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Comparing the Long Term Use of H2 Antagonists (H2RAs) and Proton Pump Inhibitors (PPIs) and the Incidence of Colitis

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Abstract

• Esophagitis, Barrett’s esophagus and Zollinger-Ellison syndrome may be complications.
• Improved awareness and increased use of treatments that cause histology.
• Clinicians seek a medication that is specific, selective, and effective for the treatment of GERD, do H2RAs or PPIs cause colitis?
• Microscopic colitis is a significant complication risk following the long-term use of PPIs. The diarrhea was most commonly loose and occurred on average 4.4 times per day ranging from 4-9 times per day.

Introduction

• Microscopic colitis is a significant complication risk following the > 4-8 week use of certain H2RAs and PPIs.
• Clinicians seek a medication that is specific, selective, and effective for the treatment of GERD, do H2RAs or PPIs cause colitis?
• Improved awareness and increased use of treatments that cause histological changes observed in microscopic colitis.

Research Question

• Microscopic colitis causing chronic diarrhea and chronic colonic inflammation continues to be a statistically significant complication risk with extended use (≥ 4-8 weeks) of certain H2RAs and PPIs.
• Among the drugs associated with microscopic colitis are H2RAs; ranitidine (Zantac) and proton pump inhibitors, lanoprazole (Prevacid), omeprazole (Prilosec), and esomeprazole (Nexium).
• Diarrhea is one of the most frequently reported adverse events during the long-term use of PPIs. The diarrhea was most commonly loose and occurred on average 4.4 times per day ranging from 4-9 times per day.

Literature Review

• PPIs reduce acid secretion by inhibiting the hydrogen-chloride (HCl) secreting pump (H+/K+ ATPase) in the stomach and are anti-secretory agents.
• PPIs enter the parietal cell through the proton pump, resulting in an irreversible pump inactivation reducing the amount of H+ that is pumped into the stomach lumen. The binding is irreversible, the effects of PPIs persist until new pumps are synthesized.
• Concerns of small and large bowel dysbiosis, microscopic colitis and lymphocytic colitis secondary to long term PPI use (> 4-8 weeks) are raised.
• Diarrhea was reported in clinical trials and observational data of lansoprazole users.
• Lansoprazole is a highly effective PPI, has been well tolerated with minimal serious adverse events. Diarrhea is reported in approximately 5% to 8% of study patients.
• In atypical colitis and lymphocytic colitis related to lansoprazole, with both clinical (cavitation of diarrhea) and histological improvement upon cessation of this medication.
• The most potent medications that suppress gastric acid are PPIs. They have been shown to be effective in treating patients with GERD, do H2RAs or PPIs cause colitis?

Discussion

• Multiple case studies suggest a causal relationship between microscopic colitis and lanoprazole, omeprazole and esomeprazole treatment, due to the temporal association of exposure, resolution of symptoms and normalization of histopathology upon drug withdrawal, and the immediate recurrence of disease with histologic abnormalities upon drug re-exposure.
• PPIs are therapeutically more effective than H2RAs in the treatment of gastrointestinal reflux disease, have a higher risk profile, increased ADRs and are more broadly implicated in microscopic colitis.
• Microscopic colitis causing chronic diarrhea and chronic colonic inflammation continues to be a statistically significant complication risk with the extended use of certain PPIs (lanoprazole (Prevacid), omeprazole (Prilosec) and esomeprazole (Nexium) and the H2RA (ranitidine (Zantac))).
• PPIs have the physiological and functional potential to interfere with gastrointestinal physiology by virtue of altering intestinal pH.
• PPIs can also interact with mechanisms and sites of action, other than that of gastric H+K+ ATPase. Colon epithelial cells also express proton pumps, which are involved in maintaining local electrolyte balance.
• Several bacteria including Helicobacter pylori and Staphylococci, as well as fungi such as Candida albicans contain H+K+ ATPase in their plasma membranes, which are highly similar to human plasma membranes.
• PPIs can influence a wide variety of microbial growth, including bacteria and fungi, by inhibition of H+K+ ATPase.

Applicability to Clinical Practice

• H2RAs and PPIs are widely prescribed worldwide by physicians and can be purchased over-the-counter by patients.
• In 2010, 54 million US prescriptions for the generic antacid medication Prilosec (omeprazole) not including OTC sales.
• PPIs interfere with gastrointestinal physiology by virtue of altering intestinal pH.
• Hydrochloric acid is required for the breakdown and digestion of food. Although considered safe, long-term use has raised safety concerns.
• Potential adverse drug reactions include Cholesterol difficult infection, dysbiosis, changes in autoimmunity, bone fractures, respiratory infections, B12, and iron malabsorption, malabsorption syndromes, watery diarrhea, enteric infections, small bowel bacterial overgrowth, inflammatory bowel disease, such as microscopic colitis, hypergastrinemia, including rebound secretion of hydrochloric acid and carcinoid tumors.
• Successful GERD management includes lifestyle and behavior modification as first line, prior to adding H2RAs or PPIs.
• In high-risk populations, such as the elderly, acid reducing medications are contraindicated.
• Patient education in avoiding GERD triggers can decrease the frequency and incidence of GERD, esophagitis, peptic ulcer disease and dyspepsia.

Statement of the Problem

• Effective and evidenced based treatments are being chosen with good safety profiles and low incidence of side effects.
• This study discusses increased IELs, inflammation of the colon, alterations in intestinal barrier function and unfavorable mucosal immune activation induced with certain H2RAs and PPIs.
• Healthcare providers may need to improve the oversight and education given to GERD patients who are treated with long term H2RA and PPI therapy to decrease the incidence of colonic inflammation.

References

[8] Chiba, M., Sugawara, T. (2009). Lansoprazole- associated collagenous colitis: Diffuse mucosal inflammation continues to be a statistically significant complication risk with the extended use of certain PPIs (lanoprazole (Prevacid), omeprazole (Prilosec), and esomeprazole (Nexium) and the H2RA (ranitidine (Zantac))).

Thanks . . .