.05 was considered statistically significant.

Results

Patient Characteristics

A total of 260 pediatric patients were included in the analysis, with a mean age of 13.6 years and a mean body weight of 23.5 kg. Slightly more than half of the patients were male (53.9%). The majority of patients (60.4%) had no documented comorbidities; among those with underlying conditions, hematology/oncology and neurological disorders were the most common. Oral administration of pantoprazole would have been clinically feasible in 89.2% of patients. Regarding prescribing indications, stress ulcer prophylaxis (SUP) accounted for the largest proportion of IV pantoprazole use (45.4%), followed by gastrointestinal bleeding (25.8%). Other indications included reflux-related conditions, peptic ulcer disease, dyspepsia, and gastric polyps. Detailed baseline characteristics and prescribing indications are summarized in Table 2.

Table 2. Patient characteristics and indications for intravenous pantoprazole (N = 260)

Variable	Category	N	%
Age (years)	Mean±SD	13.6 ± 5.1	—
Weight (kg)	Mean±SD (range)	23.54 ± 6.22 (3.5–89)	—
Sex	Male	140	53.9
	Female	120	46.1
Comorbidities	None	157	60.4
	Hematology/Oncology disorders	26	10.0
	Neurological disorders	25	9.6
	Gastrointestinal disorders	9	3.5
	Cardiovascular disorders	3	1.2
	Respiratory disorders	4	1.5
	Reflux disease	19	7.3
	Peptic ulcer disease	17	6.5
Hospital ward	Internal Medicine I	36	13.8
	Internal Medicine II	111	42.7
	Hematology	22	8.5
	Infectious Diseases	47	18.1
	Emergency	22	8.5
	Pediatric ICU	9	3.5
	Surgery	13	5.0
Eligibility for oral therapy	Eligible (PO possible)	232	89.2
	Not eligible (PO impossible)	28	10.8
Indications for IV pantoprazole	Gastrointestinal bleeding	67	25.8
	Stress ulcer prophylaxis	118	45.4
	Gastroesophageal reflux / Erosive esophagitis	26	10.0
	Dyspepsia / Nonspecific abdominal pain	17	6.5
	Gastric/duodenal ulcer	19	7.3
	Gastric polyp	13	5.0

IV: Intravenous, PO: Oral (per os), SD: Standard Deviation, N: Number of Patients, kg: kilogram.

Appropriateness of Prescriptions

Of the 260 IV pantoprazole prescriptions evaluated, 42% were classified as appropriate, based on a composite assessment in which prescriptions were deemed appropriate only when all evaluated domains — indication, dose, route of administration, and duration of therapy — were consistent with guideline criteria. The most frequent cause of inappropriate use was unjustified indication, followed by prolonged treatment duration and inappropriate IV administration despite patient eligibility for oral therapy. Dosing errors were relatively uncommon. Ward-level analysis demonstrated the highest rates of inappropriate prescribing in the Surgery (92.3%) and Emergency (72.0%) wards, whereas appropriateness was highest in the Hematology (95.5%) ward and the Pediatric Intensive Care Unit (PICU) (100%). Inappropriate indications were most observed for SUP, dyspepsia, and gastric polyps, while prescriptions for gastrointestinal bleeding were largely appropriate. A detailed breakdown of results is provided in Table 3, including domain-specific analyses for route, dose, and duration, which clearly identify the sources of error among inappropriate prescriptions.

Table 3. Appropriateness of intravenous pantoprazole prescriptions by domain, ward, and indication (N = 260)

Category	Subcategory	Appropriate N (%)	Inappropriate N (%)	P value / Notes
Domain	Indication	112 (43.1)	148 (56.9)	Based on guideline criteria
	Route (IV vs eligible for PO)	232 (89.2)	28 (10.8)	Missed switch opportunities
	Dose	245 (94.2)	15 (5.8)	Infectious ward: P=0.023
	Duration	210 (80.8)	50 (19.2)	Internal II: P=0.001; Infectious: P=0.003; Emergency: P=0.006
Ward†				
	Internal Medicine I	13 (36.1)	23 (63.9)	0.549
	Internal Medicine II	41 (36.9)	70 (63.1)	0.437‡
	Hematology	21 (95.5)	1 (4.5)	<0.001
	Infectious Diseases	23 (48.9)	24 (51.1)	0.659§
	Emergency	6 (27.3)	16 (72.7)	0.999¶
	PICU*	9 (100)	0 (0)	<0.001
	Surgery	1 (7.7)	12 (92.3)	<0.001
Indication				
	Stress ulcer prophylaxis	42 (35.6)	76 (64.4)	0.077
	Gastrointestinal bleeding	53 (79.1)	14 (20.9)	<0.001
	GERD / Erosive esophagitis	12 (46.2)	14 (53.8)	0.679
	Dyspepsia / Abdominal pain	3 (17.6)	14 (82.4)	0.042
	Peptic ulcer disease	8 (42.1)	11 (57.9)	1.000
	Gastric polyp	2 (15.4)	11 (84.6)	0.080

Data are presented as numbers (percentage). For the ward section, P values represent comparisons between appropriate and inappropriate prescriptions within each ward (Chi-square or Fisher's exact test, as appropriate). For the indication section, P values represent the overall association between indication category and appropriateness classification. A P value < 0.05 was considered statistically significant. † p-values represent comparisons between appropriate and inappropriate prescriptions within each ward, unless otherwise specified. ‡ In the Internal Medicine II ward, inappropriate prescribing was predominantly driven by prolonged treatment duration (P = 0.001). § In the Infectious Diseases ward, inappropriate prescriptions were mainly associated with inappropriate duration of therapy (P = 0.003). ¶ In the Emergency ward, treatment duration was the primary contributor to inappropriate prescribing (P = 0.006). * All prescriptions in the PICU were classified as appropriate; therefore, no P value was calculated for this ward. IV; Intravenous, PO: Oral (per os), PICU: Pediatric Intensive Care Unit, GERD: Gastroesophageal Reflux Disease, N: Number of Patients, P: P value.

Dosing and Duration Errors

Analysis of dosing indicated that the majority of prescriptions were within recommended ranges, with dosing errors accounting for fewer than 6% of all prescriptions. Mean prescribed doses are presented for descriptive purposes only and were not used to determine dosing appropriateness. Dose appropriateness was assessed categorically based on guideline-recommended dosing ranges and is reported as appropriate or inappropriate in Table 3. Overall, dosing errors constituted less than 6% of prescriptions. The only statistically significant difference was observed in the Infectious Diseases ward, where inappropriate prescriptions were associated with lower mean doses compared with

appropriate prescriptions (13.25 ± 6.18 mg vs. 20.18 ± 11.24 mg, P = 0.023). In other words, differences in dosing between appropriate and inappropriate prescriptions were not statistically significant (Table 4).

In contrast, treatment duration demonstrated greater variability across wards. In the Internal Medicine II ward, the mean duration of therapy was significantly longer in appropriate prescriptions than in inappropriate ones (4.07 ± 2.35 vs. 2.13 ± 1.63 days, P < 0.001). Similar patterns were observed in the Infectious Diseases ward (4.18 ± 2.44 vs. 3.04 ± 5.03 days, P = 0.003) and the Emergency ward (3.00 ± 0.82 vs. 1.61 ± 1.50 days, P = 0.006). In the Hematology, PICU, and Surgery wards, no statistically significant differences in treatment duration were identified; however, in the Surgery ward, the majority of prescriptions were inappropriate (91.7%). Overall, errors related to treatment duration contributed more substantially to irrational use than dose-related errors, as summarized in Table 4.

Table 4. Dosing and duration of intravenous pantoprazole by ward, stratified by appropriateness

Ward	Dose (mg) Appropriate (Mean ± SD)	Dose (mg) Inappropriate (Mean ± SD)	P value (Dose)	Duration (days) Appropriate (Mean ± SD)	Duration (days) Inappropriate (Mean ± SD)	P value (Duration)
Internal Medicine I	15.89 ± 10.34	18.48 ± 10.13	0.597	3.56 ± 1.51	3.16 ± 2.94	0.179
Internal Medicine II	22.07 ± 10.09	18.40 ± 9.96	0.054	4.07 ± 2.35	2.13 ± 1.63	<0.001
Hematology	29.57 ± 9.44	15.0 ± 0.0	0.145	6.90 ± 4.87	1.0 ± 0.0	0.114
Infectious Diseases	20.18 ± 11.24	13.25 ± 6.18	0.023	4.18 ± 2.44	3.04 ± 5.03	0.003
Emergency	24.50 ± 13.70	23.28 ± 11.91	0.863	3.00 ± 0.82	1.61 ± 1.50	0.006
PICU	17.62 ± 8.17[1]	N/A	—	4.63 ± 2.13[1]	N/A	—
Surgery	25.0 ± 0.0 (n=1)	24.21 ± 11.21 (n=11)	—	4.0 ± 0.0 (n=1)	3.83 ± 1.80 (n=11)	—

In PICU, all patients (N=9) received appropriate prescriptions; no inappropriate prescriptions were recorded. Data are presented as mean ± standard deviation. P values represent comparisons between appropriate and inappropriate prescriptions for dosing and duration within each ward. Continuous variables were compared using the independent-samples t-test or the Mann–Whitney U test, as appropriate, based on the data distribution. A P value < 0.05 was considered statistically significant. IV: Intravenous, SD: Standard Deviation, N: Number of Patients, mg: Milligram, PICU: Pediatric Intensive Care Unit, P: P value, N/A: Not Applicable.

Route of Administration and Opportunities for IV-to-Oral Switch

Among the 260 patients who received IV pantoprazole, 115 (44.2%) were clinically eligible for oral administration. However, only 22 patients (8.5%) underwent an actual IV-to-PO conversion, resulting in 93 missed opportunities (35.8%). The frequency of missed IV-to-PO switches varied across hospital wards. As illustrated in Figure 1, the hematology (88.9% missed) and surgery (100% missed) wards demonstrated the poorest adherence to IV-to-PO conversion criteria, whereas the infectious diseases (76.2% missed) and internal medicine I (77.8% missed) wards showed comparatively lower — though still substantial — rates of inappropriate continuation of IV therapy. No eligible cases for IV-to-PO conversion were identified in the Pediatric Intensive Care Unit, owing to clinical constraints.

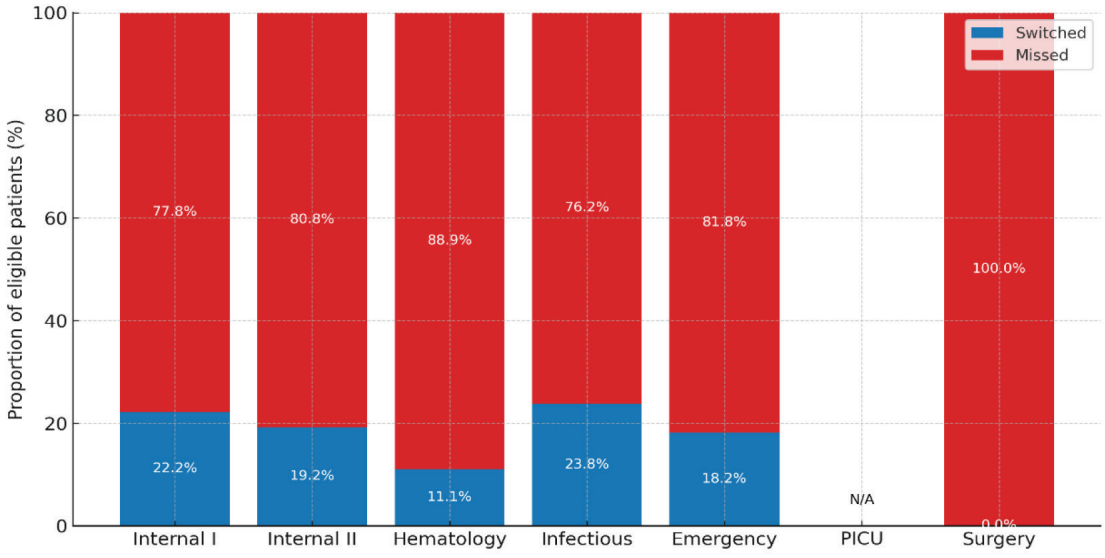

Figure 1. Distribution of IV-to-PO switch opportunities across hospital wards, showing the proportions of successful conversions versus missed opportunities among eligible patients

The forest plot (Figure 2) presents ward-specific missed IV-to-PO switch rates with corresponding 95% Wilson confidence intervals (CIs). The overall missed-switch rate was 80.9% (95% CI: 72.7 - 87.0). At the ward level, the highest rates were observed in the surgery ward (100%, 95% CI: 51.0 - 100.0) and the hematology ward (88.9%, 95% CI: 56.5 - 98.0), whereas the lowest rates were noted in the infectious diseases ward (76.2%, 95% CI: 54.9 - 89.4) and the internal medicine I ward (77.8%, 95% CI: 54.8 - 91.0).

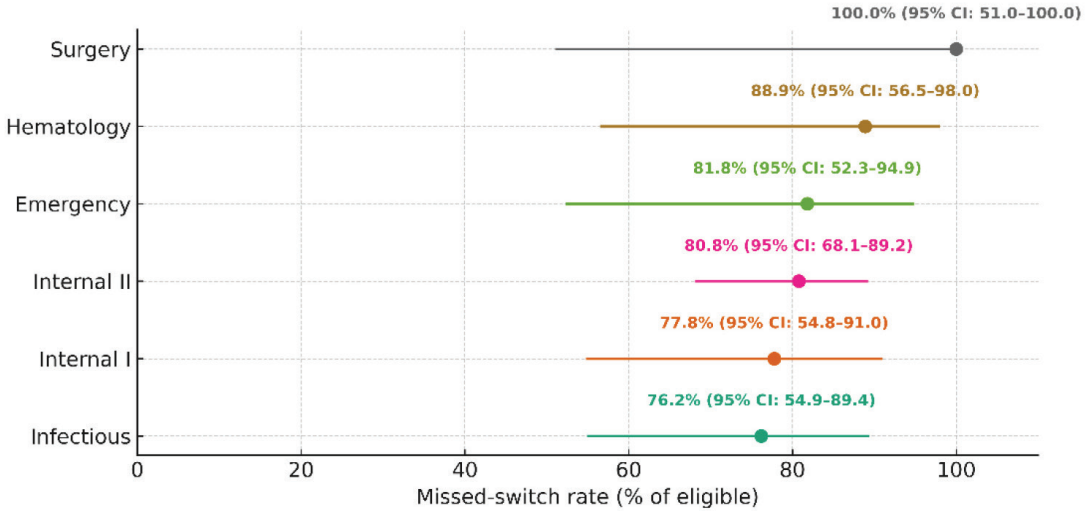

Figure 2. Forest plot of missed IV-to-PO switch rates for pantoprazole across hospital wards, with corresponding 95% confidence intervals

Cost Analysis

During the study period, total hospital expenditure on IV pantoprazole amounted to 2,045.3 million Iranian Rials (IRR), of which 1,567.4 million IRR (76.6%) was attributable to inappropriate use. The projected avoidable cost achievable through timely IV-to-PO conversion was estimated at 1,044.6 million IRR [≈8,356.8 United States dollars (USD)]. Substantial variation in excess costs was observed across hospital wards (Table 5). The internal medicine II ward accounted for the highest avoidable expenditure (≈3,322 USD) and demonstrated a significantly higher proportion of inappropriate use compared with other wards (P = 0.018). The surgery ward showed 100% inappropriate IV pantoprazole expenditure, which was also statistically significant (P = 0.009). Significant excess costs were likewise identified in the Internal medicine I (P = 0.041), infectious diseases (P = 0.037), and Emergency (P = 0.043) wards. In contrast, excess costs in the hematology ward did not reach conventional statistical significance (P = 0.052). The pediatric intensive care unit (PICU) incurred no avoidable costs, as no patients were eligible for oral conversion during the study period (Table 5).

Table 5. Cost analysis of intravenous pantoprazole utilization across hospital wards.

Ward	Total IV expenditure (IRR)	Inappropriate IV expenditure (IRR)	Inappropriate cost	Avoidable cost with IV-to-PO switch (IRR)	Avoidable cost (USD)	P value
Internal Medicine I	274,800,000	186,500,000	67.8%	122,600,000	980.8	0.041
Internal Medicine II	918,200,000	712,400,000	77.6%	415,300,000	3,322.4	0.018
Hematology	186,400,000	165,800,000	88.9%	134,200,000	1,073.6	0.052
Infectious Diseases	352,600,000	268,700,000	76.2%	198,500,000	1,588.0	0.037
Emergency	147,200,000	120,500,000	81.8%	89,300,000	714.4	0.043
PICU	52,600,000	0	0%	—	—	—
Surgery	113,500,000	113,500,000	100%	84,700,000	677.6	0.009
Total	2,045,300,000	1,567,400,000	76.6%	1,044,600,000	8,356.8	—

Data are presented as monetary values in Iranian Rials (IRR) and United States Dollars (USD), and as percentages where indicated. For each hospital ward, P values represent within-ward comparisons between inappropriate and appropriate intravenous pantoprazole expenditure proportions. These categorical comparisons were performed using the Chi-square test when all expected cell counts were ≥5 and Fisher's exact test when expected cell counts were <5. A P value < 0.05 was considered statistically significant. IV: Intravenous, IRR: Iranian Rails, USD: United States Dollars, N: Number of Patients, P: P value, PICU: Pediatric Intensive Care Unit.

Discussion

In this retrospective DUE study, inappropriate prescribing of IV pantoprazole was found to be highly prevalent in a tertiary pediatric hospital. Errors related to indication — particularly unjustified use for stress ulcer prophylaxis — were the primary contributors to irrational prescribing. Although dosing deviations were uncommon, prolonged treatment duration and failure to convert eligible patients from IV to oral therapy substantially contributed to inappropriate use. Nearly 81% of patients eligible for IV-to-PO conversion did not undergo a switch. From an economic perspective, inappropriate prescribing accounted for more than three-quarters of total IV pantoprazole expenditures, with the Internal Medicine II and Surgery wards emerging as the principal drivers of excess costs.

Our findings are consistent with international evidence demonstrating widespread overuse of IV PPIs in hospital settings. Across adult populations, more than half of IV PPI prescriptions have been reported as unnecessary or inconsistent with guideline recommendations (12,13). For example, an audit conducted in a tertiary hospital in Saudi Arabia found that only 31.7% of IV PPI courses were appropriately prescribed, indicating that nearly 68% were inappropriate (12). Similarly, a study from a Brazilian hospital reported that only 23.4% of patients receiving IV omeprazole had a justified clinical indication (13). An Iranian study in an adult hospital setting reported even lower rates of rational use, with IV pantoprazole prescribed appropriately in only 15.9% of cases (20), underscoring the extent of unwarranted use. Collectively, these studies conclude that IV PPIs are frequently overprescribed, resulting in avoidable healthcare costs and unnecessary patient exposure to potential risks (12,13). A recurring theme across studies is the inappropriate use of IV PPIs for stress ulcer prophylaxis in low-risk or non-critically ill patients (12). In the Middle Eastern audit, for instance, more than 80% of SUP-related IV PPI prescriptions were not indicated (12). Even in settings with comparatively more judicious prescribing, inappropriate use remains substantial; a recent multicenter study reported that approximately 24% of IV PPI prescriptions were inappropriate (21). Consistent findings have also been reported in Western healthcare systems. A 2025 U.S. study focusing on upper gastrointestinal bleeding found that IV PPIs were "grossly overused," even among patients with a low risk of bleeding (22). Taken together, evidence from diverse regions — including the Middle East, Latin America, and Western countries — reveals a strikingly similar pattern, in which only a minority of hospitalized patients meet strict indications for IV PPI therapy.

Although the trend of overutilization is well established in adult populations, pediatric-specific data remain limited (23-25). The present study helps to address this gap by providing what appears to be the first systematic evaluation of IV PPI prescribing appropriateness in an Iranian pediatric hospital. The available evidence suggests that pediatric inpatient settings are similarly affected by PPI overuse. For instance, a recent study conducted in Saudi Arabia among non-critically ill pediatric patients reported that omeprazole was appropriately prescribed in only 38.6% of cases, indicating that approximately 61.4% of prescriptions were inappropriate — rates comparable to those reported in adult populations (25). The authors also emphasized the scarcity of pediatric-focused studies and noted that inappropriate use of acid-suppressive therapy in adults exceeds 50% in much of the published literature (23, 26).

Our findings in the Iranian pediatric context are consistent with these observations and suggest that a similar pattern of overprescription exists among children. Increasing evidence indicates that many pediatric PPI prescriptions may be empirical or prophylactic in nature, without robust clinical justification. For example, a pharmacoepidemiologic study from the United States examining IV pantoprazole use in infants found that more than 54% of recipients had no documented diagnosis of gastroesophageal reflux disease (GERD) or erosive esophagitis, implying use without a clear indication (27). Similar empirical use of PPIs in infants and children has been reported in other regions, frequently for conditions such as infant reflux or nonspecific irritability, despite the limited number of approved indications in younger age groups (28).

Importantly, the novelty of this study lies in its focus on pediatric patients in Iran, a context in which no prior systematic data on IV PPI use were available. By comparing our findings with reports from adult hospitals in Iran and with international studies, we demonstrate that inappropriate IV PPI prescribing is a pervasive problem that transcends age groups and geographic regions. Although the magnitude of misuse varies across settings, a consistent pattern emerges — namely, excessive reliance on IV PPIs for prophylactic purposes or for mild conditions that do not warrant such therapy. This comparison highlights a critical message: There is a global need for improved stewardship of PPI prescribing. Across both adult and pediatric settings, adherence to guideline-based indications and the implementation of targeted interventions — such as prescriber education, prescription audits, and computerized order-entry controls — could substantially reduce unnecessary IV PPI use (22,29). Our pediatric-focused findings emphasize that efforts to

optimize PPI utilization should not be limited to adult care. Overall, this study corroborates prior reports of widespread IV PPI overuse in hospital settings (13,25) while uniquely identifying the pediatric population as an under-recognized component of this issue. Addressing this knowledge gap represents an essential step toward developing targeted strategies to reduce PPI misuse and improve patient care across all age groups.

In pediatric inpatients, irrational PPI use represents a significant concern, as it imposes unnecessary financial costs and increases the risk of adverse outcomes. A recent audit reported that only approximately 35% of inpatient pediatric PPI prescriptions were compliant with guideline recommendations, underscoring the extent of overuse in this population (30). Prolonged acid suppression in children may disrupt normal gastrointestinal microbiota and immune defenses, thereby increasing susceptibility to hospital-acquired infections (31). Accordingly, PPI exposure has been associated with higher rates of infections, including Clostridioides difficile infection and pneumonia, among hospitalized pediatric patients (32). A large cohort study further demonstrated an approximately 34% increased hazard of serious infections among PPI-exposed infants, reinforcing the need to restrict PPI use to clearly indicated cases (31). In addition, long-term PPI therapy has been linked to impaired nutrient absorption, such as vitamin B12 deficiency, and other potential adverse effects (33). Consequently, unnecessary PPI prescribing not only wastes healthcare resources but also exposes pediatric patients to avoidable harm.

Another important concern identified in this study is the failure to implement timely IV-to-PO medication switches. Prolonged continuation of IV therapy beyond clinical necessity may extend hospital stays, increase healthcare costs — such as those related to additional nursing workload — and cause patient discomfort due to extended use of intravenous lines. Evidence indicates that implementing structured IV-to-PO conversion protocols in hospitalized pediatric patients yields clear benefits. For example, a quality improvement study demonstrated that expediting IV-to-PO conversion reduced the median length of hospital stay by approximately 14 hours (34). Clinical pharmacy services, including DUE programs and pharmacist-led interventions, play a critical role in addressing both inappropriate initiation and prolonged continuation of IV PPI therapy. Previous studies have shown that pharmacist-driven initiatives can significantly improve appropriate PPI prescribing by reducing unindicated use and associated drug costs (35), while also promoting earlier IV-to-PO conversion and more efficient resource utilization.

Our findings are consistent with prior Iranian studies highlighting the effectiveness of targeted interventions in improving the appropriate use of IV pantoprazole. For instance, the introduction of structured order-entry forms for IV pantoprazole has been shown to enhance physicians' adherence to guideline-based prescribing, although overall compliance remained suboptimal, suggesting that complementary strategies such as ongoing education and feedback are necessary to sustain rational use (20). Similarly, implementation of a preprinted IV pantoprazole protocol has been associated with a significant reduction in overall drug consumption and an increase in appropriate administration across multiple hospital departments, demonstrating that standardized stewardship tools can effectively improve prescribing practices (36). Collectively, these findings underscore the value of pharmacist-led stewardship strategies in optimizing PPI utilization and reducing inappropriate IV use in hospital settings.

Inappropriate antibiotic use imposes a substantial economic burden on healthcare systems (37). It is estimated that 30 - 50% of antimicrobials used in hospitals are unnecessary (38), and in Iran, approximately 58% of antibiotics are prescribed without an appropriate indication (39), resulting in avoidable healthcare expenditures (40). These inefficiencies are particularly consequential given that nearly 42% of Iran's total healthcare spending occurs in hospital settings, with almost half of these costs paid out of pocket by patients (41). In the present study, reducing inappropriate IV pantoprazole prescribing was associated with a potential cost saving of approximately 8,300 USD, offering meaningful relief for constrained hospital budgets. Although studies have reported substantially larger financial losses associated with inappropriate antimicrobial therapy (42), the observed savings in this pediatric setting are nonetheless clinically and economically relevant. While pediatric care generally incurs lower absolute costs than adult care, patterns of medication misuse appear to be similar across both populations (43).

Strengths, Limitations, and Future Directions

This study has several notable strengths. It represents one of the first systematic DUEs of IV pantoprazole conducted in a pediatric hospital setting in Iran, thereby addressing an important gap in the existing literature. The retrospective design, inclusion of all eligible patients over a complete one-year period, and rigorous two-step adjudication process involving both a pediatric gastroenterologist and a clinical pharmacist enhance the reliability and validity of the findings. In addition, the integration of clinical appropriateness assessments with direct cost analysis provides a comprehensive evaluation that links prescribing quality to measurable economic outcomes.

Nevertheless, several important limitations should be acknowledged. The single-center design limits the generalizability of the findings, as prescribing practices and resource availability may vary across institutions. In addition, the exclusive focus on pantoprazole precludes assessment of inappropriate use of other PPIs or acid-suppressive agents. Clinical outcomes, such as rates of gastrointestinal bleeding or adverse drug events (ADEs), were not evaluated, which restricts the ability to directly link inappropriate prescribing to patient harm. Although the cost analysis was detailed, it included only direct drug acquisition costs and did not account for indirect costs, such as increased nursing workload or prolonged hospitalization. Finally, some subgroup analyses, including those involving the Surgery and PICU wards, were limited by small sample sizes.

Looking ahead, multicenter DUE studies conducted across pediatric hospitals in Iran and the broader region are needed to improve external validity and capture a wider range of prescribing practices. Interventional research is also warranted, particularly studies evaluating the impact of standardized IV-to-oral switch protocols or pharmacist-led stewardship rounds on prescribing appropriateness and cost reduction. Future investigations should aim to integrate clinical outcome measures with utilization and economic data to more comprehensively define the clinical and financial consequences of irrational IV PPI use.

Conclusion

This DUE study demonstrates that inappropriate prescribing of IV pantoprazole is highly prevalent in a tertiary pediatric hospital in Iran, with unjustified indications, prolonged treatment duration, and failure to convert to oral therapy identified as the primary contributors. These practices not only consume limited healthcare resources but also expose pediatric patients to avoidable risks. The cost analysis revealed that more than three-quarters of total IV pantoprazole expenditures were attributable to irrational use, with the Internal Medicine II and Surgery wards accounting for a disproportionate share of the financial burden. Although overall medication volumes in pediatric care are lower than those in adult hospitals, the observed pattern of overuse closely mirrors that reported in adult settings.

The findings underscore an urgent need for targeted stewardship strategies in pediatric care, including routine reassessment of IV therapy, strict adherence to guideline-based indications, and systematic implementation of IV-to-PO conversion protocols. Integration of clinical pharmacy services and routine DUE activities can play a pivotal role in enhancing prescribing quality, reducing unnecessary expenditures, and improving patient safety. Ultimately, rationalizing IV pantoprazole use in pediatric populations is not only essential for cost containment but also critical for optimizing clinical care and protecting children from preventable harm.

Conflict of Interest

Authors have nothing to declare.

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