Comparative drug review gastrointestinal therapies tagamet and nexium biology ess...

Tagamet and Nexium have been two of the many common drugs these days, both of which are widely used in the medical treatment of major gastric acid-related disorders like peptic ulcer disease (PUD) and gastro-esophageal reflux disease (GERD), with their respective active ingredient being cimetidine and esomerprazole.

In view of their similar uses in gastrointestinal therapies, this review addresses various major characteristics possessed by the two drugs and in an attempt to make a vivid comparison between them in accordance to their active ingredients, for providing information optimizing the selection of gastric acid-related drugs at different clinical conditions.

Mechanism

Both cimetidine and esomeprazole serve to cure gastrointestinal disorders by reducing the secretion of gastric acid, however, with different drug targets to be acted on and mechanisms to bring about their actions. Cimetidine, being a histamine H2 receptor competitive antagonist (H2RA), reversibly binds to the histamine H2 receptor on the acid-secreting parietal cell of the stomach and lead to the production of second messenger cAMP which can ultimately trigger the H+/K+-ATPase to pump more acid out of the cell. Thus, the binding of histamine released by Enterochromaffin-like (ECL) cells in the stomach to the receptors, which in turn stimulates gastric acid secretion, is inhibited. At the same time, with the blockage of the histamine H2 receptors by cimetidine, the effect of both gastrin- and acetylcholine-stimulated acid secretion would be reduced. All these result in the lowering of acidity in the stomach.

Esomeprazole, being a proton pump inhibitor (PPI), acts by an entirely different mechanism. Esomerprazole is a weak-base prodrug and it accumulates in the unique, highly acidic canalicular space of the active parietal cell, where the pH is less than 2. 0. At this pH, it is converted to the active form of the drug, which then covalently binds to one or more cysteines that are accessed from the luminal surface of the gastric proton pump in gastric parietal cells, the H+/K+ ATPase enzyme, the target of which esomeprazole acts on. As a result, this irreversibly inhibits the H+/K+ ATPase enzyme, whose activity is involved in the final step of gastric acid secretion

Therapeutic Effectiveness

Owing to their different mechanisms of action, the gastric acid-suppressive effect produced by them varies, thus leading to variation in their effectiveness for treating related diseases. In general, PPIs (e. g. esomerprazole) are more potent than H2RAs (e. g. cimetidine) because the former inhibits the H+/K+ ATPase enzyme involved in the final step of acid secretion[1], as the latter only inhibits one of the pathways involved in acid secretion. The superior acid-suppressive effect of PPI over an H2RA has been verified by comparative studies. [2-5]

Because of the different mechanism of these two drugs, esomeprazole has a longer duration than cimetidine. After converted to the active form, Esomeprazole can bind reversibly to the H+/K+-ATPase. As a result, esomeprazole will not be easily enzymatically metabolized and the major factor that leading to loss of effect of esomeprazole is largely dependent on

the production of new H+/K+-ATPase. This is reason why esomeprazole has a rather long duration of effect on inhibition of acid secretion.

In terms of therapeutic outcomes, it has been shown that higher efficacy is found in PPI treatments than in H2RA treatments for a wide range of diseases such as peptic ulcer disease, gastroesophageal reflux disease, GI damage caused by non-steroidal anti-inflammatory drugs, and Zollinger-Ellison syndrome. [6 V13], as revealed by many studies. One of these aimed to investigate oesophagitis in which a meta-analysis of 43 therapeutic trials was conducted in patients with moderate or severe oesophagitis. The proportion of patients successfully treated was almost doubled with PPIs, and the rapidity of healing and symptom relief were about twice that with H2RAs. [14] Thus, It had confirmed the advantage of PPIs over H2RAs. [15]

To sum up, up to the present stage, esomerprazole seems to be more effective and a more preferable choice than cimetidine for the treatment of most gastric acid-related diseases.

Safety

In fact, both cimetidine and esomeprazole are quite safe and they rarely have adverse effects that may be lethal. In a meta-analysis of 24 double-blind placebo-controlled studies, it shows negligible difference of incidence of side effects between cimetidine and placebo. The most commonly reported adverse effects are diarrhea, other gastrointestinal disturbances, dizziness, tiredness, rashes and headache. Furthermore, most adverse effects of cimetidine are dose-related and as the length of treatment increases, the risk is decreased which means Cimetidine is rather secure for patients who

require long-term treatment. Also, Cimetidine has significant anti-androgen effects in patient receiving high dose and this puts some male patients in fear.

Adverse effects of Esomeprazole are infrequent as Cimetidine, but some of its common side effects like headache, diarrhea and skin rashes can be severe and may need to resolve on drug discontinuation. Moreover, recognized increases in the prevalence of pneumonia and Campylobacter enteritis as well as a doubling of the risk of infection with Clostridium difficile should not be overlooked due to the role of esomeprazole as a first-line drug.

What should emphasize is that patients still need health care professionals careful indication as if both drugs are safe. Since esomeprazole is one of the most frequently prescribed medicine and 63% , 33% and 67% of hospital inpatients in Austria, Ireland and the United Kingdom did not meet the criteria for taking esomeprazole or other proton pump inhibitors. As a result, it is pharmacoeconomically unfavorable and improved clinical pharmaceutical care can be achieved by detailed indication by the cooperation of pharmacist and health care professionals. What is more, these two drugs are placed in the same Pregnancy Category by the US FDA and they are not advised for the pregnant women. Because of their inhibition of parietal cells, secretion of intrinsic factor is reduced. As a result, both drugs can lead to mal-absorption of Vitamin B12 which is important for maturation of Erythrocytes and DNA synthesis and thus Vitamin B12 therapy may be needed.

Drug interactions

They interact with a wide variety of drugs except that they both reduce absorption of acid-dependent drugs due to their effect of lowering of the stomach pH, but in fact only drugs with a narrow therapeutic index have clinical significance. The majority of interactions is due to binding of cimetidine to cytochrome P450 isoenzymes in the liver with subsequent inhibition of microsomal oxidative metabolism and increased bioavailability or plasma concentrations of drugs metabolised by these enzymes. These drugs are anticoagulants, phenytoin, theophylline, benzodiazepines, betal-blockers, lidocaine, Procainamide, ketoconazole and itraconazole.

Similarly, Esomeprazole interferes with the elimination of drugs metabolized by isoenzyme CYP2C19 and to a smaller extent by CYP3A4. Therefore, it increases the plasma level of clarithromycin, amoxicillin, diazepam, phenytoin, and warfarin. In addition, esomeprazole has a potential interaction with atazanavir which is a HIV-Protease Inhibitor to treat HIV by substantially reducing the concentration of atazanavir.

Conclusion

Summarizing all the above mentioned features, Nexium is seemingly a better drug in terms of its potency, therapeutic effects as well as its range of application in clinical conditions, comparing to Tagamet. However, its benefits and drawbacks may be revealed in the future by research works, which should be always aware of.