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Research Article

A REVIEW ON COMPARISON BETWEEN PANTOPRAZOLE AND RABEPRAZOLE FOR THE TREATMENT OF ACID-RELATED DISORDERS

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ABSTRACT

The prevalence of acid-related disorders is substantially increasing globally due to the changing lifestyles adopted by the people. During the previous two decades, significant progress has been made in the diagnosis and management of acid-related disorders. The initiation of proper therapy is necessary to withstand the deleterious effect of gastric acid on the mucosal lining. Among the various antisecretory drugs available, those included under the class of proton pump inhibitors have proven to be most effective in treating acid-related disorders. Pantoprazole and rabeprazole are the ones commonly advised by clinicians to curtail the excess gastric acid secretion either in gastric, duodenal ulcers, or reflux disease. Despite being similar in their mechanism of action, both drugs differ in their pharmacological and clinical properties. The high pKa value of rabeprazole enabled it to have a rapid activation rate and hence faster onset of action and quick symptom control in contrast to pantoprazole. However, the duration of action is relatively shorter for rabeprazole as it readily dissociates from the H+K+ATPase system. Further, rabeprazole maintains higher intragastric pH throughout the 24 hours post its first and subsequent single-dose administration than pantoprazole. These factors entitle rabeprazole to be more efficient than pantoprazole. Nonetheless, the clinician has to determine which drug to be selected depending on the degree and duration of acid suppression required for an individual patient.

INTRODUCTION

Acid-related disorders are common conditions with negative impacts on the quality of life of a large number of people caused by an imbalance between acid secretions by gastric parietal cells and mucosal defense mechanisms against the effects of the acid. Duodenal ulcer disease, gastric ulcer disease, gastroesophageal reflux disease (GERD), and Zollinger-Ellison syndrome are some of the acid-related disorders. The acid can damage gastric, duodenal, and esophageal mucosa leading to the occurrence of symptoms (epigastric pain, heartburn, dyspepsia, bloating, nausea, and vomiting) erosions, ulcerations, and other complications such as bleeding, esophageal cancer, and stricture formation. [1]

A network of central and peripheral mechanisms control gastric acid secretion. Parietal cells of the gut contain several proton pumps which are the enzyme (hydrogen potassium adenosine triphosphate, H+ K+ ATPase) that facilitates the exchange of intracellular hydrogen for extracellular potassium. Unless proton pumps migrate to and extend cysteine residues to the cell wall they remain inactive. When a proton pump becomes active, it pumps hydrogen ions into the secretory canaliculus where they combine with chloride ions to form hydrochloric acid, thereby creating an acidic environment. This constitutes the final step in the process of gastric acid secretion. [2]

Chronic use of aspirin or non-steroidal anti-inflammatory drugs (NSAIDs), *Helicobacter pylori* infection, stress, ischemia, and acid hypersecretion foster ulcer-like symptoms. Frequent lower esophageal sphincter (LES) relaxations, decreased LES pressure, abnormal presence of acid, pepsin, and bile acids in the distal esophagus, complicated by esophageal dysmotility, gastroparesis, and abnormal tissue factors in the esophagus are associated with GERD-like symptoms. A gastrin-secreting tumor causing gastric acid hypersecretion is the foremost factor for Zollinger-Ellison syndrome. [1]

Patients encountered with acid-related disorders secrete more gastric acid and their overall 24-hour intragastric pH may be lower compared with healthy individuals. Therefore, therapy should be focused on elevating gastric pH. [2]

Proton pump inhibitors (PPIs) are the compounds developed to control the effects of excessive acid secretion that binds the enzyme H+K+ ATPase (proton pumps) whereby inhibiting the

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final pathway to gastric acid secretion. Before the introduction of PPIs, antacids for neutralizing acid and histamine-2 receptor antagonists (H2RAs) for decreasing acid secretion were the standards of care. Details acquired throughout the last decade manifest PPIs to be the most effective therapy for long-term symptom control and alleviate acid-related disorders. Besides the degree of acid suppression, the duration of acid suppression is important. PPIs maintain intragastric pH > 4 for a prolonged period compared with H2RAs and antacids that correspond with more rapid and complete mucosal healing. [3] As all PPIs are prodrugs, they require an acidic environment to get activated. Following administration, PPIs are absorbed systemically and later secreted into the acidic environment of the canalicular space where they become ionized due to their weak basic nature and concentrated at the site of activity. The protonated (ionized) molecule changes its shape and converts to its active form- a sulfenamide with exposed sulfur atoms. The exposed sulfur atoms bind covalently to the sulfur atoms in the cysteine residues of the proton pump thereby inhibiting their ability to exchange potassium ions for hydrogen ions in the parietal cells and thus inactivating the proton pumps. [2]

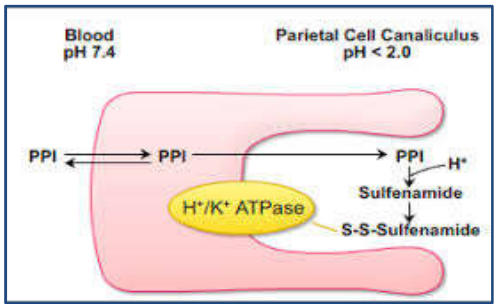

Fig 1 Mechanism of action of proton pump inhibitors

Even though all PPIs exert their effects through the same basic mechanism of action, they do not have the same pharmacological and clinical properties. They differ in their capability to control symptoms quickly and consistently. Presently accessible PPIs are omeprazole, lansoprazole, pantoprazole, esomeprazole, and rabeprazole. This review focuses on the differences between pantoprazole and rabeprazole in terms of their activation, pharmacokinetics, efficacy, safety, and pharmacoeconomics in the treatment of acid-related disorders. [2]

Both pantoprazole and rabeprazole belong to a class of antisecretory compounds that suppress gastric acid secretion by inhibiting the gastric H+K+ ATPase at the secretory surface of the gastric parietal cell and both have been proven effective in the treatment of acid-related disorders.

Activation

The reactivity or the pKa of the molecule determines the rate of acid-induced activation of an individual proton pump inhibitor. The pKa of a PPI is the pH at which half the drug becomes protonated and the other half remains unionized. Consequently, the activation rate varies depending on the pH. At a very low pH of about 1.2, the activation rates of different PPIs are very rapid and much the same. Whereas at higher pH values of about 5, the activation rates for the PPIs vary such as approximately 7 minutes for rabeprazole and 5 hours for pantoprazole. To a certain extent, this difference is correlated to the pKa of the drugs, with rabeprazole having the highest pKa of around 5.

The onsets of action of different PPIs are also associated with their pKa values. As rabeprazole has greater reactivity or higher pKa value, it is rapidly converted to the active sulfenamide derivative and shows a more quick response to the first dose than other PPIs. While pantoprazole is much more stable in an acidic environment and it's conversion to the active sulfenamide derivative is relatively slow. Furthermore, rabeprazole has the most remarkable day-1 effects because it attains about 88% of maximal acid suppression and maintains higher intragastric pH in the 24 hours following its single-dose administration compared with lansoprazole, pantoprazole, and omeprazole. [2]

Thus, rabeprazole due to its rapid rate of activation exhibits a faster onset of action and faster symptom control than other PPIs.

Mechanism of action

Structurally all PPIs are substituted benzimidazoles and share a similar mechanism of action. Once activated the protonated molecules concentrate in the secretory canaliculus of the parietal cells and form covalent disulfide bonds with surface-exposed cysteines of the active parietal cells thereby inhibiting the proton pumps. [4] Though all PPIs bind to one common specific site on the alpha subunit of the proton pump (cysteine 813 on the luminal loop between transmembrane domains 5 and 6), pantoprazole may also bind to the adjacent cysteine 822 and rabeprazole to additional sites at cysteine 892 and cysteine 321 though the clinical significance of these differences is unclear. [5]

Pharmacokinetics

Pharmacokinetic processes (absorption, distribution, metabolism, and elimination) strongly determine the concentration of a drug at its site of action. [6]

Absorption

All PPIs are formulated in an enteric coating when administered orally to protect them from rapid degradation in the stomach as the drugs are all acid-labile. Absorption of the drugs takes place rapidly in the duodenum. [5]

Distribution

All PPIs are extensively bound to serum proteins where pantoprazole and rabeprazole show about 98% and 96% of protein binding respectively. The apparent volume of distribution (Vd) of pantoprazole and rabeprazole is 0.15 l/kg and 0.34l/kg respectively. [4, 7] The absolute bioavailability of pantoprazole is 77% and that of rabeprazole is 52%.

Metabolism

All PPIs are extensively metabolized in the liver by the cytochrome P450 system, specifically by the CYP 2C19 and CYP 3A4 enzymes to varying degrees. [5, 8] CYP 2C19 has been identified with genetic polymorphisms that can significantly influence the metabolism and pharmacodynamic actions of PPIs. [6] Nevertheless, rabeprazole is less dependent on the polymorphism of CYP 2C19 as it undergoes an almost complete nonenzymatic metabolism. Hence, its antisecretory activity is more predictable and has the potential to reduce interpatient variability in both pharmacological and clinical effects as compared to that of the other PPIs, which are mainly catabolized through this enzyme. [4] Pantoprazole is also metabolized by sulphotransferase which is not part of the CYP

system and is therefore unlikely to have significant drug interactions compared with other proton pump inhibitors. [5, 8]

Elimination

About 80% of an oral or intravenous dose of pantoprazole is excreted as metabolites in urine with the remainder excreted in the feces via biliary secretion. A 20mg dose of rabeprazole is eliminated approximately by 90% in the urine and 10% in the feces. [4, 7]

Pharmacokinetic parameters

The maximal plasma drug concentration (Cmax) is considerably influenced by the rate of passage in the gastrointestinal tract, release of drug, and intraduodenal pH. [5] The Cmax of pantoprazole after a single oral dose of 40mg is 2.5mg/l. [7]. In contrast to other PPIs, the serum concentration of pantoprazole is not dose-dependent. The Cmax of rabeprazole is however proportional to the dose ingested. [4]
The area under the plasma concentration-time curve (AUC) correlates well with acid suppression, and it is significantly lower for rabeprazole 20mg (0.8 μgh/ml) or 40mg (1 μgh/ml) than for pantoprazole 20mg (2 μgh/ml) or 40mg (4.6±4.9 μgh/ml). [5]

The plasma half-lives of elimination (t ½) of all proton pump inhibitors are short and similar with approximately 1 hour and are therefore not likely to accumulate even when clearance is reduced. [5]The time (tmax) taken to reach peak plasma concentration for rabeprazole is 2.5 hours and that for pantoprazole is between 2-4 hours. [9, 10]

The irreversible covalent binding of the sulfenamide to the proton pumps (H^+K^+ ATPase) results in longer duration of acid inhibition (48±72h). However, rabeprazole has a shorter duration of action as it dissociates more readily from the H^+K^+ATPase enzyme than the other drugs. In vitro studies have revealed that pantoprazole may even have a longer duration of action than other PPIs as it is the only PPI to bind both cysteine 813 and cysteine 882 residues of the proton pump. [5]

Pantoprazole exhibits linear pharmacokinetics after both i.v and oral administration. {PK pant}The elimination half-life (t½), clearance (Cl), volume of distribution (Vd), and bioavailability are independent of the dose of drug ingested.

Special population

The pharmacokinetics of PPIs remains the same in patients with renal impairment. On the contrary, patients with hepatic impairment have witnessed a seven to nine-fold increase in the area under the plasma concentration-time curve (AUC) and a prolongation of the half-life (t½) to 4±8 hours for all proton pump inhibitors. A decrease in drug clearance and an increase in the half-life of elimination to approximately 1.5 hours are seen in the elderly population. [5] No dosage adjustment of rabeprazole is necessary for elderly, renal impairment, and mild to moderate hepatic impairment patients though an increased exposure and decreased elimination is seen post the administration of rabeprazole in patients with mild to moderate liver impairment. [9] Pantoprazole requires no dosage adjustment in patients with renal impairment, or patients undergoing hemodialysis and in patients with mild to moderate hepatic impairment. However, it shows a relative contraindication in patients with severe liver disease. [10, 11] Though no adequate and well-controlled studies have been conducted with both rabeprazole and pantoprazole in pregnant women, animal data shows certain fetal harm with rabeprazole and no impaired fertility or harm to the fetus due to pantoprazole use. Thus the pregnancy category of rabeprazole and pantoprazole is C and B respectively. [9, 10]

Table 1 Comparison of pharmacokinetic parameters of pantoprazole and rabeprazole [7, 12, 13.14, 15]

Pharmacokinetic parameters	Pantoprazole 40mg	Rabeprazole 20mg
AUC (μgh/ml)	2-5	0.8
Cmax (μg/ml)	1.1-3.3	0.4
Tmax (h)	2-4	3.1
t½ (h)	0.9-1.9	1
Cl (lh/kg)	0.08-0.13	0.50
Vd (l/kg)	0.13-0.17	0.34
Bioavailability (%)	77	52
Protein binding (%)	98	95-98
Dose linearity	Linear	Linear

AUC- area under the concentration curve; Cmax: maximum serum concentration; Tmax: time to maximum serum concentration; t½: elimination half-life; Cl: drug clearance; Vd: apparent volume of distribution

Drug interactions

Drug interactions with PPIs arise when the drugs are being metabolized through the CYP 450 system or at the absorption level when the intragastric pH determines the absorption of the affected drug. [2]

Concomitant administrations of food and antacids have shown no influence on the bioavailability of pantoprazole and rabeprazole [4, 7]. Yet the food intake delayed the absorption of rabeprazole and pantoprazole by about 2 hours or longer. [4, 9, 10]

Rabeprazole shows no significant interactions with theophylline, phenytoin, warfarin, or diazepam. However, both pantoprazole and rabeprazole may interfere with the absorption of drugs where gastric pH is an important determinant of their bioavailability (eg: ketoconazole, iron salts). Concurrent administration of diazepam, digoxin, diclofenac, glyburide, nifedipine, phenytoin, or theophylline show no alteration in the pharmacokinetic variables of pantoprazole.[16] Concomitant use of atazanavir with PPIs result in decreased atazanavir plasma concentrations and thereby reduce its therapeutic effect. Even though no formal drug interaction studies of methotrexate with PPIs have been conducted, case reports and retrospective analyses suggest that concomitant administration of PPIs and methotrexate (primarily at high dose) may elevate and prolong serum levels of methotrexate. [9, 10]

Dose-response relationships

The dose-response relationships exhibit a rectilinear manner up to a near-maximal acid inhibitory effect. A range of 60-90% acid inhibition is achieved by the doses currently used in clinical practice reflecting that the values often fall on the rectilinear part of the dose-response curve. Likewise, pantoprazole displays higher healing rates with doses from 10 to 40mg. [17] A study by Kromer et al for analyzing the dose-response relationships in the treatment of GERD, duodenal as well as gastric peptic ulcer using pantoprazole and omeprazole has shown higher healing rates with 40mg than with 20mg.[18] In another study by Dekkers et al, rabeprazole 20mg inhibits acid secretion in both peptic ulcer and reflux disease as effectively as omeprazole 20mg.[19] In the maintenance

treatment of GERD, 20mg of pantoprazole is considered sufficient although studies are showing that a dose of 10mg may be as effective. [20] Data obtained from various studies revealed that a dosage of 30-40mg of PPIs is optimal for the treatment of active ulcer disease as well as moderate to severe GERD. For mild symptomatic GERD or in maintenance treatment after the healing of erosive esophagitis, a daily dosage of 15-20mg seems adequate. The eradication of H.pylori requires a two-dosage regimen of PPIs in combination with antibiotics. In the clinical setting, all PPIs appear to have similar potential and inherent capacity to inhibit acid secretion. Nonetheless, the clinician has to decide what degree of acid inhibition he aims for in the individual patient and also need to select proper drug with an appropriate dose. [17]

Table 2 Standard therapeutic regimen for the treatment of acid related disorders [8, 9, 10, 21]

Indication	Pantoprazole	Rabeprazole
Erosive or ulcerative GERD	40mg PO (per oral) once daily for up to 8 weeks.	20mg PO once daily for 4-8 weeks.
Symptomatic GERD	40mg PO once daily for up to 8 weeks or 40mg IV infusion over 15mints daily for 7-10 days; switch to PO once patient able to swallow.	20mg PO once daily for 4 weeks.
Maintenance of healing of erosive esophagitis	40mg PO once daily.	20mg PO once daily.
Duodenal ulcer	40mg PO once daily for 2 weeks.	20mg PO once daily after morning meal for up to 4 weeks.
Zollinger-Ellison syndrome	40mg PO twice daily or 80mg IV infusion every 8-12 hours up to 7 days; switch to PO once patient able to swallow.	Starting dose 60mg PO once daily then adjust to patient needs.
H.pylori eradication	40mg PO twice daily for 7 days with morning and evening meals; take with amoxicillin 1000mg and clarithromycin 500mg twice daily.	20mg PO twice daily for 7 days with morning and evening meals; take with amoxicillin 1g twice daily and clarithromycin 500mg twice daily.

Efficacy

The healing rates attained by all PPIs in the treatment of acid-related disorders (GERD or peptic ulcer disease) are essentially the same. It is hard to find any clinically significant differences between PPIs in most patients as about 90% of healing rates are seen with these drugs. However, differences are noticeable in measures of efficacy on antisecretory activity and maintenance of higher intragastric pH for a longer period. [3]

In a cross-over, double-blind, randomized study conducted in 18 H.pylori-negative subjects, rabeprazole 20mg could reach a median 24-hour gastric pH of 3.4, compared with 2.9 for lansoprazole 30mg, 2.2 for pantoprazole 40mg, 1.9 for omeprazole capsule 20mg, 1.8 for omeprazole 20mg MUPS (multiple unit pellet system) and 1.3 for placebo post the first day of dosing. Moreover, rabeprazole maintained pH > 4 for more time (8 hours) than the other agents (7.4, 4.9, 2.9, 3.0, and 0.9 hours respectively). The results even showed that day-time and night-time pH values were higher with rabeprazole and lansoprazole than with pantoprazole, omeprazole capsule, and omeprazole MUPS tablet. Hence, rabeprazole achieved rapid and consistent acid suppression on the first day of dosing compared with other PPIs in treating acid-related disorders. [4, 22]

Similarly, a double-blind, double-dummy, two-way crossover study performed in 38 H.pylori-negative volunteers, randomized to oral rabeprazole 20mg or intravenous pantoprazole 40mg daily for 3 days after a 14-day washout period by the comparator treatment exhibited that rabeprazole has attained higher mean percentage of intragastric pH> 4 (37.7%) for 24 hours along with greater mean percentage time compared with pantoprazole (23.9%) on days 1 and 3. Therefore, oral rabeprazole 20mg produced greater acid suppression than intravenous pantoprazole 40mg and suggested to be an effective alternative in patients who can take oral medication. [23]

The degree of acid suppression, the duration of acid suppression within the 24 hours, and the duration of treatment predict the efficacy of antisecretory drugs in healing peptic ulcer disease and GERD. {0019} An open-label, randomized, two-way crossover study carried out with twenty-nine H.pylori negative GERD patients with a history of nocturnal heartburn has shown that the patients who had received a single dose of rabeprazole 20mg achieved a higher mean area under the intragastric pH-time curve (AUC) at all time intervals including night than those who had received pantoprazole 40mg with a 14-day washout period. Even the mean percentage time with pH >3 and > 4 was significantly more after dosing with rabeprazole than with pantoprazole at all time intervals. [24]

Nocturnal reflux has arisen as major trouble leading to multiple esophageal complications due to its undiagnosed and unmanaged condition. During recent years, many researchers analyzed the development of nocturnal gastric acid breakthrough (NAB) in GERD patients with nocturnal reflux symptoms. Nocturnal acid breakthrough (NAB) has been defined as the occurrence of intragastric pH falling to below 4 for at least 1 hour during the 12 hours of night sleeping period. In a study, forty patients with active peptic ulcer disease randomly received a single oral dose of rabeprazole 10mg, omeprazole 20mg, and pantoprazole 40mg where the intragastric pH was monitored 1 hour before and 24 hours after the dose was given. The pH of NAB was statistically higher in the rabeprazole group than the one in the others (1.84, 1.15 and 1.10 with rabeprazole, omeprazole, and pantoprazole respectively). Further, rabeprazole exhibited a longer time (4.65 hours) of nocturnal alkaline amplitude (NAKA) than omeprazole (3.22 hours) and pantoprazole (3.15 hours). [25]

One more similar study of double-blinded, randomized, and two-way crossover design evaluated the effects of rabeprazole and pantoprazole on nocturnal intragastric pH and gastric acid output during day 1 of therapy after the consumption of standard meals. The study involved 15 patients with a history of mild reflux and was given either rabeprazole 20mg or pantoprazole 40mg before the first of three standard meals; intragastric pH and gastric acid output were measured continuously overnight. The results revealed that the percentage of time during which the mean intragastric pH was greater than 4.0 and gastric acid output was less than 2.0 was higher for oral rabeprazole than for pantoprazole. Thus on day 1 of therapy, oral rabeprazole maintained higher intragastric pH and inhibited acid output to a greater extent as well as for a longer period than pantoprazole. [26]

The role of PPIs in the eradication of H.pylori infection along with antibiotics is significant even though their synergistic effect is unknown. The enzymatic activity of urease is

necessary for H.pylori to survive the acidic pH conditions in the human stomach, so inhibition of this enzyme may explain the antibacterial effect of PPIs. [27] Moreover, coadministration of a PPI with antibiotics makes the latter more stable and increases their effectiveness in eradicating H.pylori. PPI maintains higher intragastric pH and provides a favorable environment for antibiotics to exert their effects. Rabeprazole has a more rapid onset of antisecretory action compared with other drugs in its class and its effectiveness in combination therapy for H.pylori eradication is not strongly determined by the CYP 2C19 genetic polymorphism. [6]Further, data from a large-scale trial conducted in the United States recommended that a 7-day rabeprazole based regimen is as effective as 10-day rabeprazole and omeprazole based therapies for H.pylori eradication. [28]

Safety

All PPIs have been associated with some common adverse effects such as headache, diarrhea, rash, nausea, and constipation with incidences of 1±3 %. Slight increases in aspartate transaminase (AST) and alanine transaminase (ALT) have also been reported. The withdrawal rate due to adverse effects was 1±2 % in most studies. These agents differ significantly in their risk for pharmacokinetic interactions that may result in important toxicities. Adverse drug interactions occur either from induction (loss of therapeutic benefit) or inhibition (increased toxicity from excessive effect) of drug elimination. Generally, the risk for adverse events resulting from drug interactions was more for patients taking a PPI and warfarin, clarithromycin, corticosteroids, carbamazepine, nifedipine, or diclofenac. [6] However, long-term daily use (> 3years) of PPIs may lead to malabsorption or a deficiency of cyanocobalamin and also may be associated with an increased risk for osteoporosis-related fractures of the hip, wrist, or spine. Infrequent cases of hypomagnesemia have been reported with prolonged treatment with PPIs.

Adverse reactions of rabeprazole that occurred at a rate greater than 2% and greater than placebo included pain, pharyngitis, flatulence, infection, and constipation. [9] Numerous studies have extensively shown that rabeprazole has a very low risk for pharmacokinetic interactions that might result from CYP induction or inhibition. [6]

Adverse reactions of pantoprazole that occurred at a rate greater than 2% and greater than placebo are headache, diarrhea, nausea, abdominal pain, vomiting, flatulence, dizziness, and arthralgia. [10] Thrombocytopenia and acute interstitial nephritis associated with pantoprazole use have been outlined in isolated case reports. Headache, nausea, dizziness, flushing, and pain at the site of infection are some of the adverse effects reported in patients who received i.v pantoprazole. [11]

Pharmacoeconomics

Acid-related disorders specifically GERD require long-term maintenance therapy which imposes a great economic burden on affected individuals. Therefore, the choice of treatment has long-term cost implications. A treatment model to compare the costs and effectiveness of treatment of GERD (unconfirmed by endoscopy) with seven available PPIs (esomeprazole, lansoprazole capsules, and oro-dispersible tablets, omeprazole both generic and branded, pantoprazole and rabeprazole) was developed. [29] Generic omeprazole and rabeprazole has less cost with higher quality-adjusted life years (QALY) gains and resulted in more symptom-free days than the other PPIs. Nevertheless, rabeprazole exhibited a beneficial cost-effectiveness ratio of £3.42 per symptom-free day and £8308 per QALY gained when compared with generic omeprazole. In another similar model done in the UK for endoscopy confirmed NERD (Non-erosive reflux disease) patients, the base-case annual median costs and utilities gained with on-demand PPI therapy were lowest for rabeprazole 10mg (123 euro and 0.89), followed by pantoprazole 20mg (176 euro and 0.90), esomeprazole 20mg (190 euro and 0.89), lansoprazole 15mg (195 euro and 0.91), omeprazole 20mg (201 euro and 0.90), and omeprazole 10mg (210 euro and 0.91). [30]

CONCLUSION

Acid-related disorders have adversely affected the quality of life of individuals across the globe. Though many treatment strategies have been developed over the past several years, proton pump inhibitors (PPIs) have shown remarkable outcomes in the suppression of gastric acid secretion. Various studies have demonstrated the superior effects of proton pump inhibitors over H2 receptor antagonists and antacids. However, among proton pump inhibitors there exist slight differences in healing rates of acid-related disorders. Rabeprazole has a rapid activation rate due to its high pKa value compared to other PPIs. This unique pharmacodynamic property enables rabeprazole to exert faster onset of action and hence faster symptom control. Further, rabeprazole maintains higher intragastric pH and accomplish maximal acid suppression in the 24 hours following its single-dose administration compared with lansoprazole, pantoprazole, and omeprazole. However, rabeprazole has a short duration of action compared to pantoprazole because of its rapid dissociation from the proton pumps. Both pantoprazole and rabeprazole show linear pharmacokinetics and that remain unaltered in renal impaired patients, even though certain changes occur in liver disease patients. Rabeprazole appears to be more efficient in the management of acid-related disorders than pantoprazole due to its rapid onset of action and maintenance of higher intragastric pH. Apart from a few minor adverse effects both rabeprazole and pantoprazole are safer to use extensively in acid-related disorders. Rabeprazole has proven to be low-priced with higher quality adjusted life years gained than other PPIs in some treatment models. However, yet more studies on the comparison between pantoprazole and rabeprazole should be conducted to have a wider understanding of their differences.

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