



Deprescripción de inhibidores de la bomba de protones en atención primaria

Deprescribing Proton Pump Inhibitors in Primary Care:

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ABSTRACT

Introduction: proton pump inhibitors (PPIs) are among the most widely used drugs worldwide, and a considerable share of long-term prescriptions lacks a documented indication or periodic review, exposing patients to avoidable risks and burdening health systems. Objective: to critically describe the evidence on the extent of PPI overuse, the safety concerns associated with prolonged use, the rebound phenomenon after withdrawal and the deprescribing strategies applicable in primary care. Development: nearly one in four adults uses a PPI, and in primary care records most continuous users have no recorded indication. The evidence linking PPIs to adverse outcomes is mostly observational and of low certainty, while stopping a PPI can trigger transient acid-related symptoms. Interventions that combine a decision algorithm for the clinician with patient education and shared decision-making increase step-down or discontinuation; tapering or on-demand use suit mild disease, whereas complicated reflux disease, Barrett's esophagus, eosinophilic esophagitis and high gastrointestinal bleeding risk generally call for continuing therapy. Conclusions: deprescribing should be a periodic, individualized and shared process driven by the absence of an indication rather than by fear of adverse effects, and the primary care physician is well placed to lead it.

Keywords: proton pump inhibitors; deprescriptions; primary health care; inappropriate prescribing.

RESUMEN

Introducción: los inhibidores de la bomba de protones (IBP) se encuentran entre los fármacos más utilizados en el mundo, y una proporción considerable de las prescripciones prolongadas carece de una indicación documentada o de revisión periódica, lo que expone a los pacientes a riesgos evitables y carga a los sistemas de salud. Objetivo: describir críticamente la evidencia sobre la magnitud del uso excesivo de los IBP, las inquietudes de seguridad asociadas a su uso prolongado, el fenómeno de rebote tras la suspensión y las estrategias de deprescripción aplicables en atención primaria. Desarrollo: casi uno de cada cuatro adultos consume un IBP y, en los registros de atención primaria, la mayoría de los usuarios continuos no tiene una indicación registrada. La evidencia que vincula los IBP con desenlaces adversos es sobre todo observacional y de baja certeza, mientras que la suspensión puede desencadenar síntomas ácidos transitorios. Las intervenciones que combinan un algoritmo de decisión para el clínico con educación del paciente y decisión compartida aumentan la reducción o la suspensión; la reducción gradual o el uso a demanda se adecuan a la enfermedad leve, mientras que la enfermedad por reflujo complicada, el esófago de Barrett, la esofagitis eosinofílica y el alto riesgo de hemorragia digestiva suelen requerir mantener el tratamiento. Conclusiones: la deprescripción debe ser un proceso periódico, individualizado y compartido, guiado por la ausencia de indicación y no por el temor a los efectos adversos, y el médico de atención primaria está bien situado para liderarlo.

Palabras clave: inhibidores de la bomba de protones; deprescripciones; atención primaria de salud; prescripción inadecuada.

INTRODUCTION

Proton pump inhibitors (PPIs) are among the most prescribed drugs worldwide and have transformed the management of acid-related disorders, such as gastroesophageal reflux disease (GERD), peptic ulcer, and gastroprotection in at-risk patients.(1) A systematic review of 65 observational studies identified more than 28 million users in 23 countries and estimated that nearly a quarter of adults take a PPI.(2)

This widespread use contrasts with the proportion of prolonged treatments that lack a current indication. In an analysis of electronic medical records from 62 primary care practices in England, which included 77 356 adults on continuous PPI treatment, 62% had no recorded indication, and 40% of them had not received a medication review in the previous year.(1) Inappropriate PPI prescribing in primary care has also been documented in Switzerland(3) and among community-dwelling older adults,(4) and deprescribing remains insufficiently implemented.(5)

In addition to these observations, concerns about long-term safety, cost, and polypharmacy have led scientific societies to formulate specific documents on deprescribing, defined as the discontinuation or reduction of a drug under clinical supervision when its indication is no longer current.(6,7) A similar call has been made in general medical journals to reduce the unnecessary use of these drugs.(8)

For the family physician, this issue is especially relevant: this physician issues repeat prescriptions, knows the patient's comorbidities, and can sustain the conversation over time about whether the treatment remains necessary. In fact, the American Gastroenterological Association assigns to the primary care physician the responsibility of periodically reviewing and documenting the indication.(6)

This review article aims to critically describe the available evidence on the magnitude of inappropriate PPI use, safety concerns associated with long-term use, the rebound phenomenon after discontinuation, and deprescribing strategies applicable in primary care, in order to provide clinicians with a practical framework for deciding whom, when, and how to reduce or discontinue these drugs.

METHODS

A descriptive narrative literature review was conducted to synthesize the evidence on inappropriate PPI use, long-term safety, acid rebound, and deprescribing interventions in primary care.

Search strategy and information sources

The search targeted literature indexed in PubMed/MEDLINE, including PubMed Central, and was complemented by consulting journal websites and open-access institutional repositories. MeSH/DeCS terms and free-text words were used, combined with Boolean operators (AND, OR):

- ("Proton Pump Inhibitors" OR "PPI") AND ("Deprescriptions" OR "deprescribing" OR "Inappropriate Prescribing") AND ("Primary Health Care" OR "general practice")
- ("Proton Pump Inhibitors") AND ("adverse effects" OR "umbrella review" OR "rebound acid hypersecretion" OR "discontinuation")

Inclusion and exclusion criteria

• Inclusion criteria:

1. Systematic reviews, meta-analyses, umbrella reviews, randomized clinical trials, population-based observational studies, and clinical practice guidelines or updates from scientific societies.
2. Studies written in Spanish or English.
3. Studies that evaluate the magnitude of inappropriate IBP use, their long-term safety, acid rebound after discontinuation, or deprescribing interventions, preferably in primary care.

• Exclusion criteria:

1. Opinion editorials, letters without original data, conference abstracts without full text, and study protocols without results.
2. Studies focused exclusively on hospital use or pediatric populations.
3. Studies with data duplication or without a described methodology.

Selection of studies and analysis of information

The selection was based on the clinical relevance and perceived methodological quality of

each document, prioritizing evidence syntheses and randomized trials. No systematic screening flow was applied, and risk of bias was not formally assessed. The information was synthesized qualitatively and thematically along the following axes: magnitude of the problem, indications and situations in which treatment should not be discontinued, long-term safety, acid rebound, reduction strategies, and interventions in primary care. As a limitation inherent to the narrative design, the possibility of selection bias in the retrieved literature and the impossibility of generating combined statistical estimates are acknowledged.

DEVELOPMENT

Magnitude of the problem: global use and off-label prescribing

Beyond the overall consumption figures,(2)the central concern is the duration of treatment. In the English study, 11% of the 675 951 registered adults were on continuous PPI treatment; among those with diagnoses for which courses of up to three months are indicated (34% of continuous users), 99% had received their first prescription three or more months earlier.(1)Only 4% had a diagnosis justifying long-term use and, in 41% of them, no medication review in the previous year was recorded.(1)

The factors that explain this inertia are well known: IBPs are effective, inexpensive, easily accessible, and perceived as safe, and the lower frequency of systematic follow-up in overloaded systems allows repeated prescriptions to be renewed indefinitely.(1,9) In addition, nearly two-thirds of continuous users were 60 years of age or older and 27% were receiving 10 or more medications,(1) a profile in which each unnecessary drug adds therapeutic burden.

The problem, however, operates in two directions. In the same study, 19% of patients receiving treatments associated with gastrointestinal risk (14 826 people) had not been prescribed any gastroprotective agent, and 18% of those using clopidogrel together with a PPI received omeprazole or esomeprazole, a combination that the British regulatory agency advises against.(1)This underscores that the objective is not to withdraw PPIs indiscriminately, but to adjust their use to the indication.

Supported indications and situations in which it should not be discontinued

According to the American Gastroenterological Association, deprescribing should be considered in every patient without a definitive indication for chronic PPI, and the decision to discontinue should be based solely on the absence of an indication, not on fear of adverse events.(6)This distinction is relevant because most patients with GERD (approximately 70%) have endoscopy-negative reflux, in which PPIs provide less symptomatic relief and short courses of 4 to 8 weeks are recommended.(1,10,11)Peptic ulcer guidelines, in turn, consider courses of up to 12 weeks, unless there is a maintenance indication, such as the presence of gastrointestinal risk factors or daily use of nonsteroidal anti-inflammatory drugs (NSAIDs).(12,13)

Conversely, the AGA recommends not considering discontinuation in complicated GERD (severe erosive esophagitis, esophageal ulcer, or peptic stricture), in Barrett's esophagus, in eosinophilic esophagitis, or in idiopathic pulmonary fibrosis, and neither in patients at high risk of upper gastrointestinal bleeding, a risk that should be assessed using an evidence-based strategy before deprescribing. In those with a chronic indication who receive 2 daily doses, it suggests considering a switch to 1 daily dose.(6)Table 1 summarizes these approaches.

Long-term safety: association does not imply causation

Prolonged PPI use has been associated with enteric infections, pneumonia, chronic kidney disease, vitamin and mineral deficiencies, fractures, and cardiovascular events,(14)associations that have fueled both patients' concern and interest in deprescribing. However, it is advisable to assess the quality of this evidence.

An umbrella review of meta-analyses of cohort studies and randomized trials examined 91 associations in cohort studies: 52 were statistically significant, but none remained supported by convincing evidence after sensitivity analyses. Fracture at any site and chronic kidney disease in older adults reached convincing evidence in the primary analysis, and COVID-19 mortality showed weak evidence of an association. In the meta-analyses of trials, 38 of 63 associations were significant, but none were supported by high- or moderate-quality evidence. The authors conclude that most adverse outcomes attributed to PPIs probably reflect confounding factors.(15)

Table 1. Proposed management for prolonged IBP use in primary care

Patient situation	Proposed behavior
No definitive indication for chronic use	Consider a deprescribing trial, with tapering or discontinuation.(6)
Chronic indication with 2 times daily dosing	Consider switching to 1 daily dose.(6)
Complicated GERD (severe erosive esophagitis, esophageal ulcer, peptic stricture)	In general, do not discontinue.(6)
Barrett's esophagus, eosinophilic esophagitis, or idiopathic pulmonary fibrosis	In general, do not discontinue.(6)
High risk of upper gastrointestinal bleeding (e.g., daily NSAIDs with gastrointestinal risk factors)	Do not deprescribe; assess the risk before any change.(6,12,13)
Mild symptoms or reflux with negative endoscopy	Gradual reduction or on-demand use.(14)
Recurrent symptoms after discontinuation	As-needed use instead of complete discontinuation; reassess.(14)

IBP: proton pump inhibitors; ERGE: gastroesophageal reflux disease; AINE: nonsteroidal anti-inflammatory drugs.

Gastric cancer deserves a separate comment. A population-based cohort study from the United Kingdom, with a new user and active comparator design (PPIs versus H2 receptor antagonists), described a 45% increased risk, which increased with cumulative duration of use, although the absolute risk remains low.(16) These findings do not justify withdrawing an indicated PPI, but reinforce the desirability of periodically reassessing the need for treatment, so that prolonged exposure is reserved for those who need it.

Acid rebound and symptoms following discontinuation

The reappearance of symptoms is the main perceived barrier to deprescribing. After prolonged treatment, rebound acid hypersecretion, i.e. a compensatory increase in gastric secretion once the PPI has been withdrawn, may occur.(17) In two randomized, double-blind, placebo-controlled trials conducted in asymptomatic healthy volunteers (48 in Sweden and 120 in Denmark), those who received PPIs developed acidic symptoms after withdrawal and those who received placebo did not; symptoms appeared in 40% to 50% of PPI-exposed subjects.(17) In terms of duration, after more than one year of treatment, rebound lasted more than eight and less than 26 weeks in a study reported by that review.(17)

In patients, symptomatic recurrence depends on which patients are deprescribed. In 3 trials comparing discontinuation with daily treatment, recurrence in the discontinuation arm ranged from 20% to 68%; the success rate was higher when patients were selected because of treatment inappropriateness or uncomplicated GERD, and lower in erosive esophagitis.(14) In the 2 studies included in that review that compared abrupt versus gradual withdrawal, no significant differences were found in PPI resumption,(14) and the AGA considers both modalities acceptable.(6) Nevertheless, it is reasonable to anticipate rebound and explain to the patient that transient symptoms do not necessarily mean that the PPI remains indispensable.

Deprescribing strategies: reduce, space out, or discontinue

The available options are direct discontinuation, gradual dose reduction, switching from two daily doses to one, and on-demand use. (6,14) The systematic review of 66 studies concluded that it is not possible to recommend a universal strategy: the choice should be based on patient assessment and clinical judgment. The same review suggests that complete discontinuation may not be appropriate for recurrent symptoms, where on-demand use is an alternative, and that deprescribing is more applicable in mild illness and symptoms, where gradual reduction may mitigate the rebound associated with abrupt discontinuation.(14)

Erosive esophagitis, longer prior PPI treatment duration, and greater symptom severity were identified among the factors associated with deprescribing failure; in one study, irritable bowel syndrome, daily reflux symptoms, and concomitant dyspepsia were independent predictors.(14) In practice, since rebound can persist for weeks,(17) it seems prudent to schedule follow-up and agree with the patient on what to do if symptoms reappear.

Interventions in primary care: what works and for whom

In the systematic review of 66 studies, the most effective strategies shared 3 elements: colla-

boration among several professionals, clinical decision support algorithms, and patient participation. In randomized trials reporting this outcome, implementation rates ranged from 24% to 67%, and in the remaining studies, they ranged from 38% to more than 90%, with the lowest values in interventions aimed directly at the patient.(14)

1 cluster-randomized trial in general practices in Germany evaluated an electronic shared decision-making tool (arriba-PPI) in adults with at least 6 months of PPI use. In 49.2% of consultations with the tool, the physician and the patient decided to reduce or discontinue the PPI; at 6 months, defined daily doses decreased by 22.3% (95% CI 18.55-25.98), versus 3.3% in the control group (95% CI -7.18 to +0.62). At 12 months, the reduction remained stable in the intervention group, while the control group showed a decrease of 10.2%, bringing the results of both groups closer together.(18)

At a family medicine center in Beirut, a trial of 140 patients with chronic use evaluated an informational and motivational patient leaflet along with a deprescribing algorithm for clinicians: at six months, the proportion of participants who reduced or discontinued PPIs was 87.1% in the intervention group and 28.6% in the control group, and gap symptoms decreased over time in those who reduced or discontinued. (14,19) This is a small, single-center study, but it illustrates the potential for simple interventions.

These interventions share a common feature: they are low-cost (algorithms, educational material, and systematic medication review). This makes them potentially transferable to primary care systems with limited resources, although their effect must be verified in each context.

Barriers and considerations for practice

The main barriers described are lack of time, absence of guidelines applicable to the local setting, and prescriber attitudes, in addition to the patient's fear of symptom recurrence.(14)The most extensive systematic review suggests that the most appropriate approach is to design interventions tailored to the organizational context: where there is close collaboration with pharmacists, pharmacist-supported deprescribing may be effective, and where medical records are digitized, electronic decision support is a strategic option.(14)

Based on the cited recommendations, the following sequence can be proposed for the family physician: identify chronic users and document the indication; rule out situations in which it should not be discontinued and assess the risk of gastrointestinal bleeding; agree with the patient on a gradual reduction or an as-needed regimen, anticipating possible rebound; and document the decision and schedule its reassessment.(6)This sequence represents a synthesis of the reviewed literature and is not a validated protocol.

The evidence has limitations that should be acknowledged: considerable methodological heterogeneity, a predominance of pragmatic studies without a control group, and short-term follow-up outcomes.(14)Furthermore, the studies included in the most extensive systematic review originated from Europe, North America, Asia, and Australia,(14)which limits direct extrapolation to primary care in Latin America and justifies the conduct of local studies.

CONCLUSIONS

A significant proportion of long-term PPI treatments in primary care lack a documented indication and periodic review, whereas some patients at gastrointestinal risk do not receive the gastroprotection they need. The evidence linking PPIs to adverse outcomes is mostly observational and of low certainty; therefore, deprescribing should be based on the absence of an indication and not on fear of adverse effects. The most effective interventions combine decision algorithms for clinicians, patient education, and shared decision-making; gradual reduction or on-demand use allows for the management of rebound in mild disease, whereas complicated reflux disease, Barrett's esophagus, eosinophilic esophagitis, and high risk of gastrointestinal bleeding generally require continuation of treatment. Integrating periodic review of PPIs into primary care consultations is a low-cost measure with the potential to improve safety and therapeutic rationality.

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