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Editorial

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 H_2 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 H_2 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 continous 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

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as a result of the impact of generics, but public expenditure remains the same due to a noticeable rise in the number of prescriptions.

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 restrospective 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 incorrent 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

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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

1. Bashford JN, Norwood J, Chapman SR. Why are patients prescribed proton pump inhibitors? Retrospective analysis of link between morbidity and prescribing in the General Practice Research Database. BMJ 1998;317:452-6.
2. Heidelbaugh JJ, Kathleen L, Goldberg KL, Inadomi JM. Magnitude and economic effect of overuse of antisecretory therapy in the ambulatory care setting. Am J Manag Care 2010;16:e228-e234.
3. Leri F, Ayzenberg M, Voyce SJ, Klein A, Four-year trends of inappropriate proton pump inhibitor use after hospital discharge. Southern Med Ass 2013;106:270-3.
4. Sánchez Cuén JA, Irineo Cabrales AB, Bernal Magaña G, Peraza Garay FJ. Indicaciones inadecuadas en el consumo crónico de inhibidores de bomba de protones en un hospital de México. Estudio transversal. Rev Esp Pat Dig 2013, 131-7.
5. Naunton M, Peterson GM, Bleasel MD. Overuseof proton pump inhibitors. J Clin Pharm Ther 2000;25: 333-40.
6. Pillans PI, Kubler PA, Radford JM, Overland V. Concordance between use of proton pump inhibitors and prescribing gudelines. Med J Aust 2000;172:16-8.
7. Walker NM, McDonald J. An evaluation of the use of proton pump inhibitors. Pharm World Sci 2001;23:116-7.
8. Ntaios G, Chatzinikolaou A, Kaiafa G. Evaluation of use of proton pump inhibitors in Grece. Eur J Intern Med 2009;20:171-3.
9. Burgos Lunar C, Novo del Castillo S, Llorente Díaz E, Salinero Fort MA. Estudio de prescripción-indicación de inhibidores de la bomba de protones. Rev Clin Esp 2006;206:266-70.
10. Martín-Echevarría E, Pereira Juliá A, Torralba M, Arriola Pereda G, Martín Dávila P, Mateos J, et al. Assessing the use of proton pump inhibitors in an internal medicine departamento. Rev Esp Enferm Dig 2008;100:76-81.
11. Asensio AN, Barrientos RR, Castro PZ. Use of acid-suppresive mredications in hospitalizad patients. Ann Med Intern 2002;19:557-60.
12. Ramirez E, Lei SH, Borobia AM, Pinana E, Fudio S, Muñoz R, et al. Overuse of PPIs in patients at admission, during hospitalisation, and at discharge in a terciiary spanish hospital. Curr Clin Pharmacol 5, 288-297
13. Craig DGN, Thimappa R, Anand V, Sebastian S. Inappropriate utilization of intravenous proton pump inhibitors in hospital practice. A prospective study of the extent of the problem and predictive factors. Q J Med 2010;103:327-335.
14. Pasina L, Nobili A, Tettamanti M, Salerno F, Corrao S, Marengoni A, et al. Prevalence and appropriateness of drug prescriptions for peptic ulcer and gastro-esophageal reflux disease in a cohort of hospitalized elderly. Eur J Intern Med 2011;22:205-11.
15. Ponce J, Vegazo O, Beltrán B, Jimenez J, Zapardiel J, Calle D, et al. Prevalence and factors associated with gastro-oesophageal reflux disease (GORD) in Spain. Aliment Pharmacol Ther 2006;23:175-83.
16. Lanas A, Garcia-Tell G, Armada B, Oteo-Alvaro A. Prescription patterns and appropriateness of NSAID therapy according to gastrointestinal risk and cardiovascular history in patients withdiagnoses of osteoarthritis. BMC Medicine 2011, 9:38
17. Lanas A, Martín-Mola E, Ponce J, Navarro F, Piqué JM, Blanco FJ. Estrategia clínica para la prevención de los efectos adversos sobre el tracto digestivo de los antiinflamatorios no esteroideos. Gastroenterol Hepatol 20003; 26: 487-508, Rev Esp Reumatol 2003; 30: 393-414.
18. Cahir C, Fahey T, Teeling M, Teljeur C, Feely J, Bennet K. Potentially inappropriate prescribing and cost outcomes for older people: a national population study. Br J Clin Pharmacol 2010;69:543-52.
19. Hanzat H, Sun H, Ford JC, McLeod J, Souza RL, Mangoni AA. Inappropriate prescribing of proton pump inhibitors in older patiens. Effects on an educational strategy. Drugs Aging 2012;29:681-90.

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20. Forgacs I, Loganayagam A. Overprescribing proton pump inhibitors. Is expensive and not evidence based. Br Med J 2008;336:2-3.
21. Molloy D, Molloy A, O'Loughlin C, Falconer M, Hennessy M. Inappropriate use of proton pump inhibitors. Ir J Med Sci 2010;179:73-75.
22. Regal RE, Bostwick TR, Knauf KS. Acid suppressive therapy use on an inpatient internal medicine service. Ann Pharmacother 2006;40,1261-6.
23. Ahrens D, Chenot J-F, Behrens G, Grimmsmann T, Kochen MM. Appropriateness of treatment recommendations for PPI in hospital discharge letters. Eur Clin Pharmacol 2010;66:1265-71.
24. Ahrens D, Behrens G, Himmel W, Kochen MM, Chenot J-F. Appropriateness of proton pump inhibitor recommendations at hospital discharge and continuation in primary care. Int J Clin Pract 2012;66:767-73.
25. Krol N, Wensing M, Haaijer-Ruskamp F, Muris JX, Numans NE, Schattenberg G et al. Patient directed strategy to reduce prescribing for patients with dyspepsia in general practice: a randomized trial. Aliment Pharmacol Ther 2004;19: 917-22.
26. Batuwitage BT, Kingham JGC, Morgan NE, Barlett RL. Inappropriate prescribing of proton pump inhibitors in primary care, Postgrad Med J 2007;83:66-68.
27. van Vliet EP, Steyerberg EW, Otten HJ, Rudolphus A, Knoester PD. Hoogsteden HC et al. The effects of guideline implementation for proton pump inhibitor prescription on two pulmonary medicine wards. Aliment Pharmacol Ther 2009; 29: 213-21
28. Argüello L, Pertejo V, Ponce M, Peiró S, Garrigues V, Ponce J. The appropriateness of colonoscopies at a teaching hospital: magnitude, associated factors, and comparison of EPAGE and EPAGE-II criteria. Gastrointest Endosc 2012;75:138-45.