Rationalizing the use of PPIs: An unresolved matter

The abnormally high use of proton-pump inhibitors (PPIs) has been repeatedly denounced for many years (1), and attention has been drawn towards the economic burden it represents (2,3). Multiple scientific publications have reported this problem in many countries. In the present issue of the Journal an observational, prospective study based on a survey to analyze the inappropriate (not recommended by clinical guidelines) indication of chronic PPI use (daily for over one year) in outpatients seen at a specialty hospital in Mexico is reported (4). The authors find an overall rate of inappropriateness of 35.3 %, a figure within the lower range of those reported, which exceed 60 % in many countries including Australia (5,6), United Kingdom (7), and Greece (8), and in four studies performed in Spain (9,10-12). All these studies discuss oral therapy with PPIs, but inappropriateness is also very high (above 75 %) in terms of dosage and length of intravenous therapy (13).

The introduction of antisecretory agents in clinical practice, initially H2 antagonists and then PPIs, has brought in the treatment of conditions associated with gastric acid secretion. The indisputable greater effectiveness of PPIs makes them preferable progress to H2 antagonists. In a study that examined the indication of antisecretory agents at hospital admission and discharge for gastro-esophageal reflux disease (GERD) and peptic ulcer, two conditions where prescription is appropriate, PPIs were chosen in over 95 % of cases (14).

PPI prescription is quantitatively high because of factors inherent to these drugs (high therapeutic efficacy and safety) and the high prevalence of diseases where they are appropriately indicated. GERD—the paradigm here—accounts for almost all appropriate PPI prescriptions for chronic use, and is followed by the prophylaxis of gastric disease by non-steroidal anti-inflammatory drugs (NSAIDs). Sánchez Cuén et al. (4) note that GERD is the most common appropriate indication (31.3 %), representing over 70 % of all appropriate indications.

Disease-related factors that account for a high use of PPIs include the high prevalence and chronic nature of GERD, as well as the frequent need for prophylaxis of NSAID-related gastropathy, which is presumably increasing (population ageing associated with comorbidity and a higher number of therapies representing risk factors, including anticoagulants, antiaggregants, etc.). These factors justify a high number of prescriptions for continuous PPI therapy, as reported by health agencies. According to the latest official data, PPI use in Spain increased by 227 % during the 2004-2010 period; however, the cost for the Treasury only increased by 21.3 %, from €516 to €626 million, which is increased, nevertheless, a significant sum of money. It is of note that the increased expense principally in the first two years and has remained virtually identical (€626 million in 2006) during the last five years of the mentioned above period. Thus, costs per prescription have decreased, most likely
The fact that a high usage is fully justified in the treatment of GERD and NSAID-related gastric disease does not exclude inappropriate prescribing. This is particularly apparent in the prevention of NSAID-related gastric injury, where indications are both excessive and incorrect (16), as they do not comply with clinical practice recommendations, including Spanish guidelines (17). In this setting polypharmacy prescriptions not including any gastrolesive drugs stand out. NSAID-free polypharmacy prescriptions represented 16.6% of inappropriateness in the study by Sánchez Cuén et al. (4). This conceptual error entailing the use of PPIs as “mucosal protectors” when several drugs are used, regardless of their gastrolesive potential, must be corrected. The elderly population, in which polypharmacy and comorbidity are most commonly associated, is particularly prone to inappropriate PPI prescriptions (14,18,19). The indication for dyspepsia is also characterized by inappropriate prescribing. This would be substantially reduced should recommendations for chronic-use prescriptions be complied with (20).

Inappropriateness is therefore present both in primary (9) and specialized care (10), while a high rate (70%) has also reported in emergency care (21). The fact that hospitalization is associated with a high use of PPIs and represents a risk factor for inappropriate prescription is a cause of concern. Initial information obtained by a retrospective study carried out at Michigan University Hospital to examine antisecretory therapy revealed that 29% of patients used these agents at admission (33% received PPIs) and 74% following their discharge (84% received PPIs). It was estimated that their indication was warranted in only 10% of cases (22). In a similar analysis in a Spanish tertiary hospital 28.7% of patients were already on PPIs on admission, 82.6% received them during their stay, and 54.8% were recommended them on discharge from hospital. Prescription was deemed inappropriate in 74.5, 61.3 and 80.2% of cases, respectively (12). Another study that quantified inappropriateness by analyzing hospital discharge summaries revealed there was no information to justify the recommendation to remain on PPIs in 54.5% of cases; the indication was deemed incorrect in 12.7%, and was evidence-based in only 32.7% (23). In a later study that assessed prescription 6 months before and after hospital discharge the above data were replicated; PPI indication at discharge was found to be inappropriate in 52%, appropriate in only 35%, and uncertain in 13% of cases; of these, 58, 67 and 73%, respectively, remained on PPIs after discharge. Of note in this context two thirds of inappropriate indications have their origin in the hospital (24).

It is clear that compliance with recommendations for clinical practice is very low. According to the aforementioned studies, deficiencies in PPI indication not only remain unresolved but even increase when patients are attended to in the various healthcare scenarios (primary care, specialized care, emergency care, critical care), whatever the reason may be. Consensus action protocols have been proposed to improve prescription appropriateness (9). In view of the widespread nature of the problem, which affects all levels of care, a wider-reaching though tailored policy seems necessary. An alternative would be the development of educational programs to improve prescription practice. Educational strategies have had disparate impacts with a tendency towards dissatisfaction (19,25-27). The effect was disappointing in a study that assessed the effect of such strategies at 6 months; 24% of patients received PPIs before the intervention (54% inappropriately), and 26% (49% inappropriately) 6 months after the intervention (26).

In light of the fact that prescribers—that is, physicians at all health care levels (primary, specialized, hospital care)—are ultimately responsible for inappropriate prescribing, the most effective approach may be a more direct, proactive intervention of...
health managers and policy makers (health agencies, medical directors, department and unit coordinators, quality control commissions, pharmacy departments, etc.) by implementing different tools (audits, discharge summary reviews, prescription studies, etc.) to provide objective reports on the current situation, and to ensure the rationalization of prescriptions, which would be achieved by adherence to clinical guidelines and recommendations or to protocols agreed upon in an evidence-based setting.

Strategies for rationalization in the use of drugs such as PPIs, and by extension in diagnostic tests, where a high rate of inappropriateness also exists (28), are key to a high quality, efficient care.

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REFERENCES


