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Research

Should Patients with Low Body Mass Index and Hypoalbuminemia on Chemoradiation Be Prescribed Prophylactic Proton Pump Inhibitors?

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Abstract

Introduction: The common causes of peptic ulcer disease are H. pylori infection and NSAIDs. Other factors such as physiological stress, smoking, steroid use, and previous history of PUD also increase the risk for developing gastric ulcers. Medical therapy has become more effective and accessible, leading to a decrease in the risk of complications by 2 -3% per year and a decline of 30-40% in the USA from 1993 to 2006. However, chemoradiation, which is increasingly used in the management of cancer patients, can cause mucosal injuries and other complications. Although there is no established support for prophylactic PPIs for cancer patients undergoing chemoradiation, a subset of patients with risk factors for systemic chemotoxicity and vulnerability to stress ulcers should be carefully evaluated and prescribed short-term PPIs to reduce complications and avoid unnecessary hospitalization.

Method: No IRB approval was obtained: Two case reports of cancer patients with gastrointestinal tumors who presented to the Emergency Room with abdominal pain shortly after receiving chemoradiation are described. Both patients were not prescribed PPIs prior to their chemoradiation therapy and were found to have gastric perforation, requiring exploratory laparotomy with Graham patch and prolonged hospitalization.

Results: According to studies, chemoradiation increases the risk of mucosal injuries and consequently the risk of developing stress gastric ulcers. Patients with borderline low BMI (<18.5) and hypoalbuminemia (<3.5dg/L) who undergo such treatment have a higher risk of developing stress mucosal injuries compared to average patients.

Conclusion: These case reports highlight that low BMI and hypoalbuminemia increase the risk of developing stress gastric ulcers in patients undergoing chemoradiation due to mucosal toxicity. Therefore, this specific patient population should be carefully evaluated and prescribed short-term PPIs prophylactically to prevent gastric ulcers, thereby reducing the risk of emergent surgical intervention and unnecessary hospitalization.

Keywords: Foregut: esophagus, stomach, surgery/interventions: malignant gastric diseases

Introduction

Peptic ulcer disease (PUD) is described as a defect in the gastric or duodenal mucosa. It is often asymptomatic and is usually identified after a late complication has occurred, such as perforation, obstruction, or bleeding. PUD results from an imbalance between gastric acid secretion and the buffering mucosal barrier. The most common risk factors are H. pylori infection and nonsteroidal anti-inflammatory drugs (NSAIDs). Other risk factors include physiological stress, smoking, steroid use, and a previous history of PUD. With the increasing effectiveness and accessibility of medical therapy (metronidazole, proton pump inhibitor (PPI), and clarithromycin) for H. pylori infection, the risk of complications decreases 2-3% per year, with a decline of 30-40% in the USA from 1993 to 2006.[1]

Despite effective treatment, patients with complications such as bleeding, perforation, and obstruction often present to the Emergency Department (ED) in critically ill conditions.

Therefore, early diagnosis is essential, and patients should be resuscitated immediately within 24 hours of diagnosis. In the ED, an upright chest X-ray can be rapidly obtained for assessment, and any evidence of pneumoperitoneum requires immediate surgical consultation. If a patient is vitally stable, a contrast tomography (CT) scan could be obtained for further evaluation.

If the perforation is contained without evidence of contrast leakage; the patient will require immediate surgical intervention. Meanwhile, all patients with pneumoperitoneum should be resuscitated by nil per os (NPO), nasogastric tube for decompression, antibiotics, antifungal treatment (especially for critically ill or immunocompromised individuals), and intravenous fluid replenishment (urine output ≥0.5cc/kg/hr) to normalize lactic acidosis. Surgical intervention should not be delayed if there is a high suspicion of gastric perforation because the mortality rate increases with delayed treatment (>24 hrs). Moreover, poor surgical outcomes are associated with advanced age, multiple comorbidities, preoperative delay >24hrs, hypoalbuminemia, and sepsis (decreased urine output, tachycardia) at presentation.[1]

According to the American Cancer Society, the risk of dying from cancer (excluding skin cancer) in the USA decreased by 32% between 1991 and 2019. This significant drop is mainly attributed to early detection and availability of treatment.[2] While surgical resection could be a curative therapy for early noninvasive tumors, several studies show better outcomes with neo-adjuvant chemotherapy in selective tumors. Chemoradiation also induces chemotoxicity in healthy rapid-proliferating cells in the gastrointestinal (GI) system by impairing mucosal cell layer, increasing exposure to gastric acid. Selective chemotherapy, Bevacizumab, and other Epidermal Growth Factor Receptor (EGFR) inhibitors are associated with GI bleeding and perforation.[6] With mucosal disruption, it is more likely to cause mucosal injuries, and PPIs, which can effectively decrease gastric acid secretion by 99% when compared to alternatives, can be gastro-protective. In two studies conducted in 1996 and 2001, Satori and his colleagues showed that the use of PPIs decreased both endoscopic findings (gastritis or erosions) and symptoms in patients on chemotherapy. Currently, there is no clear indication for cancer patients on chemoradiation to receive short- or long-term PPIs.

Methods

No IRB approval was obtained for the publication of this article

Patient 1 is a 78-year-old cachectic and frail male with a BMI of 18.3 and significant past medical history of rectal cancer (currently treated with Nigro protocol, with the last treatment administered 3 days ago) and leukopenia. He was admitted to hospital for symptomatic hyponatremia (Na 125). After 48 hours of admission, the patient began experiencing diffuse abdominal pain. An upright abdominal x-ray was obtained immediately, which showed no evidence of pneumoperitoneum. However, due to persistent abdominal pain and high suspicion of gastric perforation, a CT scan of the abdomen was performed, revealing a small pneumoperitoneum. Resuscitation was initiated, and the patient was taken to the operating room within 6 hours of imaging. Intraoperatively, a 7 mm anterior gastric perforation was identified without signs of bleeding or intraluminal mass. The perforated ulcer was closed primarily, and a Graham patch repair was performed using the omentum. The abdominal cavity was thoroughly irrigated with copious amounts of saline. Two Jackson-Pratt (JP) drains were placed near the perforation and the right gutter. The patient was then transported to the intensive care unit (ICU) for further resuscitation. On postoperative day (POD) 5, the patient started receiving total parenteral nutrition and was transferred to the floor. An upper gastrointestinal (UGI) series was performed on POD 6, which did not identify any leaks. The patient's diet was advanced to clear liquids, which he tolerated well. During admission, the patient's albumin level was 3.1, and postoperatively it was 3.0. The patient recovered well and was discharged to an Acute Rehabilitation facility.

The second case involves a 70-year-old male with a BMI of 20.3 who has oropharyngeal cancer and is undergoing chemoradiation. He presented to the emergency department (ED) with unbearable abdominal pain that had lasted for one day. His last chemoradiation was two weeks ago. During admission, the patient was found to be hyponatremic (Na 129) and in septic shock (elevated lactic acid level of 6.5 and elevated creatinine of 1.3). An abdominal X-ray revealed a large amount of pneumoperitoneum. The patient was resuscitated and underwent an exploratory laparotomy within 6 hours of presentation. Intraoperatively, a large anterior perforated ulcer was identified on the first portion of the duodenum and repaired using a Graham patch, with placement of a JP drain. The abdominal cavity was irrigated with copious amounts of saline fluid. Due to the progressive nature of the patient's disease and the intraoperative stability, a gastrostomy tube was placed for feeding access. The patient was then taken back to the ICU for further resuscitation. The second patient followed a similar course as the first patient, with negative leakage during the UGI series test, and started a clear liquid diet afterward via the gastrostomy tube.

Results and Discussion

Although both patients presented to the ED with different chief complaints, they had both undergone chemoradiation within a month of hospital admission and were found to have a perforated viscus. Both patients were successfully resuscitated and underwent surgery in a timely manner.

In contrast, the first patient had leukopenia (white cell count, WBC 2.8) due to prolonged chemoradiation, whereas the second patient (WBC 14.3) had just began his chemoradiation treatments. Neither patient had a history of GERD or PUD disease prior to presentation. Common factors between the patients included borderline low BMI (18.3 and 20.3, respectively), hypoalbuminemia (3.0 and 3.1, respectively) and hyponatremia (125 and 129, respectively) prior to presenting to the ED, and neither were on PPIs.

The first patient received Nigro protocol for anorectal cancer, which consisted of mitomycin and 5- fluorouracil (5-FU) in addition to 30 Gy of radiation. The second patient received chemoradiation at another hospital and was unable to provide the name of the chemotherapy, but based on several resources, docetaxel, 5-FU, cisplatin, hydroxyurea, or combination with radiation of 150 cGy are commonly used to treat laryngeal cancer.[5] Existing preliminary data does not support the use of chemotherapy in the elderly (age >70) or in patients with extensive comorbidities due to systemic toxicity. Side effects of chemoradiation include nausea, vomiting, poor appetite, which increase the risk of poor nutritional status and decrease mucosal barrier protection. Therefore, both patients were at higher risk for developing gastritis or, as seen in these cases, gastric ulcers leading to perforation.

Conclusions

The purpose of these two case reports is to examine whether malnourished patients (defined as hypoalbuminemia <3.5dg/L) would benefit from PPI use while undergoing chemoradiation therapy. Existing data suggests that radiation therapy increases the risk of esophageal, gastric, and intestinal toxicity, especially with higher hyperfractionation (>50 Gy), concurrent chemotherapy, and underlying gastrointestinal diseases. Therefore, proton pump inhibitors are sometimes prescribed for symptomatic patients, but not necessary for asymptomatic patients due to side effects. Research indicates that cellular toxicity can occur within hours of radiation therapy administration. Stem cell damage can result directly from radiation or subsequently as a result of microvascular injuries leading to ischemic changes and fibrosis.[3,4]

The mechanism of proton pump inhibitors is to block gastric acid secretion by irreversibly binding to and inhibiting the hydrogen-potassium ATPase pump located on the luminal surface of the parietal cell membrane. PPIs effectively decrease gastric acid secretion by up to 99% by inhibiting the last step of gastric acid secretion. However, prescribing long-term PPIs to immunocompromised patients can cause other complications, such as bone fractures and C. difficile infection, although there is no research to suggesting that short-term use is associated with these complications. Currently, there is no established guideline for short-term use of PPIs in high-risk patients. These case reports highlight the potential advantages of short-term use of PPI administration for other practitioners, particularly for malnourished cancer patients on chemotherapy or chemoradiation, to prevent development of gastric ulcers and related complications, thereby reducing the need for emergent surgeries and unnecessary hospitalization.

Conflict of Interest

The authors declare no conflict of interest.

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