

The costly case of proton-pump inhibitors: a single-center experience

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Dear Editors,

We thought it might be of interest to readers to learn about our study which aimed to show the difference in patient costs in administering continuous infusion of proton-pump inhibitor (PPI) versus intermittent intravenous PPI (IIP) if recent evidence-based practice was utilized at out hospital. Upper gastrointestinal bleeding (UGIB) is defined as bleeding originating from above the ligament of Treitz. The incidence of UGIB ranges from 50 to 150 per 100,000 population each year, with a higher number of cases reported in the lower socioeconomic status groups.¹ It is the most common cause of emergency admission in gastroenterology throughout the world and has an inpatient mortality rate of 10%, which has not changed over the years despite advancements in diagnostic and treatment modalities.¹⁻³ The common causes of UGIB are peptic ulcer disease, esophageal and gastric varices, cancer, and angiodysplasia in the descending order.⁴ PPIs are fundamental in the management of UGIB. Platelet aggregation, which plays a crucial role in arresting bleeding, is inhibited by the hydrochloric acid and pepsin in the stomach. The low pH environment in the stomach also disrupts platelet aggregation significantly.^{4,5} The pH of gastric juice is inversely related to clot lysis. A pH of 7.0 and above helps to achieve hemostasis by indirectly helping in platelet aggregation, platelet calcium, and serotonin release and increases the availability of platelet factor III.^{5,6} The standard practice is to initiate a continuous PPI infusion (CPI) with 80 mg of an intravenous (IV) bolus of PPI followed by continuous infusion of 8 mg/h for 72 h.^{7,8} CPI significantly reduces the bleeding risk compared to placebo.⁹ However, in recent years, studies have shown that there was no significant difference in primary outcomes such as re-bleeding rates when IIP is compared to a CPI in nonvariceal UGIB even in bleeding ulcers with high-risk features.^{5,10}

Moreover, IIP provides the added benefit of easier administration and lower cost.¹¹ To our knowledge, no study has been done to date to compare the cost between administering a CPI and IIP. Our study aimed to show the difference in patient costs between administering a CPI and IIP if the recent evidence-based practice was utilized in a single community hospital.

A retrospective review was done to identify the number of CPIs that were ordered at our community teaching hospital in Warren, Ohio, for a period of 1 year using our pharmacy database. CPI that was started for patients with nonvariceal UGIB were included in the analysis, and CPI that was initiated for all other conditions, including variceal bleed, were excluded. The standard CPI was an 80-mg IV bolus followed by a continuous 8-mg/h IV infusion for 72 h. The standard dose of IIP was 40 mg IV twice daily. The IIP was administered at 9 AM and 8 PM. The ordering physician, duration, cost of the infusion, and the cost of an equivalent intermittent PPI dose were analyzed using IBM SPSS, version 26. A cost comparison analysis was performed to compare the patient cost of CPI to an equivalent duration of IIP.

Our analysis displays a significant difference in the cost of administering CPI when compared to using IIP for a similar duration. The study showed that 217,452 USD in patient costs could have been saved in 1 year by using IIP instead of CPI at a single hospital.⁶ The cumulative cost of CPI was 326,262 USD as compared to 108,810 USD for IIP for that given period (Figure 1). The mean cost difference of CPI was found to be significantly higher than IIP at \$1025.7/patient ($p < 0.005$). The calculated cost difference amounted to 217,452 USD over the 1-year duration of data collected. Out of the 212 patients that were started on CPI, 54% were ordered by gastroenterologists as compared to 46%, which were

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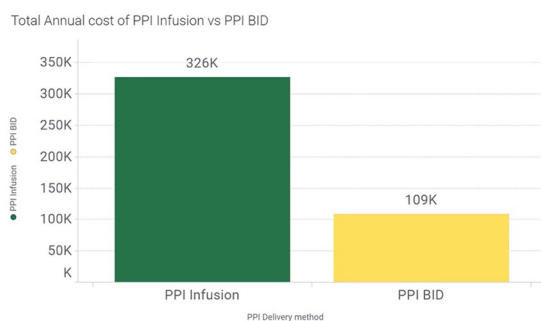


Figure 1. Total annual cost of PPI infusion versus PPI BID.

started by other physicians, including internists, intensivists, and emergency physicians. The duration of the CPI tended to be significantly longer (3.47 days) in adults > 50 years as compared to adults < 50 years (2.58 days) with a mean difference of 0.88 days ($p = 0.003$).

Our study showed that administration of CPI over 72h on a patient costed 310 USD/day more than that of an IIP administered over a similar duration. CPIs tended to be administered for a longer duration of time in patients >50 years when compared to patients <50 years (mean 3.47 days vs 2.58 days). This was significantly longer than the recommended duration of 72h. Naturally, the overall cost of administering a CPI was significantly higher in patients >50 years, as depicted in Figure 2. Whether this was due to the overall increased risk based on the risk predictors in that age group or inappropriate medication reconciliation where physicians failed to discontinue the infusion after 72h is beyond the scope of this study. Incidentally, CPIs were initiated by gastroenterologists (54.2%) more than other physicians, including internists, intensivists, and emergency physicians (45.8%). Overall, this study shows there is a significant difference in the cumulative patient cost with an estimate of 326,262 USD for CPI as compared to 108,810 USD for an equivalent duration of IIP over the period of 1 year at a community hospital with a robust gastroenterology service.

UGIB⁹ is a significant economic burden on health-care. A nationwide study showed that the hospitalization costs associated with uncomplicated and complicated nonvariceal bleed were \$3402 and \$5632, respectively, and that of uncomplicated and complicated variceal bleed were \$6612 and \$23,207, respectively.¹² A recent quality improvement study¹³ made use of electronic health record

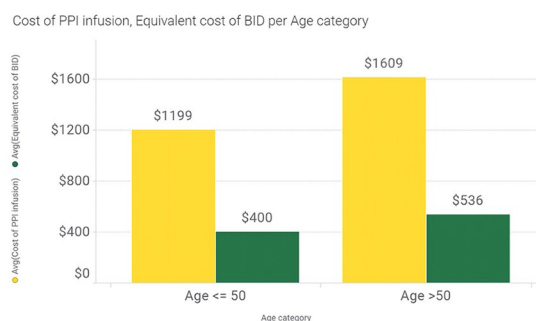


Figure 2. Cost of PPI infusion and PPI BID for an equivalent duration of administration.

alerts to reduce inappropriate use of PPI infusion. It required physicians to select an appropriate indication for ordering PPI infusions. At the end of 9 months, a 35% decrease in inappropriate PPI infusions was noted, and the study estimated saving of at least \$121,000 in terms of pharmacy costs between intermittent and continuous infusion of PPI in patients with UGIB.¹³ The results are in line with the findings of this study. A recent systematic review and meta-analysis by Sachar and colleagues compared intermittent PPI therapy to bolus plus CPI. The study showed that the risk ratio of re-bleeding within 7 days for intermittent versus bolus plus CPI to be 0.72 and the absolute risk difference to be -2.64%.¹⁴

Several studies reported that the duration of hospital stay, the necessity of blood transfusion or urgent surgery in patients who received intermittent PPI after endoscopic therapy was similar to that of patients who received CPI after endoscopic therapy.^{12,15} In addition, intermittent PPI therapy has the advantage of easier administration.¹² When high-dose and low-dose PPI were compared, there was no difference in their efficacy, rates of re-bleeding, surgical intervention or mortality, and high-dose PPIs did not prove to be superior to non-high-dose PPIs.¹⁶⁻²⁰

Limitations of this study include the retrospective observational nature of the study, the inability to comment on cost-effectiveness or outcomes as it was beyond the scope of this study. There is no universal standard pricing for CPI or IIP, as the cost depends on the manufacturer and pharmacy dispensing it in each hospital, although the variability is marginal in the United States. The cost of PPI is different in other countries and this study cannot be generalized.

Given the significant difference in the cost between a CPI and an IIP, along with the recent evidence that CPIs have noninferior outcomes compared to an IIP in nonvariceal bleed, the utility of CPI in patients with nonvariceal UGIB is debatable. Further studies comparing the cost-effectiveness of CPI versus IIP are required to re-think and revise our management guidelines in the near future.

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IRB

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Transparency declaration

The corresponding author affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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