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Original Research Article

Comparing Intravenous and Oral Esmoprazole on Intra Gastric PH in Patients with Peptic Ulcer Bleed (PUB)

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Abstract

Background: Oral and intravenous proton pump inhibitors (PPIs)are used in patients with peptic ulcer bleed (PUB) for acid suppression clot stabilisation.

Aim: To compare acid suppression produced by standard doses of oral vs. Intravenous esomeprazole in patients with peptic ulcer bleed after initial endoscopic stabilisation.

Methods: A randomized study was done on twenty patients admitted with peptic ulcer bleed with stigmata of recent hemorrhage who after initial endoscopic treatment were divided into two groups; one receiving oral while other receiving intravenous esomeprazole. The mean pH in the oral group was 7.06 ± 0.44 while the mean pH in the intravenous group was 6.78±0.27. There was statistically no difference in intragastric pH for 72 hrs with esomoprazole given either orally or IV (p=0.1). Thus oral esomeprazole is as effective as intravenous esomeprazole.

Keywords: Peptic Ulcer Bleed, Endoscopic Treatment, Oral, Intravenous, Proton Pump Inhibitors.

Introduction

Bleeding peptic ulcers remains the leading cause of upper gastrointestinal bleed with significant mortality and morbidity despite advances in diagnosis and treatment. [1] Hemostasis attained by endoscopic procedures (local adrenaline injection, thermal coagulation or clipping) reduces recurrent bleeding ,the need for surgery and mortality in patients with bleeding peptic ulcer. [2,3] However ,endoscopy therapy is associated with its own limitations like it is invasive, cumbersome, requires expertise, and is not available uniformly and complications like perforation (0.5%) and induction of uncontrolled bleeding (0.3%) after initial endoscopic hemostasis bleeding still

occurs in up to 20% of patients, and surgery is still necessary in some of these patients. [4] Therefore much of the recent work has emphasized that limitation of gastric acidity, whether by full neutralization with antacid [5] or use of H2- receptor blockers may bear importantly upon the cessation of acute mucosal bleeding. Experimental data suggest that gastric acidity plays an important role in causing clot lysis in bleeding ulcers therby impairing hemostasis. [6] It has been hypothesized that inhibiting acid production by use of proton pump inhibitors (PPIs) allows more effective and longterm acid suppression. Further, a gastric pH of <6 inhibits platelet aggregation [7] and of pH <5 inhibits plasma coagulation.(8)The efficacy of ptoton pump inhibitors (PPIs)has been demonstrated for peptic ulcers but the route of administration remains controversial.Studies have demonstrated and advocated role of intravenous proton pump inhibitors during active UGI bleed and oral proton pump inhibitors after the acute episode to reduce rebleed. [9,10,11]. In the current study, after initial endoscopic stabilization intragastric pH was monitored while patients were randomnly divided into two groups; one given intravenous esmoprazole and other oral esmoperazole to study the superiority of one over other.

Aims and Objectives

Effect on increase in gastric pH by oral versus intravenous esomeprazole in Bleeding Peptic Ulcer after endoscopic treatment and its effect on rate of re-bleed.

Materials and Methods

The prospective, randomized, double blind study was conducted in the department of Gastroenterology, Sher-i-Kashmir Institute of Medical Sciences. Twenty patients admitted to the hospital with a history of hematemesis and/or malena, or who bled while in hospital were taken for emergency endoscopy as soon as possible within 12 hrs. of bleeding or immediately after resuscitation of patients with massive bleeding or shock. Endoscopy therapies were given and if endoscopy showed peptic ulcer in the stomach or duodenum with active bleeding (spurting hemorrhage, oozing hemorrhage) or stigmata of recent hemorrhage (a non-bleeding visible vessel). Assessment of the presence of those stigmata was made after adherent clots and debris of the ulcer base had been vigorously washed away. Patients who achieved hemostasis with endoscopic therapy were eligible for entry into the study.

Exclusion Criteria

1. Patients who were under 18 years of age.
2. Those who were unable or unwilling to give written informed consent.
3. Pregnant or lactating women.
4. Those who were on anticoagulants.
5. Those who had more than one possible source of bleeding**.**
6. Those who had severe coagulopathy (prothrombin time 30% or less than normal) or platelet count less than 50,000/mm.
7. Those who had previous acid reducing surgeries (vagotomy, gastric resection)**.**
8. Those who were moribund because of terminal cancer or severe comorbid illness: or had bleeding gastric cancer.
9. Those who required treatment with NSAIDS including aspirin or clopidrogel, during IST seven days of study.
10. Those who received more than 40 gm. of PPIs within 24 hours before enrollment.
11. Those who received drugs known to interact with PPIs (phenytoin, clarithromycin, itraconazole, warfarin and other vitamin k antagonists' cisapride, atazanavir or ritonavir).

Method of Endoscopic Treatment and Intragastric PH Monitoring

Endoscopic hemostasis was achieved by using injection adrenaline (1:10,000 dilution in NS.), heat probe thermocoagulation (Olympus heat probe – 25J) are combination of both (adrenaline + heat probe) and by using endoscopic clips.

Intragastric pH Monitoring of eligible patients for 72 hrs after successful endoscopic hemostasis was done by using proxima light pH monitor which is a portable self-programmed data logger for recording of biological varibles, completely based on micro processing technology. Proximal light enables gathering of data relevant to gastric pH by means of frequency and duration.

After informed consent instrument was placed in stomach via nasal cavity and positioned under fluoroscope in the gastric corps 5cm distal to cardia. pH electrode was calibrated before and after each recording using standard buffer solution pH 4 & pH 7.

Randomization and Pharmacological Treatment

Immediately after endoscopic control of bleeding, patients 18 years or older presenting to hospital emergency departments, or already hospitalized for another reason, with overt signs of upper gastrointestinal bleeding (hematemesis, malena, or both) in the past 24 hours were eligible for randomization. We recruited patients with bleeding ulcers that showed 1 of the following endoscopic stigmata of recent hemorrhage: arterial bleeding (Forrest class Ia), oozing (Forrest class Ib), nonbleeding visible vessel (Forrest class IIa), or adherent clot (Forrest class IIb). In the case of Forrest class IIb ulcers, after attempts to remove the clot by using water irrigation or a cold snare, ulcers were either reclassified for inclusion as Forrest class Ia, Ib, or IIa or, if unsuccessful, included as Forrest class IIb. Eligible patients were randomly assigned to receive esomoprazole given as intravenous bolus of 80 gm. followed by a continuous infusion of 8 mg. per hour for 72-hour oral esomeprazole in the dosage of 80 mg bid for a period of 3 days by a pharmacist in a double-blind manner.

Randomizations were carried out in the endoscopy laboratory itself by random numbers derived from a table of random numbers in block of four by using Central Computer- Generated Block Randomisation.

Clinical Monitoring

Patients were observed for rebleeding in a high care facility of the Gastroenterology ward. All patients were given standard medical treatment (PPI's) for peptic ulcer bleeding. Patient's vital signs were checked every hour during the first 12 hours every 2 hours for the second 12 hrs and 4 hours thereafter until patients were discharged. The Hemoglobin (Hb) level and Hematocrit were checked at least once daily, and blood transfusions were given if Hb level fell to 9gm/dl or less, or vital signs deteriorated. Adverse effects were monitored throughout the study in both groups and after 3 days the patients were given esomeprazole 40gm orally once daily for 6 weeks and those +ve for H. pylori were also treated with triple therapy. Patients were clinically examined on weeks 1, 2, 4 & 6 and repeat endoscopy was done at 6 weeks, the primary end point was the rate of rebleeding. the secondary end points were 1. Surgery, 2. Death, 3. Duration of hospital stay, 4. Number of blood transfusions and 5. Number of rescue therapies required.

Statistical Analysis

The statistical Analysis of the Nominal data was done by using Test Statistics, Chi-Square test (X2) and Fischers exact test (cell frequency <5%). The Quantitative data was analyzed by using t-test for differences of Mean. These tests were two sided and were refrenced for p-values for there significance. Any value less than 0.05 ($p<0.05$) was taken to be significant otherwise non-significant. The

TYPE I, error among groups and was 0.05. The analysis of the data was done by using statistical package for social sciences (SPSS version 14.0) Chicago-USA for windows.

Observation and Results

The effect of oral versus intravenous esmoperazole on intragastric pH was studied in twenty patients; ten received oral while the remaining ten received intravenous esmoperazole after initial endoscopic stabilisation. The mean age of the patients in the oral group was 42± 15.10 while the mean age in the intravenous group was 44± 16.10. Each of the two groups had 4 patients having comorbidity in the form of hypertension, diabetes mellitus, chronic obstructive pulmonary disease or hypothyroidism. History of previous ulcer disease was seen in three patients in the oral group and four patients in the intravenous group. (p=0.833). The two groups were comparable in their modes of presentation (p=0.842) in the form of hematemesis, malena or both. The mean size of ulcer in the oral group was 1.1 ± 0.37 while in the intravenous group was 1.14± 0.35 (p=0.49). Six patients in the oral group had stigmata of reactive hemorrhage in the form of class 2b ulcer while 5 in the intravenous had class 2b ulcer (p=0.865). All the twenty patients were given initial endoscopic treatment either in the form of local adrenaline or heat probe coagulation. (P=0.9234). Table 1

Table 1: Distribution of clinical and endoscopic data of patients in group I and group II.

	I (ORAL)	II (IV)	P-Value
No. of Patients	10	10	
Mean age (yrs.)	42.00±15.10	44.50±16.10	0.27
Presentation			
Hematemesis	2	3	
Malena	4	4	0.842
Both	4	3	
Previous Ulcer Disease	3	4	0.833
Associated Comorbidity (HTN,COPD,T_2DM,LT_4)	4	4	1.00
SRH Class			
Ia.	2	3	0.865
Ib.	2	2	
IIa.	6	5	
Mean Ulcer Size	1.10±0.37	1.14±0.35	0.49
Endoscopic Treatment			
Adrenaline	7	8	0.924
Heat probe	3	2	

After the initial stabilisation, ten patients were given esmoperazole in a dose of 40mg twice a day for 48hrs and the other group received esmoperazole infusion at the rate of 8mg/hr infusion. The pH recording was done for a period of 72 hrs . The mean pH in the oral group was 7.06 ± 0.44 while the mean pH in the intravenous group was 6.78±0.27 (Table 2).

Table 2: Comparison of effect on intragastric pH of Patients on Esomeprazole in group I and group II.

Ph	I (ORAL)	II (IV)	t-Value	P-Value
Mean	7.06	6.78	1.71	0.1
Median	7.10	6.90		
S. D.	0.44	0.27		
S. E.	0.14	0.84		

This shows there is statistically non-significant difference between esomeprazole when given either IV or Orally.

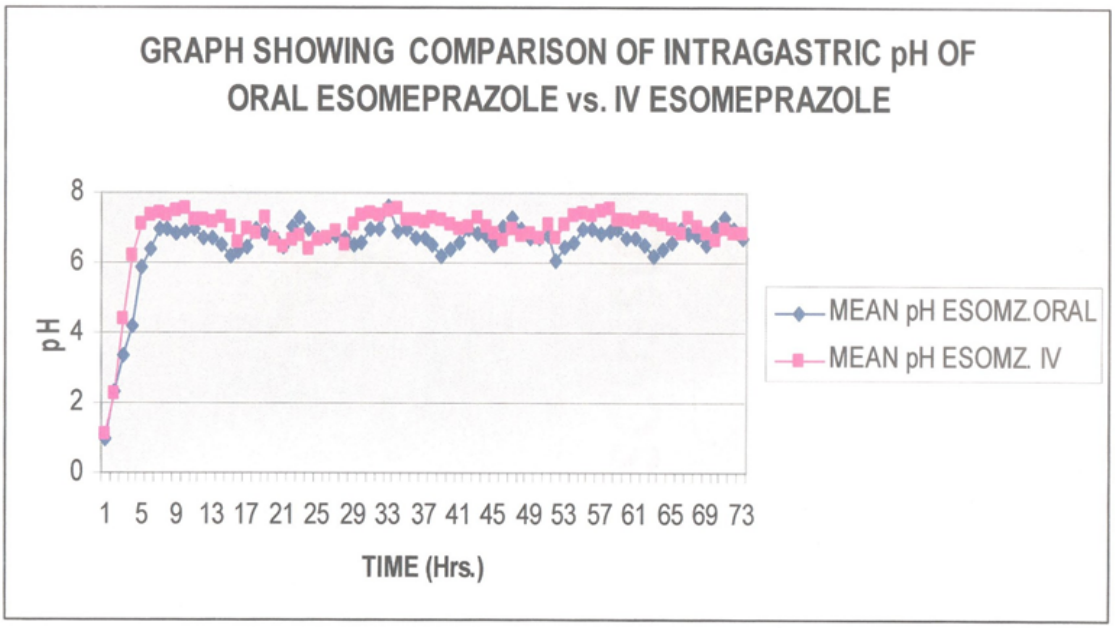

Figure 1: Comparison of intragastric pH of oral esomeprazole vs. esomeprazole

There was statistically no difference in intragastric pH for 72 hrs with esomoprazole given either orally or IV (p=0.1). The pH remained above 6. We therefore concluded that all the side effects were minor irrespective of route of administration of esmoprazole and their frequencies were similar. None of these patients required termination of drug infusion. There was statistically no significant difference among primary and secondary end points in the two groups. This shows there is statistically no significant difference between esomoprazole when given either orally or administered intravenously. Thus oral esmoprazole is as effective as intravenous esmaprazole.

Discussion

Bleeding peptic ulcer is a common and life-threatening condition. Although endoscopy therapy has become the mainstay of controlling bleeding, recurrent bleeding after endoscopic control occurs in about 20% of patients with a high associated mortality. Acid suppression has been advocated in many studies as a mainstay in the prevention of rebleed based on the hypothesis that pepsin activity is pH dependent. In the treatment of peptic ulcer bleeding (PUB), acid inhibition is based on the hypothesis that clot formation and clot lysis depend on intraluminal pH. Medications used in the prophylaxis of stress ulcer bleeding comprise antacids, H_2 receptor blockers (ranitidine) and PPIs. Two trials showed that patients who receive omeprazole run a significantly lower risk of bleeding than

patients receiving ranitidine [12,13,14]. The optimal initial treatment for bleeding peptic ulcers with active bleeding or non-bleeding visible vessel is endoscopic therapy. Among patients with non-bleeding visible vessels or adherent clots who do not undergo endoscopic therapy, acid inhibition with PPIs may significantly reduce rebleeding rate and need for surgery. After endoscopic therapy, acid inhibition with PPI may have a beneficial effect on hemostasis [15].

PPI are drugs of choice for patients with PUB because these drugs are more effective than H_2RAs or maintaining the target intragastric pH (6 or higher) and preventing the recurrence of PUB. High dose PPI therapy should be used for patients at high risk of rebleeding. Oral PPI therapy may be used for low-risk patients [16]. Lau J Y et al studied effect of i/v Omeprazole on recurrent bleeding after endoscopic treatment of bleeding peptic ulcers. It was shown that i/v Omeprazole can rapidly raise intragastric pH to more than 6, a level shown to enhance platelet aggregation and formation of fibrin clot [17]. Church N I, Palmer K R showed that acid suppression is effective in preventing bleeding from peptic ulcer. Standard dose of i/v Omeprazole may be as effective as high dose regimens. Oral Omeprazole also reduces rebleeding following endoscopic therapy for peptic ulcer [18]. In our study we compared intravenous esmoperazole with oral and found that both were equally effective in maintaining gastric pH above 6 and preventing rebleed. The findings were consistent with those of Bajaj et al who compared oral pantoprazole with iv pantoprazole in 25 patients [19]. Similar results were obtained by Focareta et al and Yilmaz et al who found oral PPIs equivalent to intravenous PPIs in regards of rebleeding, need for blood transfusion, need for surgery, need for surgery and overall mortality [20,21]. We therefore conclude and advocate that there is no difference between oral and intravenous PPIs in the outcome analysed. However, our study was underpowered due to small sample size but in a resource limited country like India considering the cost effectiveness of oral PPIs, we can safely recommend oral PPIs after initial endoscopic treatment in patients with bleeding peptic ulcers. [22]

References

1. Rotondo G. Epidemiology and diagnosis of acute nonvariceal upper gastrointestinal bleeding. Gastroenterol Clin North Am 2014; 43:643-63.
2. Cook DJ, Guyatt GH, Salena BJ, Laine LA. Endoscopic therapy fpr acute nonvariceal upper gastrointestinal hemorrhage: a meta-analysis. Gastroenterology 1992; 102:139-48.
3. Sung JJY, Tsoi KKF et al. Endoscopic clipping versus injection and thermocoagulation in the treatment of non-variceal upper gastrointestinal bleeding: a meta-analysis. Gut 2007; 56:1364-73.
4. Lee, JG, Turnipseed, S & Romano, PS et al. Endoscopy-based triage significantly reduces hospitalization rates and costs of treating upper GI bleeding: a randomized controlled trial. Gastrointest Endose 1999; 50:755-61.
5. Jensen DM. Spots and clots – leave them or treat them? Why and how to treat. Can J Gastroenterol 1999;13: 1307-11.
6. Barkham P, Tocantis LM. Action of human gastric juice on human blood clots. J Appl Physiol. 1953; 6:1-7.
7. Green FWJ, Kaplan MM, Curtis LE, et al. Effect of acid and pepsin on blood coagulation and platelet aggregation. A possible contributor prolonged gastroduodenal mucosal hemorrhage. Gastroenterology 1978; 74: 38-43.
8. Chaimoff C, Creter D, et al. The effect of pH on platelet and coagulation factor activities. Am J Surgery 1978; 136:257-9.

9. Leontiadis GI, Meintyre L, Sharma YK, Howden CW. Proton pump inhibitor treatment for acute peptic ulcer bleeding (Cochrane Review) 2004;3: ACD002094.
10. Schaffahtzky de Muckadell OB, Havelund T, Harling H et al. Effect of omeprazole on the outcome of endoscopically treated bleeding peptic ulcers. Randomized double-blind placebo controlled multicenter study. Scand J Gastroenterol. 1997; 32:320-327
11. Zed PJ, Loewen PS, Slavik RS, Maera CA. Meta analysis is of proton pump inhibitors in treatment of bleeding peptic ulcers. Ann Pharmacother 2001; 35:1528-34.
12. Labenz J, Peitz U, Leusing C, Tillenburg B, Blum AL, Borsch G. Efficacy of primed infusions with high dose ranitidine and omeprazole to maintain high intragastric pH in patients with peptic ulcer bleeding, a prospective randomised controlled study. Gut. 1997; 40:36-41.
13. Barnert J, Bittinger M, Wienbeck M. Effects of intravenous infusion of omeprazole and ranitidine on intragastric acidity in bleeding peptic ulcer patients. Gastroenterology 1994; 106: A46.
14. Kiilerich S, Rannelll T, Elsborg L. Effect of intravenous infusion of omeprazole and ranitidine on 24-hour intragastric pH in patients with a history of duodenal ulcer. Digestion 1995; 56:25-30.
15. Balanzo J Sainz S, Such J, et al. Encloscopic hemostasis by local injection of epinephrine and polidocanol in bleeding ulcer: a prospective randomized trial. Endoscopy 1988; 20: 289-291.
16. Zuckerman G, Welch R, Douglas A, et al. Active upper gastrointestinal bleeding and prevention of rebleeding. Am J Med 1984;76: 361-366.
17. Lau, JY, Sung, JJ & Lee, KK et al. Effect of intravenous omeprazole on recurrent bleeding after endoscopic treatment of bleeding peptic ulcers. N Engl J Med 2000; 343: 310-6.
18. Church NI, Palmer KR. Ulcers and non-variceal bleeding. Endoscopy. 2003; 35:122-6.
19. Bajaj JS, Dua KS, et al. Prospectuve, randomized trial comparing effect of oral versus intravenous pantoprazole on rebleeding after nonvariceal upper gastrointestinal bleeding: a pilot study. Dig Dis Sci 2007; 52:2190-4.
20. Focareta R, Ciarleglion A, et al. Proton pump inhibitor and acute peptic ulcer bleeding: effectiveness of oral esomeprazole vs. intravenous esomeprazole in reducing the risk of recurrent bleeding. Dig Liver Disease 2004; 36: S250.
21. Yilmaz S, Bayan K, et al. A head-to-head comparison of oral vs. intravenous omeprazole for patients with bleeding peptic ulcers with clean base, flat spots and adherent clots. World J of Gastroenterol 2006; 12: 7837-43.
22. Martínez J. A. P., Saavedra A. J. G., Bohorquez G. D. B., Cordero J. F. B., Barros B. D., Ríos M. K. M., Duque, L. E. D., & Martínez L. J. M. Therapeutic Potential of Heparin in Sepsis Per Gram Negative. Journal of Medical Research and Health Sciences. 2022; 5(4): 1881–1885.