

Practical Comparison of Use of Inj. Ranitidine and Inj. Omeprazole in Peri-Operative Period in Respect to Efficacy and Cost-Effectiveness for Prevention of Stress Ulcers

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How to cite this article:

Shah Bhavin K. & Asokan Aiamperumal. Practical Comparison of Use of inj. Ranitidine and inj. Omeprazole in Peri-Operative Period in Respect to Efficacy and Cost-Effectiveness for Prevention of Stress Ulcers. *New Indian J Surg.* 2019;10(3):253-256.

Abstract

Background: Since advent of Proton Pump Inhibitors (PPIs) use of H₂ receptor blockers (Ranitidine) is on decline. There is no doubt that PPIs are superior gastric acid suppressors and should be first line of therapy for peptic ulcer disease. Surgeons routinely use gastric acid suppressors for prevention of stress ulcers in peri-operative period. PPIs are more expensive, especially in injectable form. **Methodology:** We studied incidence of complications in the form of 1. Haemetemesis or bloody aspiration from Ryle's tube 2. Newly developing epigastric tenderness retrospectively in 1000 patients underwent laparotomy under general anaesthesia over the period of October 2011 to June 2018 in our surgical department. Patients were classified according to whether they were given PPI or H₂-receptor blocking agents in peri-operative period. Patients with portal hypertension and gastric surgeries were excluded from the study. **Results:** there was no statistical significant difference between use of either agent for prophylaxis of stress gastritis. **Conclusions:** H₂-receptor blockers should be used in peri-operative period instead of PPIs to reduce the cost of surgery as it does not increase risk of stress ulcers.

Keywords: Inj. Ranitidine, Inj. omeprazole, stress-ulcers, gastritis, haemetemesis

Introduction

Stress ulcers are mucosal defects in stomach or duodenum which can become complicated by upper gastrointestinal bleeding due to severe physiologic stress. Ordinary peptic ulcers usually occur in the gastric antrum and the duodenum while stress ulcers usually occur in gastric fundus. However, they can occur anywhere in the stomach and proximal duodenum. The characteristic lesions may be multiple, superficial in mucosa, similar to erosive gastritis. Occasionally, there may be a large acute ulcer in the duodenum (Curling's ulcer) [1]. They range in depth from mere shedding of the superficial epithelium (erosion) to deeper lesions that involve the entire mucosal thickness (ulceration) [2]. The ulcerations may be confined to the mucosa or they may penetrate deeper into the submucosa. Erosions cause diffuse mucosal oozing while the ulcer can erode into a submucosal vessel and produce frank hemorrhage [3].

Material and Methods

This study was carried out over a period of 6.5 years at our institution SBKS Medical Institute & Research Center in department of General Surgery, Vadodara. As the study was done for already established drugs (which did not involve any new drugs), permission of Institute Research Council was not taken. 1000 cases undergone laparotomy during this period were studied retrospectively and were divided in two parts. Those who had PPIs and those who had H₂-receptor blockers used for stress ulcer prevention.

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Received on 15.02.2019, **Accepted on** 26.03.2019

Pathogenesis

Adequate mucosal blood flow is important to maintain the mucosal barrier, and to buffer any back-diffused hydrogen ions. When blood flow is inadequate, these processes fail and mucosal breakdown occurs. Due to inadequate gastric mucosal blood flow during periods of intense physiologic stress or a breakdown in other normal mucosal defense mechanisms in conjunction with the injurious effects of acid and pepsin on the gastroduodenal mucosa [4] stress ulcers and erosive gastritis develops.

Risk factors- are broadly divided in two parts

1. Non-critically ill medical patients with two or more of the following: respiratory failure, sepsis, heart failure, hepatic encephalopathy, jaundice, kidney failure, stroke, hypertension, previous gastrointestinal disease and treatment with corticosteroids, NSAIDS, heparin, or warfarin.

2. In surgical critically ill patients, only those patients who are on a mechanical ventilator for more than 48 hours, those with a coagulopathy [5] or who develop one of the severe medical complication as mentioned above. It is also encountered in patients who sustain severe trauma (especially burns) or undergo major surgery (including neurosurgery) [6].

Stress ulcers were seen in 1.5% of patients in the 2252 patients in the Canadian Critical Care Trials group study [3]. People with stress ulcers have a longer ICU length of stay (up to 8 days) and a higher mortality (up to 4 fold) than patients who do not have stress ulceration and bleeding [7]. While the bleeding and transfusions associated with the stress ulcerations contribute to the increased mortality, the contribution of factors like low blood pressure, sepsis, and respiratory failure to the mortality independently of the stress ulceration can not be ignored. Patients who develop stress ulcers typically do not secrete large quantities of gastric acid; however, acid does appear to be involved in the pathogenesis of the lesions. Thus it is reasonable either to neutralize acid or to inhibit its secretion in patients at high risk [8]. Endoscopic means of treating stress ulceration may be ineffective and operation may require [9]. Surgical options include Vagotomy + Distal gastrectomy with oversewing of the major bleeding lesions, near total gastrectomy or Angiographic embolization. In selected patients, either endoscopic therapy or selective infusion of vasopressin into the left gastric artery may help control the hemorrhage [10].

Results & Observations

We found that out of 1000 cases studied, 210 patients were given PPIs and 790 patients were given H2-receptor blockers in peri-operative period for stress ulcer prevention. Only 2 patients had either haemetemesis or blood in Ryle's tube and 15 patients had epigastric pain in peri-operative period in those having PPIs. Only 1 patient had either haemetemesis or blood in the Ryle's tube and 5 patients had epigastric pain in those having H2-receptor blockers (Inj. Ranitidine). There was no mortality from either group and in most patients bleeding was stopped by increasing dose of given drug. Only 1 patient needed endoscopy to stop bleeding from fundus of stomach.

Discussion

Stress gastritis is a peculiar entity that has all but disappeared from the clinical (if not endoscopic) lexicon, largely due to better critical care and acid suppression or cytoprotective agents (e.g., sucralfate) in the intensive care unit (ICU). Modern intensive care, with emphasis on adequate tissue perfusion and oxygenation, has undoubtedly decreased the severity of gastric mucosal injury seen in the ICU today. Although it is still common to see small mucosal erosions when performing upper endoscopy in the ICU, it is rare for these lesions to coalesce into the larger bleeding erosions that plagued the ICU patient 30 to 50 years ago. The need for medications to prevent stress ulcer among those in the intensive care unit is unclear. The quality of the evidence is poor [11]. It is unclear which agent is best or if prevention is needed at all [12]. Benefit may only occur in those who are not being fed [13]. Drugs used include antacids, H2-receptor blockers, sucralfate, and proton pump inhibitors (PPIs). Some study shows tentative evidence to support that PPIs may be better than H2 blockers [14].

As some studies show that prevention may not be needed in all patients but prevention of the stress bleeding from the stomach is much easier than treating it, and hence the routine use of H2-antagonists with or without barrier agents, such as sucralfate, in patients who are on intensive care. These measures have been shown to reduce the incidence of bleeding from stress ulceration. Histamine2-receptor antagonists and antacids are associated with the a trend toward lower clinically important bleeding rates than with sucralfate is [15]. Concerns with the use of stress ulcer prophylaxis

agents include increased rates of pneumonia and Clostridium difficile colitis.

These injections are one of the most commonly used drugs in the world. They have reduced incidence of stress ulcers to negligible. It is debatable which drug is more effective.

Alhazani published his trial of comparing both and showed that PPI are more effective than H2-receptor blockers. However, there was no difference in mortality. In his own words "The robustness of this conclusion is limited by the trial methodology, differences between lower and higher quality trials, sparse data, and possible publication bias" [16].

Michal Leavy compared Inj. Ranitidine with oral omeprazole and found that oral omeprazole is safe, effective, and clinically feasible for stress ulcer prophylaxis [17]. Low number of patients (only 67) and higher number of risk factors in ranitidine group [The ranitidine treated group had 2.7 risk factors per patient while the omeprazole-treated group had 1.9 ($p < 0.05$)] may have an impact in outcome.



Fig. 1: M.R.P. 60 Rupees

Some believe that routine ulcer prophylaxis in patients without a history of peptic ulcer disease has only been of proven benefit in those with a coagulopathy or prolonged ventilator dependence; however, it is a common practice to use antiulcer agents in all patients who are nil per os (n.p.o.) for a prolonged period of time [18]. Acid suppression for the prevention of stress ulcer is regularly practiced in peri-operative period in India. In our hospital

these agents are used during surgery and in post-operative period for at least 5 days in all patient undergone laparotomy whether patient had been in ICU or not. Many of these patients were young and relatively healthy. This may be one reason why our study result is differing from others who show PPIs somewhat better than H2-receptor blockers.



Fig. 2: M.R.P. 2.80 Rupees

As we can see in figures 1 and 2, if Inj. Ranitidine is used 8 hourly the cost is 9 rupees/day, means 45 rupees for 5 days, while if Inj. Pantoprazole is used 12 hourly the cost is 120 rupees/day, means 600 rupees for 5 days. This is a big saving of 555 rupees for a poor patient, which can be used for necessary antibiotics like inj. Amikacin 500 mg. coming at 50 rupees/ ampoule, 100 rupees/ day and 500 rupees for 5 days ($p < 0.05$).

Conclusion

In surgical patients, at least in elective laparotomies, routine use of PPIs should be replaced by H2-blockers as it is as effective as PPIs in preventing stress ulcers and saved valuable resource can be used for more necessary drugs so that in country like India (where poverty is a huge national problem) treatment becomes more affordable.

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