REVIEW ARTICLE

EFFECTS OF DEPRESCRIBING OF PROTON PUMP INHIBITORS

EFEITOS DA DESPRESCRIÇÃO DE INIBIDORES DE BOMBA DE PRÓTONS

Rebeca Martins de Paula da Mota Silveira[1/+], Fábio Menezes de Melo[2]

[1] Medical Student at the Faculdade de Medicina de Olinda – FMO; [2] Gastroenterology Specialist and Professor at the Faculdade de Medicina de Olinda - FMO

ABSTRACT

Introduction: Proton pump inhibitors (PPI) are the most prescribed medications worldwide due to their effectiveness in treating gastric diseases, low toxicity, and ability to inhibit acid secretion. However, prolonged use of PPI may lead to serious complications and health risks for patients. Increasing attention has been given to the deprescription of PPI to reduce dosage or discontinue medications that may cause harm — considering the benefits, treatment purpose, convenience, age of the patient, and cooperation. **Objective:** To conduct a literature review on the positive and negative effects of deprescribing PPI. **Methods:** A narrative review was conducted using the Brazilian Virtual Health Library, SCIELO, and LILACS databases, with the following descriptors: deprescription, toxicity, gastric acid, and esophagitis. A total of 15 articles published in the last 12 years were selected, focusing on three main themes: PPI effect on gastric secretion, complications associated with prolonged use, and the importance of deprescription. **Results:** Several patients self-medicate or continue previous treatments without medical supervision. Moreover, using multiple medications without prior analysis for pathology may lead to complications. In this context, deprescription (especially of PPI) plays a key role in preventing adverse effects, worsening of diseases, and complications of pre-existing conditions. Deprescription also enhances patient safety by reducing exposure to adverse drug reactions, medication errors, drug interactions, and unnecessary hospitalizations. **Conclusion:** PPI are unnecessary for all digestive disorders but effective for gastric conditions. Therefore, a multidisciplinary team is essential for evaluating treatment and implementing safe deprescription strategies. Deprescription should follow a comprehensive therapeutic approach aimed at minimizing harm to the health and well-being of the patient.

Keywords: Deprescription; Toxicity; Gastric acid; Esophagitis.

RESUMO

Introdução: Entre os medicamentos mais prescritos mundialmente encontram-se os inibidores da bomba de prótons (IBPs), amplamente utilizados no tratamento de doenças gástricas por sua eficácia, baixa toxicidade e ação sobre a secreção ácida. No entanto, o uso prolongado desses fármacos pode causar sérias complicações e prejuízos à saúde dos pacientes que os utilizam de forma contínua. Com o intuito de reduzir a dose ou interromper o uso de medicamentos potencialmente prejudiciais, tem-se investido na desprescrição de IBPs, processo que deve considerar os benefícios, a finalidade do tratamento, a comodidade, a idade e a cooperação do paciente. **Objetivo:** Realizar uma revisão de literatura sobre os efeitos negativos e positivos da desprescrição dos inibidores da bomba de prótons. **Métodos:** Revisão narrativa realizada nas bases de dados da Biblioteca Virtual em Saúde (BVS), SCIELO e LILACS, utilizando os descritores: desprescrição, toxicidade, ácido gástrico e esofagite. Foram selecionados 15 artigos publicados nos últimos 12 anos, abordando três núcleos temáticos: ação dos IBPs sobre a secreção gástrica, complicações decorrentes do uso prolongado e a importância da desprescrição. **Resultados:** Muitos pacientes recorrem à automedicação ou mantêm tratamentos anteriores sem acompanhamento médico. Além disso, o uso simultâneo de múltiplos fármacos, sem análise adequada da patologia, pode resultar em diversas complicações. Nesse contexto, a desprescrição, especialmente dos IBPs, surge como estratégia para prevenir efeitos indesejados, agravamento de doenças e complicações associadas a condições pré-existentes. Sua importância reside em evitar o uso prolongado e indiscriminado desses medicamentos, garantindo a segurança do paciente e minimizando riscos como reações adversas, erros de medicação, interações medicamentosas e hospitalizações.

Conclusão: Embora os IBPs sejam eficazes no tratamento de doenças gástricas, são desnecessários em

alguns casos de patologias digestivas. Assim, destaca-se a relevância da atuação de uma equipe multidisciplinar na avaliação do tratamento e na condução da desprescrição. Conclui-se que essa prática requer uma abordagem integral, voltada à escolha terapêutica que cause o menor impacto possível à saúde e à qualidade de vida do paciente.

Palavras-chave: Desprescrição. Toxicidade. Ácido gástrico. Esofagite.

INTRODUCTION

Using multiple medications is effective and sometimes necessary for addressing specific clinical conditions. However, the potential harm of polypharmacy often outweighs the benefits, raising concerns that have been included among the three priority areas of the Third Global Patient Safety Challenge of the World Health Organization.[1]

This challenge seeks to dismantle the concept of polypharmacy, commonly seen in the treatment of conditions such as gastric disorders, through strategies such as deprescription. Deprescription is one of the key approaches used to reduce polypharmacy and, consequently, its associated risks.[2,3]

Among the most prescribed medications worldwide are proton pump inhibitors (PPI). These drugs have been widely used to treat gastric conditions due to their efficacy in suppressing acid secretion and relatively low toxicity.[4]

Although effective in short-term use, long-term PPI therapy has been related to serious complications since it hinders the absorption of vitamins and minerals that depend on gastric acidity. Moreover, the altered gastric pH may impair the absorption of other medications, potentially compromising their therapeutic effect[5].

To reduce exposure to potentially harmful medications, significant efforts have been made to deprescribe PPIs. This process must consider the benefits and purpose of treatments, patient convenience, age, and cooperation.[6]

Deprescribing is not a random decision and requires identifying and discontinuing the use of unnecessary, ineffective, unsafe, or potentially inappropriate medications. Although PPI may be beneficial, simultaneous use with other drugs may render them ineffective and lead to harmful effects.

This study is justified by scientific evidence and empirical observation suggesting that despite being intended for short-term treatment, patients often continue taking PPI indefinitely without knowing their long-term consequences. The present study is a narrative review aiming to compile secondary data on PPI use and discuss its implications.

This research highlights current knowledge, presenting new perspectives on the topic, and supporting the notion that inappropriate PPI prescription may be harmful and compromise patient health.

METHODS

This study is a narrative review. The data presented are based on scientific articles published between 2007 and 2019. Books, doctoral theses, and a manual published by the Brazilian Ministry of Health were also considered to support the theoretical and historical foundation and enrich the discussion.

The literature search used the Brazilian Virtual Health Library SCIELO, and LILACS databases. The following descriptors were used: deprescribing, toxicity, gastric acid, and esophagitis. Abstracts were reviewed, and articles were selected according to the following inclusion criteria: publications from the last 12 years, available online, and written in English.

From this perspective, three thematic areas emerged: PPI effect on gastric secretion, complications associated with prolonged use, and the importance of deprescribing PPI.

RESULTS AND DISCUSSION

PPI effect on Gastric Secretion

The H^+/K^+ ATPase enzyme (proton pump) is responsible for secreting hydrochloric acid into the stomach lumen. These enzymes are activated by different stimuli generated by histamine, gastrin, and acetylcholine, and are involved in the acid production process using hydrogen (H^+) and potassium (K^+) ions exchange, a process that requires ATP.[4]

PPI inhibits gastric acid production, making the gastric pH more alkaline. These drugs block the final step in the hydrochloric acid production pathway in gastric disorders. This mechanism provides strong acid suppression, making PPI the first-line therapeutic option.[7]

Moreover, the covalent binding of the drug to the enzyme occurs at the cysteine residue, leading to irreversible inhibition. After this interaction, the proton pump is not regenerated, and acid production resumes only after synthesizing a new enzyme. This irreversible inhibition ensures an effect that lasts between 24 and 48 hours.[6]

Complications: Long-Term Use of PPI

The currently available PPI in the pharmaceutical market include omeprazole, lansoprazole, pantoprazole, esomeprazole, dexlansoprazole, and rabeprazole.[3] Among these, omeprazole is the most prescribed drug[8] for treating digestive system disorders, such as gastric and duodenal ulcers, gastroesophageal reflux disease, and erosive esophagitis.[9]

A study conducted in Germany with 74,000 individuals aged 75 years or older found a high prevalence of dementia among patients undergoing continuous PPI treatment. The most frequently used PPI included omeprazole, esomeprazole, lansoprazole, pantoprazole, and rabeprazole.[10]

Chronic PPI usage might increase the risk of fractures,[11] as PPI may inhibit the proton pumps in osteoclasts, thus interfering with bone metabolism.[12]

A retrospective study in Pennsylvania showed that prolonged PPI use reduces calcium absorption and bone integrity. Patients who used PPI for more than one year had a 44% increased risk of fractures in the coccygeal region.[13]

Research by Herzin and colleagues revealed that reduced gastric acidity may lead to bacterial overgrowth and subsequent pneumonia in outpatient and hospitalized patients.[12] This microbial proliferation occurs because the elevated gastric pH (above 4) facilitates their growth. On the other hand, when the stomach pH returns to its normal acidic state, microbial growth is suppressed.

Regarding gastric alterations, PPIs are indicated for treating peptic ulcers (duodenal and gastric), reflux esophagitis, and Zollinger-Ellison syndrome. However, a controversy regarding their use exists, as PPI has been associated with proliferative changes in the gastric mucosa.[14]

Additionally, when combined with medications to treat *Helicobacter pylori*, PPI may contribute to gastric cancer due to the change from an antral-predominant chronic gastritis to a corpus-predominant chronic gastritis, which increases the risk of gastric neoplasia.[15]

Due to reduced gastric acidity, long-term use of PPI also affects absorbing other micronutrients, such as vitamin B12 and iron.[15] In older patients who may already suffer from gastric atrophy, often caused by *H. pylori* infection, chronic PPI use may further reduce serum vitamin B12 levels.[15] Vitamin B12 deficiency exacerbates conditions, such as dementia, especially in older adults.[10]

As for iron absorption, heme and non-heme iron may be affected during long-term PPI treatment.[16] However, this effect is generally mild and has not been directly linked to an increased risk of iron deficiency.[15]

Importance of PPI Deprescription

Several patients self-medicate- or continue previous treatments without medical supervision. Furthermore, the use of multiple drugs without prior analysis of patients conditions may lead to several complications, as previously discussed.

Therefore, deprescribing medications, particularly PPI, is one of the strategies to avoid undesirable effects, new illnesses, and conditions worsening. Deprescription must follow specific steps and needs to be a medical decision that should be planned and supervised, since dose reduction or abrupt discontinuation may also lead to adverse consequences, such as symptom relapse.[3]

Thus, this approach also aims to bring together interdisciplinary healthcare teams in the process and to ensure monitoring for adverse withdrawal reactions, especially in older patients.[11]

The importance of deprescription lies in preventing PPI from being prescribed for an indefinite period, often without the awareness of patient of the reasons for the treatment. It also promotes patient safety by avoiding exposure to adverse reactions, medication errors, drug interactions, and hospitalizations resulting from such complications.[2]

Deprescription should be considered particularly in older patients who have completed at least four weeks of PPI therapy. Tapering the daily dose, discontinuing treatment, or switching to an as-needed basis is advisable. An H2 receptor antagonist may also be considered as an alternative to PPI.[5]

FINAL CONSIDERATIONS

PPIs are used empirically, either by prescrip-

tion or self-medication, to treat or prevent digestive diseases.

PPI is the most advanced pharmacotherapeutic option for treating digestive disorders (the most potent inhibitors of acid secretion), playing a key role in managing several gastric pathologies.

However, PPI use is unnecessary for some digestive disorders. These findings highlight the importance of a multidisciplinary team during treatments to reduce the prescription of gastric secretion inhibitors.

Finally, to implement deprescription, we suggest adopting a comprehensive approach to treatment and selecting the least harmful option to their health.

REFERENCES

1. World Health Organization. Medication Without Harm – Global Patient Safety Challenge on Medication Safety. Geneva:World Health Organization; 2017.
2. Garfinkel D, Ilhan B, Bahat G. Routine deprescribing of chronic medications to combat polypharmacy. Therapeutic Advances in Drug Safety 2015; 6: 212-33.
3. Mcgrath K, .Hajjar ER, Kumar C, Hwang C, Salzman B. Deprescribing: a simple method for reducing polypharmacy. J Fam Pract 2017; 66: 436-45.
4. Morschel CF, Mafra D, Carraro EJC. Inibidores da bomba de prótons e sua relação com a doença renal. J. Bras. Nefrol. 2018, 40(3):301-6.
5. Strand DS, Kim D, Peura DA. 25 Years of Proton Pump Inhibitors: a comprehensive review. Gut Liver. 2017; 11: 27-37.
6. Brinkworth MD, Aouthmany M, Sheeha NM. Histamine 2 Receptor Antagonists and Proton Pump Inhibitors. Dermatitis 2016; 27: 100-9.
7. Braga MP, Silva CB, Adams AIH. Inibidores da bomba de prótons: revisão e análise farmacoeconômica. Saúde. 2011; 37: 19-32.
8. Brewster UC, Perazella, MA. Lesão renal aguda após terapia com inibidor da bomba de prótons. Kidney Int. 2007; 71: 589-93.
9. Nadri Q, Althaf MM. Granulomatous tubulointerstitial nephritis secondary to omeprazole. BMJ Case Rep 2014;2014. pii: bcr2014203842
10. Gomm W, von Holt K, Thomé F, Broich K, Maier W, Fink A, et al. Association of proton pump inhibitors with risk of dementia: a pharmacoepidemiological claims data analysis. JAMA Neurol 2016.
11. Kuller L. Do proton pump inhibitors increase the risk of dementia? JAMA Neurol 2016.
12. Herzig SJ, Howell M, Ngo LH, Marcantonio ER. Acid- suppressive medication. Use and the risk for hospital- acquired pneumonia. J Amn Med Assoc. 2009; 301: 2120-8.
13. Ho PM, Maddox TM, Wang L, Fihn S, Jesse R, Peterson ED, et al. Risk of adverse outcomes associated with concomitant use of clopidogrel and proton pump inhibitors following acute coronary syndrome. J Am Med Assoc. 2009; 301: 937-44.
14. Menegassi VS, Czeczko LEA, Czeczko LSG, Ioshii SO, Pisani JC, Ramos Júnior O. Prevalência de alterações proliferativas gástricas em pacientes com uso crônico de inibidores de bomba de prótons. Arq Bras Cir Dig:2010; 23: 145-9.
15. Thomson AB, Sauve MD, Kassam N, Kamitakahara H. Safety of the long-term use of proton pump inhibitors. World J Gastroenterol. 2010; 19: 2323-30.
16. Sohaily SA, Duggan A. Long term management of patients taking proton pump inhibitors. Austr Pres. 31: 5-7, 2008.