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Potential Adverse Effects of Proton Pump Inhibitors Mimicking Other Conditions

Saumya H Mittal, Tuhina Govil[1]

Department of Medicine, HIMS College, Jolly Grant, Dehradun, Uttarakhand, [1]Department of Pediatrics, Jagrani Hospital, Lucknow, Uttar Pradesh, India

Abstract

Proton pump inhibitors, the most potent and safest acid inhibitory agents available, irreversibly bind and inhibit H^+, K^+-ATPase. They inhibit all phases of gastric acid secretion. Proton pump inhibitors are considered extremely safe and are regularly prescribed. They may, however, have side effects. They affect the clearance of other medicines. And the reactions to them may mimic other conditions and side effects of other medicines.

Key words: Adverse reactions, allergies, proton pump inhibitors, reactions, side effects

Introduction

Proton pump inhibitors, the most potent and safest acid inhibitory agents available, irreversibly bind and inhibit H^+, K^+-ATPase. They inhibit all phases of gastric acid secretion.[1]

Onset of action is rapid, with a maximum acid inhibitory effect between 2 and 6 h after administration and duration of inhibition lasting up to 72–96 h. With repeated daily dosing, progressive acid inhibitory effects are observed. These agents potently inhibit all phases of gastric acid secretion. With repeated daily dosing, progressive acid inhibitory effects are observed.[1]

The side-effect profile [Table 1] can mimic many other conditions and the side effects of the other concomitant medicines in use.

Discussion

Proton pump inhibitors are considered extremely safe and are regularly prescribed. In almost all the patients, a proton pump inhibitor is usually prescribed.

Everything we consume may contain bacteria that colonize and infect the stomach and the intestines. Gastric acid precludes infection from such ingested bacteria. Proton pump inhibitors reduce the secretion of the acid, and the patients on these antacids may therefore have raised gastric bacterial concentration. Clostridium difficile is one of the commonest organisms found to have raised concentration. Possibility of community acquired and nosocomial pneumonias are also raised.[2]

Long-term proton pump inhibitor users show raised gastrin levels (up to 1.5–2 times the normal). If the use of proton pump inhibitors is stopped, the levels return to normal in 3–4 weeks. Hypergastrinemia is associated with hyperplasia of enterochromaffin-like cells. However, risk of colon cancer has not been found to be raised. No major teratogenic effects have been noted in 1st trimester. Caution is however advised.[3]

A decreased absorption of oral cyanocobalamin may be the cause of these low levels of Vitamin B 12 in people with prolonged use of proton pump inhibitors. Similarly, an impaired bioavailability of dietary Vitamin C has also been reported.[4] Malabsorption of food-bound minerals (iron, calcium, zinc) is noted but deficiencies have not been reported.[2] It has been considered that raised risk and incidence of hip fractures may be due to calcium malabsorption secondary

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Address for correspondence: Dr. Saumya H Mittal, Department of Medicine, HIMS College, Jolly Grant, Dehradun, Uttarakhand. E-Mail: saumyamittal1@gmail.com

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Table 1: Original Work, Side Effects of Proton Pump Inhibitors

Proton pump inhibotors: Side effects	
Infections	Gastrointestinal infections like Clostridium difficile
	Pneumonia: Community acquired, nosocomial
Nutritional deficiencies	Subnormal levels of Viamin B12, Vitamin C,
	Malabsorbtion of Iron, Calcium, Zinc and fat
Gastrointestinal effects	Nausea, vomitting, constipation, diarrhoea, abdominal pain , flatulance
	Benign gastric fundal polyps, ECL hyperplasia (no colon cancer)
Hepatic effects	Hepatotoxicity and raised liver enzymes
	Cytochrome P 450 inhibition- affecting drug bioavailability like warfarin, phenytoin)
Cardiac issues	Myocardial infarction, heart failure, sudden cardiac death*
Neurological issues	Myopathy, polymyositis, rhabdomyolysis
	Arthralgia, myalgia
	Headache and fever
	Anxiety, panic attacks, episodic night terrors, confusion, attention deficit
Hematological issues	Leucopoenia, agranulocytosis, thrombocytopenia and pancytopenia
Renal issues	Interstitial nephritis, raised urea and creatinine
Dermatological issues	Toxic bullous skin lesions, exfoliative dermatitis, erythema multiforme,
	Toxic erythema, dermatomyositis, lichenoid reaction, and vitiligo
Anaphylaxis and allergies	

*FDA concluded no long term association

to proton pump inhibitor-induced acid suppression.[5] On the other hand, it is known that iron absorption needs an acidic environment. In the absence of acid production secondary to proton pump inhibitors, the iron absorption may be reduced.[1] The increased bacterial growth cause increased deconjugation of bile acids in the jejunum, thereby leading to fat malabsorption.[6]

Gastrointestinal side effects include nausea, abdominal pain, constipation, flatulence, and diarrhea. Some of these side effects, chiefly diarrhea and abdominal pain, are reported in as high as 1–5% cases. A reversible association was observed with development of small benign gastric fundal polyps.[7] Hepatotoxicity is commonly seen in patients with hepatic cirrhosis. In other patients, raised liver enzymes have been noted.[8-10]

Inhibition of hepatic cytochrome P450 may lead to increase in the half-life and therefore the bioavailability of many drugs, e.g. benzodiazepines, warfarin, and phenytoin.This inhibition was higher for earlier drugs in this group (omeprazole, lansoprazole). The newer drugs (rabeprazole, pantoprazole, and esomeprazole) interact with cytochrome P450 system significantly less.[3]

Cardiac issues have been raised intermittently about possibly increased risk of conditions like myocardial infarction, cardiac failure, and sudden cardiac death. The Food and Drug Administration, however, has concluded that association of these cardiac problems with the long-term use of proton pump inhibitors is unlikely.[11,12]

Subacute myopathy has been reported, probably by the whole group. The induction of autoimmune antibodies may be the possible mechanism. Myalgia, polymyositis, and rhabdomyolysis have been reported too. Fever and headache can occur along with myalgia. Two possible mechanisms are suspected for fever: (a) Hypersensitivity reaction and (b) effect on hypothalamic regulatory centers of body temperature.[13-17]

Many neuropsychiatric symptoms have been reported to occur in patients that resolved on stopping the drugs. These include ataxia, anxiety with panic attacks, episodic night terrors, confusion, and attention deficit.[18]

Hematological manifestations are rarely reported including one or all cell lineages-leucopoenia, agranulocytosis, thrombocytopenia, and pancytopenia.[19-21]

Dermatological manifestations are reported. These include toxic bullous skin lesions, exfoliative dermatitis, erythema multiforme, toxic erythema, dermatomyositis, lichenoid reaction, and vitiligo.[22-27]

Renal manifestations have been reported in the form of interstitial nephritis. The patients presented with variable symptoms of weight loss, malaise, fever, nausea, polyuria, and polydypsia. Patients had raised urea and/or creatinine levels.[28-30]

Some other miscellaneous reports have been found reporting anaphylactic reactions, gynecomastia (reduced after stopping medicines). In a report, intractable, dry, non-productive cough was reported.[19,29-33]

Conclusion

Proton pump inhibitors are commonly used effective medicines for acid peptic disease and gastroesophageal reflux disease. But these medicines are probably overprescribed and should be prescribed only when required. These medicines can have side effects as well.

The side-effect profile can mimic many other conditions and the side effects of the other concomitant medicines in use. This may be more important in the Intensive Care Unit setup of seriously ill patients as well where the effects of the proton pump inhibitors may cause the critical care physician to consider other illnesses and complications. The use of these medicines should therefore be planned for population that needs the medicine.

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Conflicts of interest

There are no conflicts of interest.

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