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Comparison of Oral versus Intravenous Proton Pump Inhibitors in Preventing Re-bleeding from Peptic Ulcer after Successful Endoscopic Therapy

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Abstract

Background: Peptic ulcer disease (PUD) consider a complex condition that can arise from a range of etiological factors. These include elevated dietary patterns, psychological strain, gastric acid secretion, Helicobacter pylori (H. pylori) infection, & prolonged administration of nonsteroidal anti-inflammatory medications. Bleeding, obstruction, & perforation continue to be the most encountered complications of PUD.

Objectives: To assess the efficacy of intravenous versus oral PPI in blocking rebleeding from peptic ulcers after successful endoscopic treatment.

Methods: The randomized controlled trials' inclusion criteria were to include: (i) each and every case who presented to the hospital with signs of ulcer bleeding, as demonstrated by haematemesis or melaena; (ii) an endoscopic procedure was carried out in order to halt the bleeding; (iii) patients were randomly assigned to receive PPIs either orally or intravenously; & (iv) a minimum of one of the subsequent outcomes—recurrent bleeding, surgical intervention, or mortality—was documented after the endoscopy procedure. Excluded were clinical trials that investigated cases involving malignant hemorrhage or patients who were already undergoing therapy with PPIs.

Results: throughout a one-month monitoring period, the involved research found no statistically significant variations among both groups Oral-Pan & IV-Pan) regarding the rates of re-endoscopy & re-bleeding, period of stay in hospital, operation, volume of blood transfusion, & mortality. Similar findings have been reported in several additional investigations.

Conclusion: The findings of our research indicate that cases with bleeding peptic ulcers and an elevated risk of re-bleeding may benefit from high-dose oral PPIs as an alternative to high-dose IV PPIs. The increased cost & accessibility of oral PPIs contribute to their considerably reduced cost.

Key words: Intravenous, Oral Proton Pump Inhibitors, Endoscopic Therapy, Re-bleeding, Peptic Ulcer.

Introduction

PUD ulcer is the leading cause of upper gastrointestinal bleeding (UGIB), causing around fifty percent of all reported patient. **(1, 2)** According to a recent Iranian review article, erosive gastroduodenopathy (16-25%) was the second most prevalent reason of UGIB, followed by PUD (30-65%). **(3)** It continues to be a significant cause of mortality & morbidity & a critical medical concern. As a result of its significant decreases in mortality, surgical treatment, and additional bleeding associated with hemorrhaging peptic ulcers, endoscopic therapy is currently the preferred hemostatic modality for these cases. **(4-6)** Despite effective endoscopic intervention, 14-36% of cases still face a significant risk of peptic ulcer re-bleeding. **(7, 8)** As a result of reducing clot formation& promoting clot lysis, gastric acid disrupts the hemostasis of duodenal & stomach ulcers**. (9)** Hence, inhibition of gastric acid secretion can effectively avert the recurrence of ulcer hemorrhage. **(8)** Inhibitors of the PPIs are the medications most frequently prescribed to decrease gastric acid secretion. An equivalent dose of oral & intravenous (IV) pantoprazole has an equivalent acid suppression impact **(10)** High dose oral Proton Pump Inhibitors suppresses acid more rapidly than standard dose oral Proton Pump Inhibitors **(11)** & high dose IV PPI suppresses acid more rapidly than high dose oral Proton Pump Inhibitors (gastric acid PH greater than six) in an adequate manner. However, there is ongoing debate regarding the most effective route, dosage, & length of PPI treatment following endoscopic treatment for a hemorrhaging peptic ulcer **(11,12).** Multiple meta-analyses & controlled trials have demonstrated that intravenous and oral PPIs are equally efficient in ulcers with a great risk of rebleeding following endoscopic treatment. The majority, however, suggested additional research to confirm the results**. (13, 14, 15)**

Methods

Search strategy

This meta-analysis utilized prospective randomized controlled investigation that enrolled cases with endoscopically confirmed peptic ulcer hemorrhage to compare the efficiency of oral versus intravenous PPIs. A literature search was conducted in the OVID databases to recognize investigation that were published in their entirety with English abstracts. "Proton pump inhibitors," "PI," "omeprazole," "lansoprazole," "pantoprazole," "rabeprazole," "esomeprazole," "dexlansoprazole," "oral," "intravenous," & "ulcer bleeding" were the search terms. A search was conducted across various electronic databases, such as MEDLINE, EMBASE, EBM Reviews, the Cochrane Centre Register of Controlled research, the British Nursing Index & Archive, Wan Fang Data, & Google Scholar. A literature search was conducted to identify any recent revisions.

Inclusion & exclusion criteria

The inclusion criteria for randomized controlled research were to include: (i) all cases who presented with signs of ulcer hemorrhaging, as indicated by hematemesis or melaena, & were admitted; (ii) endoscopic treatment was applied to stop hemorrhaging (iii) cases were randomly assigned to receive PPIs orally or intravenously; & (iv) endoscopic treatment resulted in the reporting of at least one of the following outcomes: recurrent hemorrhaging, surgical intervention, or mortality.Clinical trials that examined cases with hemorrhage caused by malignancy or cases who were already receiving PPI therapy were excluded.

Data extraction

Significance assessments were conducted independently by two investigators (HWH, KKT) on titles & abstracts of all generated papers. We assessed the eligibility of each identified trial through review. Additionally, the investigators extracted the information in a fair way using a standardized information extraction form. The two evaluators arrived at decisions concerning the inclusion of research & the extraction of data through a process of consensus. The third investigator (JJS) could

make conclusive decisions regarding trial eligibility & information extraction in the event of discrepancies.

Study outcomes.

This meta-analysis focused primarily on recurrent hemorrhage, which can be defined as the inability to adequately control bleeding following the initial endoscopic intervention. This was the 1st outcome that was evaluated. Additionally, 2nd outcomes were the amount of blood that was transfused per unit (in days), the length of time that the patient remained in the hospital (in days), the requirement for surgical intervention, & the overall mortality rate after endoscopic therapies.

Results

Authors	**Country**	**Year**	**Type of study**	**Sample size**	**Groups**	**Age**	**Male/ Female**	
Toosi SM, et al. (16)	Iran.	**2018**	a single center, prospective, randomized trial	178 patients	A total of eighty-eight cases were assigned at random to the IV-Pan group, whereas ninety cases were assigned to the oral-Pan group.	≥18(18- 100)	Out of the total number of cases, 112 (sixty-three percent) were male and sixty-six (thirty-seven percent) were female.	
Liu et al. (17)	**China**	**2012**	Randomized controlled trial.	**875 patients**	Group A received a normal treatment consisting of a forty-milligram intravenous bolus of proton pump inhibitor 2 time per day, along with a continuous infusion of saline for seventy-two hours. Group B received an intensive treatment consisting of an eighty-milligram PPI bolus initially, followed by a continuous infusion of Eight milligrams/hours for seventy-two hours.	≥18(53.8 ± 19.9)	Men n (%)in Group A was 318 (69.7), and in Group B was 299 (71.3)	
Karim et al. (18)	Pakistan	**2020**	A prospective,	200 patients	Group A consisted of	The mean age of the	There were 59 (61.5%) men &	

			comparative study		ninety-six cases, accounting for forty-eight percent of the total, whereas Group B comprised 104 cases, representing fifty-two percent.	individuals in the research was 56.3 years, with a standard deviation of ±4.1 years.	37 (38.5%) women.	
Yen et al.(19)	**Taiwan**	**2012**	a single center; prospective, randomized trial	100 patients	While the intravenous group had a re-bleeding rate of four percent (2/50), the oral group had a re-bleeding rate of four percent (2/50). Both the ESO group & the LAN group each have fifty members.	≥18(62.7 (2.3	Males, and females in group A were 37 (74%), and 34 (68%)respectively. In group B males and females were13 (26%), and 16 (32%) respectively.	
Phulpoto et al. (20)	Pakistan	**2013**	Prospective, randomized, reoccurred in 5 cases of oral omeprazole controlled clinical trial	44 cases	cases were randomly omeprazole vs intravenous omeprazole in allocated into oral omeprazole group & 41 to IV omeprazole group.(PO-OMPN=41) and (IV OMP n=41)	≥18 (57.25 16. 45)	Male to female ratio in group A was 33/11, & in group B was 30 /11	

Table (2) showing the main findings of the included studies.

Authors	**The main findings**
Toosi SM, et al. (16)	throughout the one-month monitoring period, their research found no statistically significant variations among both groups that received oral pan or IV pan: rates of re-endoscopy & volume of blood transfusion, re-bleeding, length of hospital stays, operation, or mortality. They reached the conclusion that high-dose oral PPIs may serve as an acceptable replacement for high-dose IV PPIs in cases with hemorrhaging peptic ulcer.
Liu et al.(17)	The standard dose of intravenous proton pump inhibitor (forty milligrams bolus twice daily for seventy-two hours) was less effective than the high dose (eighty milligrams bolus followed by a continuous infusion of eight milligrams/hours) in

	decreasing the frequency of recurrent bleeding, the need for blood transfusions, & the length of stay in hospital. It was determined that high-dose PPI infusions are more effective in decreasing the incidence of rebleeding, the need for blood transfusions, & the length of hospitalization. Late endoscopy is less efficacious & safer than early endoscopy.
Karim et al. (18)	According to their research, 104 (52%) cases received oral pantoprazole compared to 96 (48%) in the IV group. The administration of IV pantoprazole resulted in notable enhancements in hemoglobin (Hb) levels beginning twenty-four hours after the medication commenced (p: 0.01). Additionally, the group exhibited improvements in supine systolic blood pressure at forty-eight hours (p: 0.04) & diastolic blood pressure at both twelve & forty-eight hours, in comparison to the oral pantoprazole group (p: 0.05). Similarities were observed in the mean length of hospitalization, the necessity for blood transfusions & repeat endoscopies, rebleeding, & mortality rates among both groups (p above 0.05). No statistically significant distinction was noticed amongst the oral & parenteral routes of pantoprazole administration in terms of preventing rebleeding in cases following effective therapeutic endoscopy.
Yen et al.(19)	No significant variations were observed amongst both groups in terms of length of hospitalization, blood transfusion volume, surgical procedures performed, or mortality rate. In the oral lansoprazole group, the average length of hospitalization was 1.8 days, whereas in intravenous esomeprazole group, it was 3.9 days ($p > 0.01$). An oral proton pump inhibitor reduces the length of hospitalization for patients. No evidence exists to support a distinction in clinical outcomes among the administration of PPIs orally or intravenously.
Phulpoto et al. (20)	Oral high-dose Proton-pump inhibitors was as effective as intravenous great-dose Proton-pump inhibitors in lowering mortality, hospital stay, hemorrhage rate, & blood transfusion in cases with peptic ulcers who received endoscopic treatment, according to their analysis. It might be feasible to substitute PO PPI with IV PPI.

Discussion

Acute UGIB continues to be a prevalent medical issue that is correlated with significant mortality & morbidity. The annual occurrence of acute UGIB is assessed to be among fifty & 170 per

100,000 individuals, with peptic ulcer affecting about fifty percent of adult cases. **(21)** Endoscopic interventions, including hemoclipping or thermocoagulation, are widely advised as initial treatments for peptic ulcer bleeding due to their demonstrated efficacy in reducing mortality, recurrent bleeding, & surgical intervention requirements. On the other hand, gastric acidity disrupts hemostasis & impedes clot formation on bleeding ulcers; thus, it is critical to neutralize the intragastric level of pH to solidify clot formation. It decreases the rate of rebleeding. Proton pump inhibitors are highly effective agents that suppress gastric acid by impeding the enzymatic transfer of acidic hydrogen ions into the stomach, thereby decreasing acid secretion **(22, 23).** In cases of peptic ulcer hemorrhage, the adjuvant use of intravenous Proton-pump inhibitors following endoscopic treatment has been demonstrated to be effective. However, the ideal dosage & most effective methods of administration are still uncertain. Oral &intravenous PPIs have demonstrated comparable efficacy in elevating intragastric pH levels **(24, 25).**

Any variation in intragastric pH occurs only within the initial hours following medicine administration.16 Oral Proton-pump inhibitors may have the potential to substitute intravenous PPIs during the 24-hour intragastric pH monitoring in cases afflicted with hemorrhaging ulcers. Furthermore, it has been observed that PPIs administered orally or intravenously in the same dosage can elevate the intragastric pH level above six for a duration of three days following successful endoscopic hemostasis. **(26)**

Numerous randomized controlled trials have compared the efficiency of oral& I/V PPI in treatment of peptic ulcer hemorrhage in recent years; however, most of these research have been constrained by comparatively small sample sizes **(27, 28).**

Comparing intravenous versus oral PPI for the prevention of rebleeding from peptic ulcers following successful endoscopic treatment was the purpose of our research.

In 2008, Tsai and colleagues performed research in which 156 cases who were at high risk for developing peptic ulcers were separated into 2 groups. For the initial seventy-two-hour period following therapeutic endoscopy, the participants were administered either oral PPI or IV PPI. All patients were subsequently administered standard doses of oral PPI. Rebleeding, transfusion requirements, mortality, surgical complications, & duaration of hospitalization were comparable among the two groups. **(29)**

Furthermore, in 2011, an investigation that was carried out by Mostaghni and colleagues revealed that there weren't no significant variances observed in the volume of blood transfusion, rate of re-bleeding, or duration of hospitalization among eighty-five cases diagnosed with high-risk PUD who had been given high-dose oral omeprazole or intravenous pantoprazole within the initial seventy-two-hour duration following therapeutic endoscopy treatments. In a 2014 single-center, randomized, controlled, double-blind, double-dummy research, 244 cases who had undergone therapeutic endoscopy & suffered hemorrhage PUD were included. **(15)**

For a duration of seventy-two hours, 126 cases received high dose oral esomeprazole in addition to a placebo, while 118 cases received high dose IV esomeprazole in conjunction with an oral placebo. cases were observed for a duration of thirty days after index hemorrhage. There wasn't significant variance reflected in the outcomes of blood transfusion requirement, re-bleeding, days of stay in hospital, or re-endoscopy among both groups, as indicated by the results. Nevertheless, due to the premature termination of this study, the findings regarding the equivalence or non-inferiority of two therapy regimens cannot be definitively determined. **(32)** Following therapeutic endoscopy, in 2013, Tsoi and colleagues compared the results of oral versus I/V PPI administration in cases with high-risk PUD using a meta-analysis. A total of 6 randomized clinical research was assessed between 2006 and 2011, involving 615 cases (302 cases in the oral PPI group & 313

cases in the I/V PPI group). There were no significant variances observed in the results of volume of blood transfusion, re-bleeding, days of stay in hospital, surgical necessity, & all-cause mortality between the two groups. **(21)** In summary, meta-analyses & two recent systematic reviews indicate that post-endoscopic therapy of high-risk ulcers can be effectively managed with both oral & IV PPI. **(30, 31)**

Conclusion

cases with blood loss peptic ulcer illness may benefit from high-dose oral Proton-pump inhibitors as an alternative to high-dose intravenous Proton-pump inhibitors, according to the findings of our research. In addition, the accessibility & reduced cost (around thirty times) of oral PPI make its utilization considerably more economically viable.

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