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Mini Review

Rabeprazole: The Unique PPIs

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Abstract

Rabeprazole is a proton pump inhibitor (PPI). Rabeprazole is a rapid and potent inhibitor of H^+, K^+-ATPase. Rabeprazo has many advantages over the other currently available proton pump inhibitors in terms of chemical activation rate, onse of action, degree of inhibition of gastric acid secretion, metabolism, and gastric mucus and mucin production. Current review article is undertaken to discuss these unique features.

Keywords: rabeprazole; proton pump inhibitor; unique

Introduction

Rabeprazole belongs to proton pump inhibitor that is used to treat conditions requiring a reduction of gastric acid secretion, such as erosive or ulcerative gastroesophageal reflux disease, nonerosive reflux disease, duodenal and gastric ulcers, and other pathological hypersecretory conditions, including Zollinger-Ellison syndrome. It is also used as a part of combination therapy for the eradication of H. pylori, a pathogen frequently implicated in the development of gastric and duodenal ulcers. The other PPIs that are available in market are omeprazole, lansoprazole, or pantoprazole. The aim of the current review is to provide an update on the pharmacology and clinical profile of rabeprazole. [1]

Unique pharmacological properties

Chemical Activation

Rabeprazole has the same mechanism of action as other proton pump inhibitors. All the proton pump inhibitors are substituted benzimidazole prodrugs that require an acid-induced activation. The activation rate of PPIs depends environmental pH. [2] The chemical activation rate of rabeprazole is faster than other PPIs as shown in Table 1.

Chemical activation half-lives	Rabeprazole	Pantoprazole	Omeprazole	Lansoprazole
At pH 1.2	1.3 min	4.6 min	2.8 min	2.0 min
At pH 5.1	7.2 min	282 min	84 min	90 min

Table 1: Chemical activation half-lives of PPIs

pKa

The degree of acid inhibition during the first 24 hours depends on pKa of PPIs. Rabeprazole, omeprazole, lansoprazole and pantoprazole has pKa 5.0, 4.0, 3.9 and 3.8 respectively (Figure. 1). [3] Rabeprazole compared with omeprazole, esomeprazole, lansoprazole and pantoprazole is less dependent on low pH for conversion to its active form owing to its higher pKa therefore, rabeprazole undergoes rapid activation over a wider pH range. This difference in pKa of rabeprazole accounts for the early onset of proton pump inhibition with a potent acid-inhibitor compared with the other proton pump inhibitors. [3]

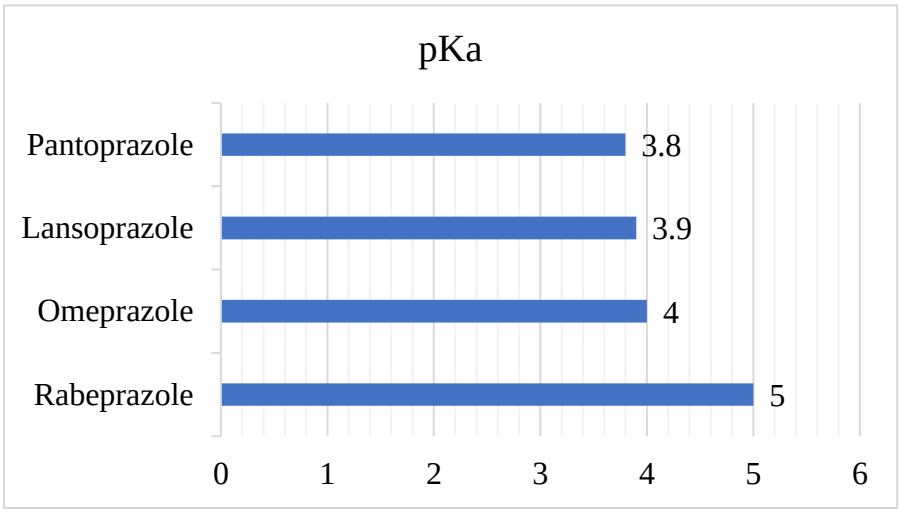

Figure 1: pKa of PPIs

Rate of inhibition of the ATPase

The rate of inhibition of the ATPase by rabeprazole was faster than other PPIs. In fact, rabeprazole inhibited the enzyme fully at 5 min. Pantoprazole, omeprazole and lansoprazole showed only 20%, 47% and 66% inhibition at 5 min, and inhibition increased to 49%, 83%, 100%, by 45 min respectively (Figure. 2). [1]

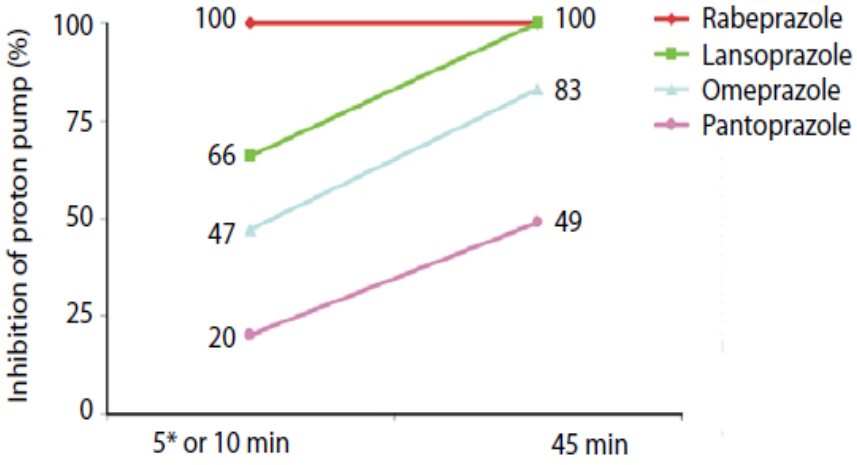

Figure 2: Rate of inhibition of the ATPase by different PPIs

Metabolism

The PPIs like omeprazole, lansoprazole, esomeprazole, and pantoprazole are extensively metabolized by CYP2C19 and CYP3A and metabolism of proton pump inhibitors could be inhibited by other drugs metabolized by these two isoenzymes. Moreover, a genetic polymorphism of CYP2C19 could be a clinical concern in the treatment of acid-related diseases with proton pump inhibitors. [1] In contrast, rabeprazole is metabolized mainly via a nonenzymatic pathway and minor involvement of CYP2C19 and CYP3A4. Therefore the acid-suppressive effect of rabeprazole is considered to be less affected by CYP2C19 genotype extensive metabolizers and poor metabolizers. Therefore, to overcome or minimize the effect of the CYP2C19 genotype, the appropriate PPIs and treatment plan should be selected according to the genotypes of CYP2C19. [2]

Mucin

Rabeprazole is the only proton pump inhibitor that enhances the content of gastric mucin. In reflux esophagitis, mucin secretion is significantly impaired. The administration of rabeprazole 20 mg QD for 8 weeks was associated with significant increases in the rate of secretion of esophageal mucin both in basal conditions (during mucosal exposure to initial saline) and following mucosal challenge with HCl/pepsin, mimicking the natural gastroesophageal reflux scenario. [2] In a double-blind placebo-controlled study rabeprazole (20 mg QD) for 7 days resulted in a significant increase in gastric mucin secretion by 167%. [3] In another double-blind placebo-controlled crossover-designed study administration of naproxen (500 mg BID) for 7 days results in significant decline of gastrin mucin production by 49%. However, coadministration, of naproxen (500 mg BID) with rabeprazole (20 mg QD) resulted in significant restoration of an impairment in mucin production by 67%.[i] Therefore, this unique pharmacological property of rabeprazole increases the production of gastric mucus and mucin, and may translate into additional clinical benefits in protecting the upper alimentary tract mucosa during acid-related challenge.

Relative Potency

All PPIs are effective for healing reflux esophagitis when given in their standard dosages but there are wide variations in the acid-suppression potency of the different PPI preparations. The potency of individual PPIs may be helpful when switching between PPIs and for assessing the cost-effectiveness of specific PPIs. Based on the mean 24-h gastric pH, the relative potencies of the five PPIs compared to omeprazole were 0.23, 0.90, 1.00, 1.60, and 1.82 for pantoprazole, lansoprazole, omeprazole, esomeprazole, and rabeprazole, respectively (Figure. 3).[ii]

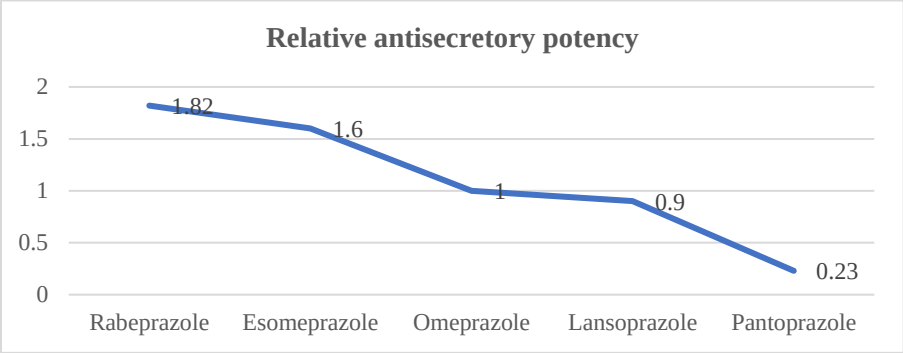

Figure 3: Relative Potency of PPIs

Conclusion

Rabeprazole has unique pharmacological & pharmacokinetics properties among the available PPIs. Rabeprazole acts by the same mechanism of action as other proton pump inhibitors with fast chemical activation rate, early onset of action, increases the production of gastric mucus and mucin and metabolism by non-enzymatic pathways. Further clinical trials must assess whether these advantages result in clinical benefit for patients of acid peptic disorders.

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