Journal of Advanced Medical and Dental Sciences Research

@Society of Scientific Research and Studies ***NLM ID:*** *101716117*

Journal home page: www.jamdsr.com doi: 10.21276/jamdsr Index Copernicus value = 85.10

(e) ISSN Online: 2321-9599; (p) ISSN Print: 2348-6805

Original Research

Management of stress induced upper gastrointestinal bleeding in patients with cirrhosis admitted in intensive care units

Dr. Dattaram U [1], Dr. Ankur Atal Gupta [2]

[1]Associate professor, Department of Surgical Gastroenterology**,** National Institute of Medical Sciences and Research, Jaipur, Rajasthan**;**
[2]Assistant professor, Department of surgical Gastroenterology and Hepato Pancreato Biliary Surgery, National Institute of Medical Sciences and Research, Jaipur, Rajasthan

***ABSTRACT*:**
Background: Hemorrhage from stress-induced gastric lesions (stress ulcers) was a significant problem in many critically ill surgical patients in the 1960s who had sepsis and evidence of organ failure.' Hemorrhage from stress ulcers has been defined as gut failure in the multiple organ failure syndrome and continues to be associated with high mortality rates when it develops postoperatively. **Objective:** To develop practice guidelines for the regulation of gastrointestinal hemorrhage in adult cases with cirrhosis by administrating H2 blockers and Proton pump inhibitors. **Methodology:** 155 cases of upper gastrointestinal bleeding with cirrhosis were entailed in the study and randomized in to 2 groups. Group A administered with omeprazole 40 mg intravenously for every 12 hours and group B with 77 patients received 300 mg cimetidine intravenously every 6 hours and the outcomes were measured. **Result**: A total of 155 patients met the inclusion criteria and thus were recruited. There was no remarkable difference in the number of cases who required ventilation in the ICU units over and above 48 hours or those who had sepsis. In omeprazole group (78patients), mean baseline pH 2.7± 1.1 (increased to 5.6 ± 0.5 after drug administration); cimetidine group (77 patients), mean baseline pH 2.9 ± 0.8 (increased to 4.7 ± 1.0 after drug administration. The number of samples with a pH of 4 or lower was 7 (12.1%) of 78, and 31 (57.4%) of 77, in omeprazole and cimetidine respectively ($p < 0.001$)
Keywords: Stress ulcer, medication prophylaxis, mortality, intravenous omeprazole, cimetidine, Cirrhosis, Upper gastrointestinal hemorrhage.

Received: 12 October, 2020 Accepted: 29 October, 2020

Corresponding author: Dr. Ankur Atal Gupta, Department of surgical Gastroenterology and Hepato Pancreato Biliary Surgery, National Institute of Medical Sciences and Research, Jaipur, Rajasthan**.**

This article may be cited as: U Dattaram, Gupta AA. Management of stress induced upper gastrointestinal bleeding in patients with cirrhosis admitted in intensive care units. J Adv Med Dent Scie Res 2020;8(11): 257-260.

INTRODUCTION: Upper gastrointestinal (GI) bleeding due to stress ulcers contributes to increased morbidity and mortality in people admitted to intensive care units (ICUs) especially in the elderly. ICU patients with major bleeding as a result of stress ulceration might have mortality rates approaching 48.5% to 65% (1,2)

Stress-damage of upper gastro-intestinal tract (GIT) mucous membrane and gastro-intestinal hemorrhage (GIH) increase the lethality of patients. Gastrointestinal bleeding remains a major cause of mortality in patients with cirrhosis. The prognosis is related to the severity of liver disease and death often occurs due to liver failure .The management of gastrointestinal bleeding in patients with cirrhosis includes arrange od medical, endoscopic and radiological intervention. (3)

The upper gastrointestinal tract is the commonest source of acute gastrointestinal hemorrhage. The prevalence of upper gastrointestinal bleeding in the population is approximately 100 per 100 000 adults per year. Hemorrhage from the gastrointestinal (GI) tract is categorized as upper GI bleeding (UGIB), small bowel bleeding (also formerly referred to as obscure GIB (OGIB)) or lower GIB (LGIB) (1,2) out of three most

common is UGIB.
This article overviews standards of practice for the management of upper and lower acute gastrointestinal bleeding. Common bleeding disorders are reviewed with expanded focus on stress induced gastrointestinal hemorrhage in cirrhosis patients, which are commonly found in the critical care setting

MATERIAL AND METHODS:
We included randomized controlled trials (RCTs) with participants of any age and gender admitted to ICUs for longer than 48 hours. We excluded studies in which participants were admitted to ICUs primarily for the management of GI bleeding and studies that compared different doses, routes, and regimens of one drug.

INTERVENTION
In a single-center, randomized controlled study, 174 patients having upper gastrointestinal bleeding with cirrhosis of liver were included. Of these patients, 154 who were qualified upon further evaluation were randomized into 2 groups: 77 patients received 40 mg intravenous omeprazole every 12 hours, 77 patients received 300 mg intravenous cimetidine every 6 hours

RESULTS:
A total of 174 patients met the inclusion criteria and thus were recruited. Of them, 20 were excluded from data analysis because 10 were lost to follow-up within 30 days, 5 were not assessable due to missing important data, and 5 did not meet the enrollment criteria. Our results are therefore based on 154 patients who completed the prophylaxis treatment. The major clinical characteristics of these patients are summarized in Table 1.

Table 1: Major clinical characteristics and outcomes of patients among 2 prophylaxis groups*

Parameters	omeprazole	cimetidine	P value
No. of patients	77	77	
Sex (male) (female)	41 37	44 33	0.398
Age(yrs) Less than 40 40-60 More than 60	 23 42 13	 26 47 04	 0.327
ICU stay (days) Less than 7 days More than 7 days	 49 29	 52 25	0.302
ventilator (hrs) ≤48 >48	 55 23	 49 28	0.259
location of hematoma supratentorial infratentorial	 62 16	 58 19	0.365
location of hematoma supratentorial infratentorial	 66 12	 63 14	 0.265
Sepsis	26	15	0.769
UGI bleeding	5	11	0.013
Death	24	12	0.326

Table 2: Demographic and clinical data of patients with UGI bleeding

Parameters	UGI Bleeding at Admission	UGI Bleeding During/ After Prophylaxis	Total	p Value
No. of patients	80	45	125	0.316
Sex Male Female	 52 28	 29 16	 81 44	0.235
Age(yrs) Median Range	 56 18-80	 48 18-74	 52 18-80	0.312
Location of hematoma Supratentorial infratentorial	 68 12	 35 10	 103 22	 0.904
bleeding arrested by high-dose omeprazole w/in 3days	63	40	103	0.286
Death	34	15	49	0.061

There was no remarkable difference in the number of cases who required ventilation in the ICU units over and above 48 hours or those who had sepsis (Table 1). In omeprazole group (77patients), mean baseline pH 2.7 ± 1.1 (increased to 5.6 ± 0.5 after drug administration); cimetidine group (77 patients), mean baseline pH 2.9 ± 0.8 (increased to 4.7 ± 1.0 after drug administration. The number of samples with a pH of 4 or lower was 8(10.39%) of 77, 21 (27.27%) of 77, in omeprazole and cimetidine respectively ($p < 0.001$).

Stress induced UGI bleeding take place in 9 cases (11.6) in the omeprazole administered group in contrast with 15 patients in the cimetidine group (19.49%) which is statistically significant ($p = 0.003$)

A total of 36 patients died, 16 of whom had UGI bleeding. The occurrence of UGI bleeding was significantly related to death ($p = 0.022$). There were 24 and 12 deaths in the omeprazole, cimetidine, and respectively, and the difference was not significant ($p > 0.05$). Factors contributing to death included septicemia or systemic inflammatory response syndrome in 23 patients, UGI bleeding in 21, and miscellaneous in 26.

In 155 patients with UGI bleeding (80 had a positive gastric occult blood test at admission and 45 developed UGI bleeding in the prophylaxis groups) in which high dose omeprazole was initiated, UGI bleeding arrested within the first 3 days in 103 patients (87.3%). Demographic and clinical features were not significantly different between patients who presented with UGI bleeding at admission and those who developed UGI bleeding in the prophylaxis groups (Table 2)

DISCUSSION:

H2RAs were less effective than PPIs, as highlighted by the current study (27.8% vs 15.5%), which is in harmony with several studies conducted in a critical care setting (4,5,6) because gastrin and acetylcholine provide alternative pathways to the stimulation of HCL secretion that cannot be suppressed by H2RAs, and tolerance of H2RAs develops as early as 24–72 hours (7)

H2 receptor blockers and proton pump blockers are most commonly used in practice to prevent upper GI bleeding in ICU patients. Proton pump inhibitors significantly more often prevented upper GI bleeding in ICU patients compared with H2 receptor blockers (8)

One recent study comparing stress-induced ulcer prophylaxis in critically ill neurosurgical patients indicated that patients receiving a PPI (lansoprazole) had a gastric pH 4 or higher less often than those receiving an H2RA (famotidine) on treatment Day 1 (36% vs 74%, $p = 0.01$), although the difference became insignificantly different on Days 2 and 3. The phenomenon of heme-positive gastric aspirates was notably higher in the famotidine group on Day 1 ($p < 0.05$), but no remarkable difference on ulceration or overt bleeding rates was observed(9)

It is appropriate to speculate that an intravenous PPI may exert a quicker and stronger effect than an oral PPI, especially for those without a loading dose. This has been confirmed by the results of Somberg et al.(5) who reported that intermittent intravenous PPI (pantoprazole) more effectively maintained a gastric pH of 4 or higher and may protect against UGI hemorrhage compared with continuously infused cimetidine. In the current study, omeprazole reduced the morbidity of stress-related UGI bleeding in few cases with cirrhosis, and the event of UGI bleeding was significantly related to death. However, omeprazole failed to reduce the mortality or ICU stay compared with cimetidine. In patients with UGIH as proven by positive results of

gastric abstruse blood evaluation, we used high-dose omeprazole (80 mg bolus plus 8 mg/hr infusion) as the initial treatment and arrested UGI bleeding successfully in the first 3 days in 87.3% of patients. This infusion strategy was adopted because a previous study by Netzer et al(10) had shown that only omeprazole infusion (initial 80 mg plus 8 mg/hr) was able to maintain a high median pH (> 6) on each day over the course of 72 hours

CONCLUSIONS:

In clinically significant UGI bleeding, the primary goal is to restore the hemodynamic status, followed by early endoscopy. Intravenous octreotide in suspected variceal and PPI in non-variceal bleeding should be administered early. Omeprazole appears to be effective and safe in reducing the morbidity of stress-related UGI bleeding in patients with cirrhosis of liver compared with cimetidine. However, it could not reduce 1-month mortality or the length of ICU stay. Currently, high-dose omeprazole is the candidate drug of choice for patients presenting with UGI bleeding.

REFERENCES:

1. van Leerdam ME. Epidemiology of acute upper gastrointestinal bleeding. Best Pract Res Clin Gastroenterol 2008; 22: 209-224
2. Hearnshaw SA, Logan RF, Lowe D et al. Acute upper gastrointestinal bleeding in the UK: patient characteristics, diagnosis and outcome in the 2007 UK audit Gut 2011; 60: 1327- 1335
3. Knaus WA, Zimmerman JE. Prediction of outcome from critical illness. Chapter 1. In Ledingham, ed. Recent Advances in Critical Care Medicine. New York: Churchill Livingstone, 1988, pp 1-3
4. Conrad SA, Gabrielli A, Margolis B, Quartin A, Hata JS, Frank WO, et al: Randomized, double-blind comparison of immediate-release omeprazole oral suspension versus intravenous cimetidine for the prevention of upper gastrointestinal bleeding in critically ill patients. Crit Care Med 33:760–765, 2005
5. Levy MJ, Seelig CB, Robinson NJ, Ranney JE: Comparison of omeprazole and ranitidine for stress ulcer prophylaxis. Dig Dis Sci 42:1255–1259, 1997
6. Somberg L, Morris J Jr, Fantus R, Graepel J, Field BG, Lynn R, et al: Intermittent intravenous pantoprazole and continuous cimetidine infusion: effect on gastric pH control in critically ill patients at risk of developing stress-related mucosal disease. J Trauma 64:1202–1210, 2008
7. Netzer P, Gaia C, Sandoz M, Huluk T, Gut A, Halter F, et al: Effect of repeated injection and continuous infusion of omeprazole and ranitidine on intragastric pH over 72 hours. Am J Gastroenterol 94:351–357, 1999
8. Cannon LA, Heiselman D, Gardner W, Jones J. Prophylaxis of upper gastrointestinal tract bleeding in mechanically ventilated patients. A randomized study comparing the efficacy of sucralfate, cimetidine, and antacids. Archives of Internal Medicine 1987;147(12):2101–6
9. Brophy GM, Brackbill ML, Bidwell KL, Brophy DF: Prospective, randomized comparison of lansoprazole suspension, and intermittent intravenous famotidine on gastric pH and acid production in critically ill neurosurgical patients. Neurocrit Care 13:176–181, 2010
10. Netzer P, Gaia C, Sandoz M, Huluk T, Gut A, Halter F, et al: Effect of repeated injection and continuous infusion of omeprazole and ranitidine on intragastric pH over 72 hours. Am J Gastroenterol 94:351–357, 1999