We Are Using Too Many PPIs, and We Need to Stop: A European Perspective

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Not many years ago, acid-related disorders were among the most common clinical problems facing gastroenterologists, surgeons, and primary care physicians. Peptic ulcer disease (PUD) and its complications were the most common causes of hospitalization. The development of H2-receptor antagonists was an important step forward, but it is the commercialization of omeprazole and other proton pump inhibitors (PPIs) that has definitively enhanced our ability to control acid-related diseases. Today, it is difficult to imagine clinical gastroenterology without the availability of these potent and highly effective agents. Indeed, the efficacy, tolerability, and safety of PPIs have led to their widespread use worldwide. No doubt, the quality of life of patients suffering from gastroesophageal reflux disease or PUD has improved markedly with these drugs. Moreover, the widespread use of PPIs is one of the main reasons for the observed decrease in hospitalizations due to PUD and its complications in many countries; nonsteroidal anti-inflammatory drug (NSAID) and aspirin (ASA) treatments are the cause of 50% of PUD complications, and PPI treatment has become the gold standard in the prevention of NSAID gastropathy in this context.

In recent years, prescription of NSAIDs and ASA has continued to rise because of a progressively aging population. Guidelines from different scientific societies, expert consensus reports, and regulatory bodies recommend PPI co-therapy as one of the main options for prevention of complications in at-risk patients treated with NSAIDs or ASA. The “bibliographic pressure” to increase PPI prevention therapies in this population has been high, as preliminary reports have shown a tremendous gap between guideline recommendations for high-risk patients and actual clinical practice (underuse of PPIs). This pressure has had a positive effect, and more recent studies report that this gap has been reduced substantially. However, at the same time, these studies have detected growing and worrisome inappropriate prescription of PPI co-therapy (overuse). A similar pattern of overuse has been described in other clinical situations such as dyspepsia. The loss of patent protection and the availability of most PPIs as generic drugs have lowered the price significantly and contributed to their increasing use.

The proportion of PPI use is especially high in some European countries. For example, in Spain, omeprazole ranked number one in drug sales in 2010, representing 5.5% of total drug packaging invoiced. According to data provided by the Organization for Economic Cooperation and Development (Figure 1) (1), the use of antil ulcer agents in Spain has increased almost four times since the year 2000, primarily due to an increase in PPI use. Similar trends are seen in other countries including the Netherlands, Iceland, the United Kingdom, and Belgium.

The number of reports showing overuse of PPI and potentially inappropriate prescription for non-approved indications is growing and indicates that once a PPI is prescribed for a patient, they often continue the treatment long term. Inappropriate prescription of PPIs occurs in both hospital and ambulatory settings, as well as in academic or private centers (2). Most reports indicate that between 30 and 50% of prescriptions of PPIs in ambulatory or hospitalized patients were issued for non-registered indications; the proportion was greater in nonacademic hospitals. The most common inappropriate indication for PPI treatment is prevention of gastric damage, often associated with drugs that have not proved to be harmful to the gastric mucosa. Prophylaxis for stress ulcer during hospitalization in low-risk patients is another common inappropriate indication. Often, no clear indication is identified. In some reports, inappropriate PPI prescription rates at admission remain identical at discharge (indicating that these medications are not routinely discontinued), with figures as high as 75% of all cases without an acceptable indication.

Studies of adverse events associated with PPI use are also growing and gaining the attention of regulatory bodies. Today, these adverse effects include enteric infections (especially Clostridium difficile-associated diarrhea), pneumonia, bone fractures, nutritional deficiencies of vitamin B12 and magnesium, acute interstitial nephritis, and increased risk of drug–drug interactions, among others. Most of these adverse events have been detected in observational studies, and, evidence is weak at best, as no clinical trials are available to confirm these outcomes. However, these potential adverse events should not be dismissed. The magnitude of the use of these compounds, the growing evidence of inappropriate
prescription worldwide, together with their potential association with serious adverse events, although low in frequency, may represent vast numbers of patients in absolute terms. Hence, they must be considered a health issue that needs to be reanalyzed and ultimately more carefully regulated. Furthermore, the total costs of inappropriate PPI use are high and unacceptable. On the basis of US data, the estimated cost for 1,034 patient-years of inappropriate PPI use in one study was $1,566,252 based on average wholesale price costs.

What can we do to curb this trend of PPI overuse? Changing prescription habits is not an easy task, but now that we have clear evidence of inappropriate PPI use with potentially important implications for our health-care systems we need to act. As always, education is the key. Although there are reports pointing out some groups of prescribers (those with increasing number of years after graduation or some surgical specialties for example) who are less prone to follow guidelines and who should be specifically targeted, a general approach for all physicians should be implemented. We, the gastroenterologists, should be the first to eradicate inappropriate PPI prescription and should expand good prescription habits to our colleagues. Expansion of good habits in PPI use within hospitals should also be our responsibility. Increasing awareness and providing evidence of the potential consequences of inappropriate PPI use are also needed in the scientific community. Likewise, I believe the “bibliographic pressure” that was so successful in improving the gap between guidelines and lack of gastro-protective measures in at-risk patients taking NSAIDS or ASA can now be also quite successful in helping to reduce the overuse of PPIs. Now that most PPIs are generic in most countries, incentives from pharmaceutical companies to use their compounds should decrease and make this task easier. In the era of informatics, other initiatives should be carried out at the same time. For example, positive experiences with web-based quality improved tools have been reported (3). The success of those initiatives has been limited, which suggests that an active interventional strategy is likely to be required. Finally, the analysis of the main differences in prescription habits between countries of the same region may also provide important clues to stop PPI overuse.

CONFLICT OF INTEREST

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REFERENCES