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Review Article

A REVIEW ON PROTON PUMP INHIBITOR FOR THE TREATMENT OF PEPTIC ULCER

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ABSTRACT

Ulcers are sores or open wounds that occur on the skin or along the lining of the digestive tract due to loss of tissue. Peptic ulcers are craters or open sores in the lining of the upper gastro intestinal tract. Occurs due to imbalance between defenses and aggressive factors. ***Proton-pump inhibitors*** *(**PPIs**) are a group of drugs whose main action is a pronounced and long-lasting reduction of gastric acid production. it act by irreversibly blocking the hydrogen/potassium adenosine triphosphatase enzyme system (the H^+/K^+ ATPase, or more commonly gastric proton pump) of the gastric parietal cells. The proton pump is the terminal stage in gastric acid secretion, being directly responsible for secreting H^+ ions into the gastric lumen, making it an ideal target for inhibiting acid secretion.*

Key wards: *Peptic ulcer, Proton-pump inhibitors, Omeprazole.*

INTRODUCTION

Peptic ulcers are craters or open sores in the lining of the upper gastro intestinal tract. They include duodenal ulcers (those that are located in the top of the small intestine or duodenum) and gastric ulcers (those found in the stomach). Peptic ulcers are common and usually occur singly. But it is possible to have two or more, or even both duodenal and gastric ulcers at the same time. Duodenal ulcers are more common than Gastric ulcer. [1]

TYPES OF ULCER

Lesions in the inner lining of the stomach, duodenum, and mouth are the most common types of ulcerations. Besides these, there are ulcers in other parts of the body that may be caused due to mineral deficiency and other reasons.

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Ulcers are sores or open wounds that occur on the skin or along the lining of the digestive tract due to loss of tissue. The digestive tract includes the esophagus, stomach, duodenum, and the intestines. The different ulcers are classified according to their location along the digestive tract. Peptic ulcers are the most common type of ulcers that include sores that occur in the stomach, esophagus, and duodenum (beginning of the intestine). There are other types like bedsores, genital and mouth ulcers.

Peptic Ulcers:

It is a broad term which includes sores of digestive tract in the stomach or the duodenum. Earlier it was believed that one developed these types of sores due to stress and spicy food. However, recent research has shown that these are just the aggravating factors. The causative agent is infection caused by the bacteria H. pylori or reaction to certain medicines like non-steroidal anti-inflammatory drugs (NSAIDs). The symptoms include

abdominal discomfort and pain 2-3 hours after one has taken a meal or when on empty stomach. Other symptoms include weight loss, poor appetite, bloating, nausea, and vomiting. Some may also experience blood in stool and vomit, and black stools that indicate gastrointestinal bleeding. Ulcers of the duodenum are called duodenal ulcers, whereas those in the stomach are called stomach or gastric ulcers.

Mouth Ulcers:

Sores that develop in the inner lining of the mouth are referred to as mouth ulcers. Anemia, measles, viral infection, oral candidiasis, chronic infections, throat cancer, mouth cancer and vitamin B deficiency are some of the common causes of sores in the mouth. These mouth sores are round or oval in shape and white, yellow or gray in color. They are inflamed around the edge and commonly occur on the inner lining of the lips, cheeks, floor of the mouth and the underside of the tongue. They cause pain and discomfort usually during drinking or eating. These are usually cured within 10-14 days. However, in severe cases it may take several weeks for these to heal completely.

Esophageal Ulcers:

They are lesions that occur in the esophagus (the food pipe). These are most commonly formed at the end of the food pipe and can be felt as a pain right below the breastbone, in the same area where symptoms of heartburn are felt. They are associated with acid reflux or GERD, prolonged use of drugs like NSAIDs, and smoking.

Pressure Sores:

These lesions are caused in patients who are confined to bed due to some debilitating illness or are on their way to recovery in hospital. In medical terms, these are called decubitus ulcers. Alternatively bedsores are also called pressure sores as they are caused due to pressure being exerted on skin for long periods. In the initial stages a bedsore manifests itself as a persistent area of red skin that hurts and feels warm. It may also be accompanied with itching. As the severity increases there is loss of the upper layer of skin and subsequent damage to the underlying tissue. These occur on parts like back, hips, shoulders and buttocks that are in contact with the bed as one lies down.

Genital Ulcers:

They are caused due to sexually transmitted diseases like syphilis, genital herpes, or thrush. Non-sexual causes of genital ulcers are infections caused by yeast, scabies, pyoderma, genital trauma and Behcet's disease. They manifest as single or multiple ulcers which are mostly painful. They may also be associated with rashes and itching. [2]

CAUSES OF PEPTIC ULCER

Peptic ulcers are caused by acid and pepsin (an enzyme) produced in the stomach. Patients who develop ulcers often produce greater amount of acid than people without ulcers. Also, the ulcer patient May not have strong enough natural defenses in the stomach or Intestinal wall to resist the effect of acid and pepsin and in 90% of cases it is caused by gram negative bacteria H.pylori.

"Doctors do not yet know all the reasons too much acid is produced, but many believe the key to healing an ulcer is to control the amount of acid produced". Or Imbalance between defenses and aggressive factors. [3]

Defensive factors:

- Mucus: continually secreted, protective effect.
- Bicarbonate: secreted from endothelial cells.
- Blood flow: good blood flow maintains mucosal integrity.
- Prostaglandins: stimulate secretion of bicarbonate and mucus, promote blood flow, and suppress secretion of gastric acid.

Aggressive factors:

- Helicobacter pylori: gram negative bacteria can live in stomach and duodenum, May breakdown mucus layer, inflammatory response to presence of the bacteria also produces urease forms CO_2 and ammonia which are toxic to mucosa.
- Gastric Acid: needs to be present for ulcer to form, activates pepsin and injures

mucosa.

- Decreased blood flow: causes decrease in mucus production and bicarbonate synthesis,promote gastric acid secretion.
- NSAIDS: inhibit the production of prostaglandins.
- Smoking: nicotine stimulates gastric acid production.[4]

CELLS OF THE GASTRIC GLAND:

Parietal cells- Produce and secrete HCl

Chief cells

- Secrete pepsinogen, a proenzyme.
- Pepsinogen becomes pepsin when activated by exposure to acid.
- Pepsin breaks down proteins (proteolytic Primary site of action for many acid-controller drugs.

Mucoid cells

- Mucus-secreting cells (surface epithelial cells).
- Provide a protective mucous coat.
- Protect against self-digestion by HCl.

Hydrochloric Acid:

- It mainly secreted by the parietal cells when stimulated by food.
- Maintains stomach at pH of 1 to 4.

Secretion also stimulated by:

- Large fatty meals.
- Excessive amounts of alcohol.
- Emotional stress.

CLINICAL MANIFESTATIONS

- Many people have symptomless ulcers.
- In 20% to 30% hemorrhage may occur.
- Pain stimulates the exposed nerve endings.
- 1-Pain is usually relieved by eating or by taking alkali or by taking antacid.
- Burning sensation in the midepigastrium.
- Pyrosis (heartburn).
- Vomiting.
- Constipation or diarrhea (Diet and medications).
- Bleeding 15% patients. [5]

SIGNS AND SYMPTOMS

Symptoms of a peptic ulcer can be:

- Abdominal pain, classically epigastric with severity relating to mealtimes, after around three hours of taking a meal (duodenal ulcers are classically relieved by food, while gastric ulcers are exacerbated by it).
- Bloating and abdominal fullness.
- Water brash (rush of saliva after an episode of regurgitation to dilute the acid in esophagus - although this is more associated with gastro esophageal reflux disease).
- Nausea and copious vomiting.
- Loss of appetite and weight loss.
- Hematemesis (vomiting of blood), this can occur due to bleeding directly from a gastric ulcer, or from damage to the esophagus from severe/continuing vomiting.
- Melena (tarry, foul-smelling feces due to oxidized iron from hemoglobin).
- Rarely, an ulcer can lead to a gastric or duodenal perforation, which leads to acute peritonitis. This is extremely painful and requires immediate surgery. [5,6]

ASSESSMENT AND DIAGNOSTIC FINDING

- Physical examination may reveal pain, epigastric tenderness, and abdominal distention.
- Endoscopy is the preferred diagnostic procedure. Because it:
- Allows direct visualization of inflammatory changes, ulcers, and lesion.
- It may reveal lesions that are not evident on x-ray studies because of their size or location. Stools may be tested for occult blood.
- H. pylori infection may be determined by biopsy and histology with culture.
- Serologic test for antibodies to the H. pylori antigen.
- Breathe test that detects H. pylori. [5]

TREATMENT OF PEPTIC ULCER DISEASE

Medications **-** medications that decrease the amount of acid produced by the stomach are used to provide quick pain relief and promote rapid healing.

- Other equally effective medications, such as coating agents called carafate, antacids, and one called Omeprazole, are available.

- Most peptic ulcers heal within 4 to 6 weeks of treatment. Take your medications regularly as directed, otherwise your ulcer may not heal completely and your symptoms could return. Symptoms may disappear in a few days, but DO NOT STOP taking your medication.
- Nighttime is the most important time to heal ulcers, since many people produce large amounts of stomach acid while they sleep.
- Take antacids as needed between meals and at bedtime to neutralize stomach acid and reduce pain.
- Aspirin and anti-inflammatory products should be avoided. Let your doctor know if you have been taking these, so alternate medications may be prescribed.
- Side effects from the medication used to treat peptic ulcer disease are very infrequent (less than 5percent), but many include mild diarrhea, dizziness, nausea, drowsiness, rash or headache.
- Remember, people are different and no single medicine is best for everyone. If your symptoms worsen, notify your doctor immediately.[5]

NATURAL THERAPY FOR ULCER RELIEF

There are many herbs, nutrients, and plant products that have been found to play a role in Protecting or helping to heal stomach and peptic ulcers. Some of the common examples are:

- ***Probiotics*** such as those found in yogurt Probiotics are friendly bacteria such as Acidophilus, Lactobacillus and Bifido bacterium.
- ***Aloe Vera herb*** may help with gastric ulcer healing.
- ***Artichoke leaf*** extract has been tested in rodents as a beneficial supplement to reduce gastritis.
- ***Prickly pear fruit,*** also known as cactus pear, grows on nopal or cactus leaf.
- ***Amla*** is used in Ayurvedic medicine. You can find amla research below on its influence on ulcer.
- ***Asparagus*** extract has been studied for ulcer prevention.

PEPTIC ULCER DIET

- Along with medical treatment for peptic ulcer, you need to follow a diet that assists your body to some symptoms of indigestion.
- Following are some peptic ulcer diet 'do and don't' guidelines.
- Do not eat foods in bulk. They add an extra workload on your digestive system. Try to eat 5-6 times a day and keep the amount of food small. This will avoid the periods of hunger and will also curb overeating.
- Rest and relax, both before and after every meal. Try to eat slowly and chew the food well. This will ease their digestion.
- Include a rich source of protein at each meal. Such foodstuffs can be milk, eggs, meat and cheese.
- Do not eat anything at least three hours before bedtime.
- Avoid foods that are fried and spicy. Also, decrease the intake amount of caffeine containing drinks, like coffee and tea.
- Do not take carbonated drinks, chocolate and tomato based products, as they work towards increasing acidity.
- Quit smoking and cut down on the consumption of alcohol.
- Take the antacids as recommended by the doctor. Generally, they are taken 1-3 hours after every meal and prior to bedtime.
- Avoid magnesium containing antacids as they may cause diarrhea. [7,8]

PEPTIC ULCER DIET: FOODS

Cereals: Whole grain cereals are mostly safe to eat with peptic ulcer. Generally, whole-grain, seedless breads, tortillas, bagels, English muffins and hot dog buns form a part of the diet for peptic ulcer. You may also take enriched rice, noodles, pastas and spaghetti macaroni without any discomfort. You may have French toasts, pancakes, muffins and waffles with low fat content once a while. Their increased amount may cause some uneasiness. Very coarse cereals such as bran, wild rice, breads with seeds and bread products with nuts and dried fruits are not meant to be included in the diet for peptic ulcer disease.

Fruits: 2-3 daily servings of fresh, frozen and canned fruits are tolerated to some extent. Fruits like papaya, watermelon and apples can be eaten on a regular basis. Citrus fruits such as grapes, pineapples, oranges and tangerines are not advisable for patients with peptic ulcer, as they increase acidity and thus further worsen the condition.

Vegetables: 3-4 daily servings of fresh, canned and frozen vegetables except tomato can be taken without much concern. If you feel some discomfort with the intake of a particular vegetable, omit that from you peptic ulcer diet. Some vegetables are gas forming in nature. Hence, they are not included in this diet. A few examples of such vegetables are cabbage, broccoli, Brussels sprouts, onion, cauliflower, cucumber and sauerkraut.

Dairy Products: Milk causes a neutralization effect during the initial hours of its intake. Therefore, it is good for patients with peptic ulcers. Various dairy products like plain mild cheese, low fat cottage cheese and no fat yogurt are recommended for intake. Certain flavors of milk and its products are a big no-no, in diet for peptic ulcer. These are chocolate milk, buttermilk, evaporated whole milk and cream and strong flavored cheese.

Meat and its Substitutes: All lean, tender pork, beef, lamb and poultry without the skin can be taken safely. Even fresh, canned and frozen fish packed in water are considered safe for consumption. 3-5 egg yolks can be taken a week. Highly seasoned and heavily marbled meat, poultry and fish are not meant to be included in peptic ulcer diet. [7,8]

PROTON PUMP INHIBITORS

Proton-pump inhibitors (**PPIs**) are a group of drugs whose main action is a pronounced and long-lasting reduction of gastric acid production. They are the most potent inhibitors of acid secretion available today. The group followed and has largely superseded another group of pharmaceuticals with similar effects, but different mode-of-action, called H_2-receptor antagonists. These drugs are among the most widely-selling drugs in the world and are generally considered effective. The vast majority of these drugs are benzimidazole derivatives; however, promising new research indicates that imidazopyridine derivatives may be a more effective means of treatment. High dose or long-term use of PPIs carries a possible increased risk of bone fractures. [3,5]

DRUGS USED AS PROTON PUMP INHIBITOR

Omeprazole (Brand names: Gasec, Losec, Prilosec, Zegerid, ocid, Lomac, Omepral, Omez).

Lansoprazole (Brand names: Prevacid, Zoton, Monolitum, Inhibitol, Levant, Lupizole)

Dexlansoprazole (Brand name: Kapidex, Dexilant).

Esomeprazole (Brand names: Nexium, Esotrex, esso).

Pantoprazole (Brand names: Protonix, Somac, Pantoloc, Pantozol, Zurcal, Zentro, Pan, Controloc).

Rabeprazole (Brand names: AcipHex, Pariet, Erraz, Zechin, Rabecid, Nzole-D, Rabeloc, Razo. Dorafem: combination with domperidone).

Ilaprazole (Brand names: Ilapro, Lupilla, Adiza). [6,9]

PROTON PUMP INHIBITOR PHARMACOKINETICS

Proton pump inhibitors are prodrugs that require activation in an acid environment.

- Oral forms are prepared as acid resistant formulations that release the drug in the intestine (because they are degraded in acid media).
- After absorption, they are distributed by blood to parietal cells.
- They irreversibly inactivate the proton pump molecule (providing 24 to 48 hour suppression of

acid secretion, despite the much shorter plasma half-lives of the parent compounds.

- They should be given on an empty stomach because food affects absorption.
- They should be given 30 minutes to 1 hour before food intake because an acidic pH in the parietal

cell acid canaliculi is required for drug activation, and food stimulates acid production.

- Maximal effect is reached after 3 to 4 days

of administration (the time required to fully inactivate the proton pumps).

- Their effects persist for 3 to 4 days after stopping the drug (the time required for full recovery of the proton pumps).
- Metabolized by the liver (dose reduction is necessary in severe liver impairment).
- Minimal excretion by the kidney (no dose reduction is necessary in renal impairment). [10]

PHARMACODYNAMICS OF PPIS

While the pharmacokinetics describes what the body does to the drug, the pharmacodynamics (PD) explore what a drug does to the body. PPIs in the systemic circulation are available for binding to the gastric H+/K+-ATPase of the proton pumps. This results in inhibition of the acid secretion, followed by elevation of the intragastric pH. pH metry is the most frequently applied method to study the efficacy of acid-inhibitory drugs continuously. pH metry is a technique that measures the pH by a probe placed in the esophagus or stomach. This technique is shown to be suitable for detection of small changes in pH, especially when the probe is placed in the stomach (10 cm below the lower oesophageal sphincter). pH metry obtains a profile of intragastric pH over a 24-hour time period. Intragastric pH is measured by a miniature glass or antimony electrode connected to a portable data logger with a sampling rate of 4 per second. Every two seconds, the median of 8 voltage measurements is calculated and stored. Data analysis is based on median pH values over 6 seconds. [11]

Mechanism of action

Proton pump inhibitors act by irreversibly blocking the hydrogen/potassium adenosine triphosphatase enzyme system (the H^+/K^+ ATPase, or more commonly gastric proton pump) of the gastric parietal cells. The proton pump is the terminal stage in gastric acid secretion, being directly responsible for secreting H^+ ions into the gastric lumen, making it an ideal target for inhibiting acid secretion.

Targeting the terminal step in acid production, as well as the irreversible nature of the inhibition, results in a class of drugs that are significantly more effective than H_2 antagonists and reduce gastric acid secretion by up to 99%. ("Irreversibility" refers to the effect on a single copy of the enzyme; the effect on the overall human digestive system is reversible, as the enzymes are naturally destroyed and replaced with new copies). The lack of the acid in the stomach will aid in the healing of duodenal ulcers, and reduces the pain from indigestion and heartburn, which can be exacerbated by stomach acid. However, lack of stomach acid is also called hypochlorhydria, the lack of sufficient hydrochloric acid, or HCl. Hydrochloric acid is required for the digestion of proteins and for the absorption of nutrients, particularly of vitamin B_{12} and of calcium.

The proton pump inhibitors are given in an inactive form. The inactive form is neutrally charged (lipophilic) and readily crosses cell membranes into intracellular compartments (like the parietal cell canaliculus) that have acidic environments. In an acid environment, the inactive drug is protonated and rearranges into its active form. As described above, the active form will covalently and irreversibly bind to the gastric proton pump, deactivating it. [3,10]

THERAPEUTIC USES OF PROTON PUMP INHIBITORS

- Gastro esophageal reflux disease (GERD).
- Gastric and duodenal ulcers.
- Prevention of recurrence of nonsteroidal anti-inflammatory drug (NSAID)-associated gastric ulcers in patients who continue NSAID use.
- Reducing the risk of duodenal ulcer recurrence associated with H. pylori infections.[5,6]

DRUG INTERACTIONS

The elevation of gastric pH induced by the PPIs can affect the absorption of a number of medications. However, this antisecretory action rarely has clinically important effects on drug

pharmacokinetics, except when the PPIs are given with ketoconazole or digoxin. Ketoconazole requires stomach acid for absorption, and this drug may not be absorbed effectively after PPIs have inhibited gastric

acid secretion. Conversely, an elevated gastric pH facilitates the absorption
of digoxin, resulting in higher plasma levels of this agent. If a patient requires both PPI and antifungal therapy, it is recommended that an agent other than ketoconazole be chosen. For patients treated concomitantly with PPIs and digoxin, clinicians should consider monitoring plasma digoxin levels. Because the PPIs are metabolized by the CYP system, there is potential for them to alter the metabolism of other drugs that are eliminated by CYP enzymes. Among the available PPIs, Omeprazole appears to have the greatest potential for such drug interactions and has been shown to delay the clearance of Warfarin, diazepam, and phenytoin. Lansoprazole, Pantoprazole, and Rabeprazole do not appear to interact significantly with drugs metabolized by the CYP system. Even with Omeprazole, however, clinically important drug interactions are uncommon. [3, 12]

IMPACT OF PROTON PUMP INHIBITOR–INDUCED HYPERGASTRINEMIA

PPIs and other antisecretory agents cause Hypergastrinemia by inhibiting gastric acid secretion. The rise in serum gastrin levels is usually modest. The elevated gastrin values return to normal Within 4 weeks after PPI therapy is discontinued. In addition to stimulating acid secretion, gastrin has been shown to have trophic effects on the gastrointestinal (GI) mucosa. In the stomach, these trophic effects are manifested predominantly in the ECL cells. Female rats in which protracted Hypergastrinemia has been induced by treatment with PPIs also have ECL cell hyperplasia and gastric carcinoid tumors. However, there are no reports of gastric carcinoid tumors attributable to Antisecretory therapy in humans. Even in patients with Zollinger-Ellison syndrome who have Severe Hypergastrinemia, carcinoid tumors are uncommon and occur predominantly in patients With multiple endocrine neoplasia (MEN). [13]

TOLERANCE AND REBOUND ACID HYPER SECRETION

Tolerance to the antisecretory effects of PPI therapy has not been seen during short-term Investigations. Rebound acid hyper secretion after PPI therapy has been shown for both basal and maximal acid output by 14 days after cessation of treatment. Rebound hyper secretion is found in H. pylori–negative, but not H. pylori–positive, subjects, possibly owing to the influence of the enhanced oxyntic gastritis that occurs during PPI therapy. The phenomenon can persist for at least 2 months after prolonged treatment. It has been suggested that PPI-induced Hypergastrinemia exerts trophic effects on the oxyntic mucosa. The clinical relevance of this phenomenon remains unknown. [14]

OMEPRAZOLE

Omeprazole (Prilosec and generics) is a proton pump inhibitor used in the treatment of dyspepsia, peptic ulcer disease (PUD), and gastro esophageal reflux disease (GORD/GERD), and laryngopharyngeal reflux (LPR) and Zollinger–Ellison syndrome. Omeprazole is one of the most widely prescribed drugs internationally and is available over the counter in the countries.

Clinical data

Legal status - Prescription only, Routes - oral, i.v.

Pharmacokinetic data

Bioavailabiability - 35 – 76%, Protein binding - 95%, Metabolism – hepatic, Half life – 1 to 1.2 hours, Excretion - 80% Renal and 20% Faeces.

Medical Uses:

- As Proton pump inhibitor
- Used to treat GERD (gastro esophageal reflux disease), gastric and duodenum ulceration and gastritis.
- Use in Helicobacter pylori eradication

Omeprazole is combined with the antibiotics clarithromycin and amoxicillin (or metronidazole in penicillin-hypersensitive patients) in the 7–14 day eradication triple therapy for Helicobacter pylori. Infection by

H. pylori is the causative factor in the majority of peptic ulcers.

Mechanism of action:

Omeprazole is a proton pump inhibitor that suppresses gastric acid secretion by specific inhibition of the H+/K+-ATPase in the gastric parietal cell. By acting specifically on the proton pump, Omeprazole blocks the final step in acid production, thus reducing gastric acidity.

Adverse effects:

Some of the most frequent side effects of Omeprazole (experienced by over 1% of those taking the drug) are:

Headache, Diarrhea, Abdominal pain, Nausea, Dizziness, Trouble awakening, And sleep deprivation, although in clinical trials the incidence of these effects with Omeprazole was mostly comparable to that found with placebo. Other side effects may include iron and vitamin B12 deficiency, although there is very little evidence to support this.

Proton pump inhibitors may be associated with a greater risk of osteoporosis related fractures and Clostridium difficile -associated diarrhea. Patients are frequently administered the drugs in intensive care as a protective measure against ulcers, but this use is also associated with a 30% increase in occurrence of pneumonia. The risk of community-acquired pneumonia may also be higher in people taking PPI. [15]

LANSOPRAZOLE

Lansoprazole is a proton-pump inhibitor (PPI) which inhibits the stomach's production of gastric acids. It is manufactured by a number of companies worldwide under several brand names. In the United States it was first approved by the Food and Drug Administration (FDA) in 1995.

Lansoprazole has been available as a generic drug since Prevacid patent protection expired on November 10, 2009. Since 2009 Lansoprazole has been available over the counter (OTC) in the U.S. in a 15 mg dose marketed by Novartis as Prevacid 24HR.

Lansoprazole is a proton-pump inhibitor (PPI) in the same pharmacologic class as Omeprazole. Lansoprazole has been marketed for many years and is one of several PPIs available. Lansoprazole is a racemate [1:1-mixture of the enantiomers Dexlansoprazole (Kapidex) and levolansoprazole].

Clinical data

Legal status – prescription only, Routes - oral, i.v.

Pharmacokinetic data

Bioavailabiability - 80%, Protein binding - 97%, Metabolism – hepatic, Half life - 1 to 1.5 hours, Excretion renal and faeces.

Lansoprazole is indicated for:

- Taking twice daily for 10 or 14 days Lansoprazole 30 mg, amoxicillin 1,000 mg, and clarithromycin 500 mg. Treatment of ulcers of the stomach and duodenum, and NSAID-induced ulcers.
- Adjunctive treatment of Helicobacter pylori infection, alongside antibiotics. Treatment to kill Helicobacter pylori (H. pylori) causing ulcers or other problems involves using two other drugs besides Lansoprazole. This treatment is known as "triple therapy", and involves Treatment of gastro esophageal reflux disease(GERD) and Treatment of Zollinger-Ellison Syndrome.[16]

PANTOPRAZOLE

Pantoprazole (sold under various brand names including Somac, Tecta, Pantoloc, Protium, Protonix, Pantecta, Pantoheal, Pantpas, Ppi-40, and Neoppi) is a proton pump inhibitor drug that inhibits gastric acid secretion.

Clinical data:

Legal status - Prescription only, Routes - Oral, i.v.

Pharmacokinetic data:

Bioavailabiability - 77%, Metabolism – hepatic, Half life - 1 hour, Excretion – Renal.

Uses:

Pantoprazole is used for short-term treatment of erosion and ulceration of the esophagus caused by gastro esophageal reflux disease. Initial treatment is generally of eight weeks' duration, after which another eight week

course of treatment may be considered if necessary. It can be used as a maintenance therapy for long term use after initial response is obtained.[17]

ESOMEPRAZOLE

Nexium is the brand name of Esomeprazole and is not available in a generic, as of 2009. It comes in 20 and 40 mg caps. It can also be given intravenously. The oral form is most often taken one time a day for four to eight weeks, but a repeat four- to eight-week course is FDA approved, as is use in children down to age one.

The most likely side effects are headache, dizziness, rash, diarrhea, nausea or vomiting, and change in taste. [15]

DEXLANSOPRAZOLE

Dexlansoprazole, known by its brand name Kapidex, received FDA approval in early 2009. It is supplied in 30 mg and 60 mg caps that are administered once daily. It is not recommended for children, but adults may take it for up to six months for some conditions. It may be associated with stomach upset, abdominal pain or upper respiratory infections, but is generally well tolerated.[18]

RABEPRAZOLE

Rabeprazole is available as the brand name drug Aciphex or in generic versions. It comes in 20 mg tablets and is usually taken once daily. It is approved for use in those over age twelve for up to 16 weeks. The most frequent side effect is headache. [19]

ADVERSE EFFECT OF PROTON PUMP INHIBITORS

Short-term: In general, proton pump inhibitors are well tolerated, and the incidence of short-term adverse effects is relatively uncommon. The range and occurrence of adverse effects are similar for all of the proton pumps inhibitors, though they have been reported more frequently with Omeprazole. This may be due to its longer availability and, hence, clinical experience.

Common adverse effects include:

- Headache (in 5.5% of users in clinical trials),
- Nausea,
- Diarrhea,
- Abdominal pain,
- Fatigue and
- Dizziness.
- Long-term use is associated with hypomagnesaemia.

Because the body uses gastric acid to release B_{12} from food particles, decreased vitamin B_{12} absorption may occur with long-term use of proton-pump inhibitors and may lead to Vitamin B_{12} deficiency. Infrequent adverse effects include rash, itch, flatulence, constipation, anxiety, and depression. In rare cases PPI use may cause 'idiosyncratic' reactions such as erythema multiforme, pancreatitis, Stevens–Johnson syndrome, and acute interstitial nephritis.

It has been observed that gastric acid suppression, using H_2-receptor antagonists and proton pump inhibitors, is associated with an increased risk of community-acquired pneumonia. It is suspected that acid suppression results in insufficient elimination of pathogenic organisms. Therefore, it has been suggested that patients at higher risk of pneumonia should be prescribed proton pump inhibitors only at lower doses and only when necessary.

Long-term:

In the specific but common case of the use of proton-pump inhibitors as long-term treatment for managing GERD, medical societies recommend that patients use the minimal effective dosage to achieve the goals of the therapy. Theories as to the cause of the increase are the possibility that the reduction of stomach acid reduces the amount of calcium dissolved in the stomach or that PPIs may interfere with the breakdown and rebuilding of bone by interfering with the acid production of osteoclasts. The reduction of vitamin B_{12} may also increase bone fragility by raising homocysteine).

A recent study also suggested that proton pump inhibitors significantly decreased the

effect of clopidogrel on platelets, as tested by VASP phosphorylation. The clinical impact of these results must be assessed by further investigations, but a PPI treatment should not be added to the antiplatelet dual therapy without formal indication. [1,5]

CONCLUSION

Now a day's peptic ulcer is a common problem associated with g.i.t and is affecting most of the total population due to present life style, intake of unhealthy foods and lack of exercise resulting in imbalance between defensive and aggressive factors of the body which leads to peptic ulcer. There are number of drugs which are used for the treatment of peptic ulcer disease. We have studied about proton pump inhibitors. These are the drugs which blocks the synthesis and release of HCl even when all the drugs fails to control the release of HCl. It has an advantage over all the other anti secretory drugs that these have less adverse effects than the others as these drugs particularly acts on proton pump.

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