EDITORIAL

# Proton pump inhibitors are not antacids!

Proton pump inhibitors (PPIs) are among the most commonly prescribed drugs in clinical practice. Since the introduction of these potent acid-suppressing agents in the late 80s, they were listed in the Guinness Book of World Records as the most prescribed in human history. Yet, to be effective in inhibiting the proton pump enzyme ($H^+/K^+$ ATPase) in the parietal cells, these drugs should be taken 1 hour before meals.

In this issue of the Journal, Mui and Fan[1] report that less than 1% of prescriptions by doctors specified that PPIs should be given before a meal, and even among gastroenterologists only a minority did so. According to Mui and Fan's audit, none of the cardiologists, internists, family physicians, and surgeons gave proper instructions on prescribing PPIs. This is astounding when compared to the results of a similar study in the United States. In a survey of practising primary care physicians from the American Board of Medical Specialties and practising gastroenterologists from the American Gastroenterological Association, Barrison et al[2] reported that 33% of the former and 95% of the latter prescribed PPIs before meals. Sub-optimal dosing impacts on the efficacy of acid suppressing therapy in the treatment of peptic disorders such as gastro-esophageal reflux disease.[3] In fact, if a PPI is taken only when the patient starts to experience heartburn after a big meal, it may not compare favourably even to antacids.

In recent years, PPI usage has switched from the treatment of peptic ulcer disease to the control of symptoms of gastroesophageal reflux disease. In order to expand the market, the pharmaceutical industry has advocated their use as required in symptom control. Thus, on-demand therapy for patients experiencing reflux symptoms without erosive oesophagitis has been evaluated in two industry-sponsored, randomised, double-blind studies.[4,5] Patients enrolled in these studies had previously received short-term treatment with omeprazole or esomeprazole and showed complete resolution of heartburn. The primary efficacy endpoint was the time to discontinuation of therapy (due to unwillingness to continue in the study). Patients received on-demand therapy with once-daily esomeprazole 20 or 40 mg or placebo for 6 months. The secondary endpoint was the time to discontinuation because of insufficient control of heartburn. On-demand therapy proved beneficial according to the stated primary and secondary efficacy endpoints. Moreover, markedly fewer patients randomised to PPI discontinued treatment than in the placebo group. The major reason for discontinuation of treatment was inadequate control of heartburn. Based on these results, PPIs have been advocated as on-demand therapy for symptom control in gastroesophageal reflux disease. In many countries, PPIs are now available as over-the-counter medication, which will no doubt further encourage resorting to these drugs whenever patients feel the 'acid' or 'burning'. Inevitably, such symptom-driven on-demand therapy is more likely to be taken after a meal instead of before food. By implication, if PPIs are taken before meals, much smaller doses are likely to suffice, whereas post-prandial use renders them inefficient and constitutes reduced efficacy.

Besides failing to achieve optimal therapeutic effects with recommended dosing, the lack of appropriate advice on usage of PPIs may lead to more serious consequences. Potential interactions between PPIs and other medications can influence the pharmacokinetic profiles of many commonly administered medications. This may ensue by (i) elevating intra-gastric pH, which can alter drug absorption, and (ii) interacting with the cytochrome P (CYP) 450 enzyme system, which can affect drug metabolism and clearance.[6] Such interactions are particularly important when they affect the pharmacokinetics of drugs with narrow therapeutic ranges, such as warfarin and digoxin. Under these circumstances, drug-drug interactions can result in significant toxicity and even death. Among the PPIs, omeprazole has the greatest potential to alter CYP 450 activity and change the pharmacokinetics of other drugs. The newer PPIs, rabeprazole and pantoprazole, are less likely to affect this enzyme system and thereby influence the metabolism of other medications. However, with the emergence of generic omeprazole, such drug interactions are more liable to occur, as many physicians are not sufficiently aware of this problem.

Clearly, the liberal use of PPI should be discouraged. After all, PPIs are not antacids and these two drug classes should not be regarded as one!

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## References


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