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EXCESSIVE USE OF PPIS ASSOCIATED WITH THROMBOCYTOPENIA IN GENERAL POPULATION

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Abstract:
Proton pump inhibitors (PPIs) are the most commonly used class of drugs for the treatment of gastric acid-related disorders. The main objective of the study is to analyse the excessive use of PPIs associated with thrombocytopenia in general population. This cross-sectional study was conducted in Mayo hospital, Lahore during June 2019 to January 2020. The data was collected from 50 patients who were used PPIs. Then we collect the blood sample of these 50 patients to count the thrombocytes in blood. All the patient had a past medical history of a duodenal ulcer. The data was collected from 50 patients. We found a trend of slight decrease in white blood cells and neutrophils in all the patients. On review of medications, since there were no other drugs (except for one prophylactic dose of heparin) that could be attributed to thrombocytopenia, it was recommended to hold the PPI. The PPI was then stopped, and platelet count recovered to 99 × 10^3/mm^3 within two days. It is concluded that PPIs should be among the differential diagnosis of thrombocytopenia.

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INTRODUCTION:

Proton pump inhibitors (PPIs) are the most commonly used class of drugs for the treatment of gastric acid-related disorders. PPIs inhibit gastric acid production by inhibiting the gastric parietal cell hydrogen potassium ATPase, which is needed for the final step of acid secretion[1]. PPIs are the most potent inhibitor of this enzyme currently available and hence their therapeutic role in the treatment of acid-related disorders is well-established. Conditions in which PPIs are more effective and commonly used include peptic ulcer disease, gastroesophageal reflux disease (GERD), Zollinger-Ellison syndrome, eradication of Helicobacter pyloriinfection, treatment of bleeding gastroduodenal ulcers and esophageal strictures, and the maintenance therapy for Barrett's esophagus[2].

Employment of PPIs steadily and remarkably increased after starting clinical use for treatment of acid-related diseases, and they are now some of the most frequently prescribed drugs throughout the world, with large numbers of affected patients provided ongoing treatment with PPI administration for several years[3]. Along with their popularity, adverse events possibly related to long-term administration of PPIs have been reported, though the level of risk is not high. In this review, we describe the pharmacological characteristics of PPIs and compare them with those of H2RAs[4].

PPIs are the most widely used medication for gastric acid inhibition in the world. All the PPIs available in Japan, including omeprazole, esomeprazole, lansoprazole, and rabeprazole, have a benzimidazole nucleus in their molecules along with various types of branch structures. These drugs covalently bind to SH residues of cysteine molecules in the alpha-subunit of proton pumps on the secretary canalicular membranes of gastric parietal cells and inhibit the acid secretory function of those pumps[5], resulting in inhibition of gastric acid secretion. Since all currently available PPIs share the same molecular structure, they also have similar pharmacological characteristics. A PPI is unstable in an acidic condition. Therefore, an enteric coating or co-administration with an acid-neutralizing agent such as sodium bicarbonate is necessary to obtain adequate per-oral bioavailability[6].

Aims and objectives

The main objective of the study is to analyse the excessive use of PPIs associated with thrombocytopenia in general population.

MATERIAL AND METHODS:

This cross sectional study was conducted in Mayo hospital, Lahore during June 2019 to January 2020. The data was collected from 50 patients who were used PPIs. Then we collect the blood sample of these 50 patients to count the thrombocytes in blood. All the patient had a past medical history of a duodenal ulcer. The patient had taken non-steroidal anti-inflammatory drugs. Upper gastrointestinal endoscopy had revealed a duodenal bulb deformity with a deep, penetrating ulcer over the anterior wall five months ago. Laboratory tests indicated hemoglobin 11 g/dl (13–15 g/dl), total leucocyte count 12.000 cells/cc (4.000–11.000 cells/cc) and platelet count 350x103 /cc. Prothrombin time was done.

The data was collected and analysed using SPSS version 19.0. All the values were expressed in mean and standard deviation.

RESULTS:

The data was collected from 50 patients. We found a trend of slight decrease in white blood cells and neutrophils in all the patients. On review of medications, since there were no other drugs (except for one prophylactic dose of heparin) that could be attributed to thrombocytopenia, it was recommended to hold the PPI. The PPI was then stopped, and platelet count recovered to 99 × 10^3/mm^3 within two days. Upper endoscope performed at that time revealed nonspecific gastritis. Biopsies were found to be negative for Helicobacter pylori infection. Due to the spontaneously improved platelet count, antibodies to heparin-platelet factor 4 complex were not checked to rule out heparin-induced thrombocytopenia. Since all the patients platelet count normalized after stopping PPI, this current episode of thrombocytopenia was deemed likely secondary to PPI use.

Table 01: Classification of thrombocytopenia by mechanism

Decreased production	Increased destruction	Splenic sequestration
Aplastic anemia	DIC	Portal hypertension with splenomegaly
MDS	TTP	Cirrhosis with congestive splenomegaly
Leukemia	HIT	Gaucher disease
DITP	DITP	Myelofibrosis with myeloid metaplasia and splenomegaly
ITP	ITP	Viral infections with splenomegaly

DISCUSSION:

The majority of adverse effects related to PPI administration are reported to occur after long-term administration has been given. For symptom control in patients with low grade reflux esophagitis, intermittent or on-demand administration may be effective enough[7]. Low grade reflux esophagitis, such as Los Angeles grade A or B, has repeatedly been reported not to progress to high grade reflux esophagitis or develop clinically relevant complications, including bleeding and esophageal stricture, even without intensive treatment[8]. Therefore, long-term PPI administration may be necessary for maintenance treatment mainly in patients with high grade reflux esophagitis, Los Angeles grade C or D. Patients with high grade reflux esophagitis are reported to comprise only 5–10% of all cases of reflux esophagitis. For treatment of low-grade reflux esophagitis and non-erosive GERD, long-term PPI administration should be avoided, if possible[9].

Long-term PPIs are also frequently given for prevention of NSAID- or aspirin-related ulcers. High dose NSAID/aspirin administration, elderly age, past history of ulcers, and bleeding ulcers are well known to increase the risk for ulcer recurrence[10]. Therefore, for risky cases, PPI administration for prevention of recurrence is considered to be a reasonable option. However, for patients without such risks, long-term PPI use should be avoided[11].

CONCLUSION:

It is concluded that PPIs should be among the differential diagnosis of thrombocytopenia. All the known risks of long-term PPI administration must be considered in clinical practice, though the majority of evidence presented in regard to such risks is not consistent or adequate to make firm conclusions.

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