Protease Inhibitors and PPIs

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Proton pump inhibitors (PPIs) are the most potent inhibitors of gastric acid secretion currently available. They have become the treatment of choice for acid-related upper gastrointestinal (GI) symptoms and diseases. In addition to the classical indications for PPI therapy, some drug regimens produce a high incidence of GI side effects. For example, in a survey of HIV patients receiving highly active antiretroviral therapy, a majority reported heartburn and gastroesophageal reflux disease. Thus, the potential for drug interactions between antiretroviral drugs and acid suppressive therapy including antacids, histamine-2 receptor antagonists (H2RAs), and PPIs for heartburn and gastroesophageal reflux disease is large. In this review, we will focus on the interactions between protease inhibitors and PPIs.

Atazanavir appears to be most sensitive to pH changes caused by PPIs. Studies have noted marked reductions in atazanavir area under the plasma concentration-time curve (AUC) when it is administered with PPIs including omeprazole and lansoprazole. Atazanavir minimum plasma concentrations in patients treated with PPIs have been reported to be unaffected by concomitant PPI use. The differences in these reports may be due to different subject types, PPI doses, and small sample sizes. Pending further data, PPIs should be avoided in patients taking atazanavir.

Fosamprenavir is a prodrug for amprenavir. Its solubility is reduced when the pH exceeds 3.3. One might expect PPIs would reduce its absorption. Studies where fosamprenavir is administered simultaneously with esomeprazole, however, did not detect a significant reduction in amprenavir plasma concentrations. It may be that administering the fosamprenavir at the nadir of the PPI’s acid-suppressing action limits the potential effect. It is common for the gastric pH to drop below 3 during the morning before the effects of the PPI are maximized. It is noteworthy that H2RAs produce a greater (30%) reduction in amprenavir plasma concentrations. It may be that administering the fosamprenavir with atazanavir may result in lower plasma concentrations.

Due to the limited number of published studies often involving small numbers of healthy subjects, the mean changes in protease inhibitor plasma concentrations remains to be defined. Reduced efficacy or the development of resistant strains of HIV may result from lowered plasma concentrations.

For a list of references, go to www.PharmacyTimes.com.