

Nocturnal Acid Breakthrough In Patients With GERD

Lead author: Kay Shaver, Pharm.D., Assistant Editor

Background

Proton pump inhibitors are the most effective treatment for gastroesophageal reflux disease (GERD). They heal esophagitis and relieve symptoms more frequently and more rapidly than other drugs. They are effective in about 80% to 90% of patients with typical GERD.¹⁻³

Nocturnal Acid Breakthrough

There are some patients with GERD who need greater acid suppression than can be achieved with twice daily proton pump inhibitors (PPIs).² Nocturnal acid breakthrough can occur with virtually any proton pump inhibitor regimen, even twice daily dosing. It is estimated that nearly 75% of patients with GERD have nocturnal acid breakthrough while taking PPIs.⁴

One study looked at the degree of stomach acid suppression with proton pump inhibitors in three groups: a group of patients with GERD taking omeprazole (*Prilosec*) 20 mg twice daily, a group of volunteers taking omeprazole 20 mg twice daily, and a group of volunteers taking lansoprazole (*Prevacid*) 30 mg twice daily. The results showed that 73% of patients had nocturnal acid breakthrough. Acid breakthrough occurred when the stomach pH fell below four for at least one hour. The return of acid secretion usually occurs during the second six hours after the evening PPI dose.²

Mechanism

An increase in stomach acid secretion occurs in response to three substances: histamine, gastrin, and acetylcholine. These substances bind to specific receptors on the parietal cell to induce acid secretion.^{5,6} The final step in stomach acid production depends on the H/K ATPase enzyme system. Proton pump inhibitors (*Prilosec*, *Prevacid*, *Protonix*, *Aciphex*) bind irreversibly to this enzyme, which inactivates the proton pump.⁴

PPIs only inhibit ACTIVE proton pumps that are stimulated by meals. In addition, they have a short half-life and are quickly eliminated from the body. Their long duration of action is due to the irreversible inactivation of active proton pumps. As a result, the efficacy of a PPI is determined by the number of active pumps which are available for binding during the short time it is in the circulation. New pumps can activate during the night after the PPI has been eliminated. These pumps are then able to be stimulated by histamine or acetylcholine.^{2,4,5}

It is thought that nocturnal acid secretion is either mediated by histamine or both histamine and acetylcholine. It is also thought that acid secretion might follow a circadian pattern, with a peak in acid secretion around midnight.^{2,5}

Since a bedtime dose of a PPI is not taken with a meal, the number of active pumps available for binding with the PPI at this time is small. The action of H₂ antagonists does not depend on food, so they are better able to suppress nighttime acid secretion. Even small doses of ranitidine (*Zantac*), such as the 75 mg OTC dose, can help control nocturnal acid secretion.^{4,5} Different H₂ antagonists can generally be used interchangeably.¹

Studies

One study looked at nighttime gastric acidity in twelve volunteers. Participants received omeprazole 20 mg twice daily for seven days. After seven days, they received a bedtime dose of either omeprazole 20 mg, ranitidine 150 mg, ranitidine 300 mg, or placebo in addition to twice daily omeprazole. They measured the percent time that stomach pH was less than four. Patients who took ranitidine at bedtime had better control of nighttime acid secretion (5% and 6% for 150 mg and 300 mg respectively) than patients who took

omeprazole (31%) or placebo (48%).⁵

Another study was done to determine if a bedtime dose of an H₂ antagonist would be effective enough to eliminate the need for a second daily dose of PPI. This study was a randomized, double-blind, crossover design. Patients received either omeprazole 20 mg twice daily and placebo at bedtime, or omeprazole 20 mg in the morning and ranitidine 150 mg at bedtime for seven days. There was a one-week washout between study periods. The results showed that omeprazole 20 mg twice daily was more effective in controlling nighttime stomach pH than when a ranitidine was substituted for the second dose of omeprazole. Sixty percent of patients on omeprazole twice daily had acid breakthrough during the night compared to 75% of patients taking omeprazole in the morning and ranitidine at bedtime.⁷

Commentary

While the above two studies were not large trials, they do suggest that there are patients who might benefit from a dose of an H₂ antagonist in addition to twice daily PPI therapy. These include patients who don't get relief from a twice daily PPI regimen and patients in whom tight control of acid secretion is desirable (severe esophagitis, Barrett's esophagus, or extraesophageal manifestations of GERD).^{2,3,5}

A bedtime dose of an H₂ antagonist does not replace the need for two daily doses of PPIs. However, it can potentially save on costs when used in place of a third daily dose of PPI. PPIs can cost more than \$3.50 per tablet or capsule, while generic prescription strength ranitidine costs less than \$1.00 each. Over-the-counter *Pepcid AC* and *Zantac 75* can cost less than 50 cents per tablet.

Remind patients taking proton pump inhibitors to take their doses before meals in order to inhibit the most pumps and get the greatest effect.