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Behind the proton pump inhibitor prescription: an international survey on physician practices and knowledge

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HIGHLIGHTS

- The study aims to evaluate physician prescribing patterns, assess their knowledge of proton pump inhibitors, and identify factors influencing their knowledge.
- An online survey of Latin American and Spanish physicians assessed proton pump inhibitor usage patterns and case-scenario responses, categorizing knowledge, and conducting subgroup analysis based on training, experience, specialty, and literature review timing.
- Thirty-eight percent of surveyed physicians commonly prescribed proton pump inhibitors, and among them, 80% were unfamiliar with deprescribing strategies, with 54.4% rarely reviewing ongoing indications.
- Sufficient knowledge was correlated with recent literature reviews and medical specialty affiliations.

ABSTRACT – Background – Proton pump inhibitors (PPIs) are widely prescribed worldwide, often resulting in their overuse. Consequently, it is essential to identify the likely causes of this overuse to facilitate their appropriate prescription. **Objective –** This study aims to assess physician prescribing patterns, their knowledge of PPIs, and factors affecting their knowledge. **Methods –** An online survey was conducted among Latin American and Spanish physicians, collecting the following data: professional information, patterns of PPI usage, familiarity with published evidence, and the management approach in three hypothetical case-scenarios. Participant knowledge was categorized as sufficient or insufficient based on the results of the case scenarios. Subsequently, subgroup analysis was performed based on physician training level, years in practice, specialty, and time since the last PPI literature review. **Results** – A total of 371 physicians participated in the survey. Thirty-eight percent frequently prescribe PPIs, primarily for prophylactic purposes (57.9%). Eighty percent were unfamiliar with PPI deprescribing strategies, and 54.4% rarely reviewed the ongoing indication of patients taking a PPI. Sixty-four percent demonstrated sufficient knowledge in the case-scenarios. A significant association was observed between specialty type (medical vs surgical: 69.4% vs 46.8%, $P<0.001$), the timing of the PPI indication literature review (<5 years vs >5 years: 71.4% vs 58.7%, $P=0.010$), and sufficient knowledge. **Conclusion –** While most participants prescribed PPIs regularly and for prophylaxis purposes, the majority were unfamiliar with deprescribing strategies and rarely reviewed ongoing indications. Sufficient knowledge is correlated with recent literature reviews and medical specialty affiliation.

Keywords – Proton pump inhibitors; drug therapy; inappropriate prescribing; deprescription.

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INTRODUCTION

Acid peptic disorders, including gastritis, peptic ulcer diseases, and gastroesophageal reflux disease, represent highly prevalent gastrointestinal conditions. Consequently, acid-suppressive therapies like proton pump inhibitors (PPIs) and histamine 2 receptor antagonists (H2RAs) have become extensively prescribed in both primary and specialized healthcare settings worldwide[1]. Currently, the number of prescriptions for PPIs in the United States is estimated to be about 113 million per year, positioning these drugs among the top twenty most frequently prescribed medications during office visits in that country[2,3]. In addition, it has been reported that approximately one out of five elderly individuals in the United States take PPIs, and a significant portion of them use these medications on a long-term basis[4-6]. Furthermore, in the United Kingdom, there has been reported a substantial increase in PPI users from 0.2% in 1990 to 15.0% in 2014[7]. These trends may be explained by the relative safe side effect profile, good tolerance and their availability over-the-counter in many countries[1,8].

The potential for serious side effects, such as *Clostridium difficile* and other enteric infections, intestinal colonization by multidrug-resistant microorganisms, hospital- and community-acquired pneumonia, dementia, osteoporotic fractures, hypomagnesemia, acute kidney injury, and chronic kidney disease, has made the overprescription of PPIs of significant concern in recent decades[8-12]. Moreover, overprescribing PPIs also carries a considerable economic burden. For instance, in the United States, the annual expenditure on PPI prescriptions is estimated to amount to approximately 10 billion dollars[13,14]. Furthermore, it is estimated that nearly £2 billion is spent unnecessarily worldwide each year as a result of PPI prescription[15,16].

Considering the reasons mentioned above, evaluating the potential causes behind the overprescription of these medications is essential for implementing strategies aimed at promoting a more rational and appropriate use. Therefore, studying the patterns of PPI usage and the level of knowledge regarding their use is important since it may be related to PPI overuse. We conducted an international survey with the aim of identifying prescribing patterns of PPIs among physicians and assessing their level of knowledge about these drugs. Additionally, we aimed to identify potential factors that could influence their knowledge levels.

METHODS

Ethics

This study was approved by the ethical review board of *Escuela de Ciencias de la Salud "Francisco Battistini Casalta", Universidad de Oriente*, Venezuela.

Study design

An observational cross-sectional study was conducted through an online survey among physicians, involving participation from interns, residents and attending physician across various medical adult specialties in Latin America and Spain. There was no explicit exclusion criterion.

In this study, the estimated sample size was calculated using the Raosoft online sample size calculator (Raosoft Inc., Seattle, Washington). The selected settings were as follows: a confidence level of 95%, an assumed response distribution of 50%, and a maximum margin of error set at 5%. As a result, the determined sample size for the study was 341.

Survey and data collection

A group of gastroenterologists designed the survey using Google Forms® (Google, Mountain View, California) and formulated the questionnaire in accordance with established guidelines for PPI usage and previous research[3,17,18]. Subsequently, it was distributed to various physician networking groups through emails and WhatsApp® messages. Data were collected from May to June 2023. Participants completed the survey on a voluntary and anonymous basis.

The survey was divided into three parts, comprising a total of 18 questions. The first part collected information on physicians' demographics and professional information. In the second section, participants were queried about their patterns of PPI usage in their practice and their familiarity with published evidence regarding PPI use and its associated side effects. Finally, the third part included three hypo-

thetical clinical scenarios in which physicians were asked to select the management option they would employ in their practice for each scenario. The correct answers were obtained from evidence-based literature[3,18-20]. The total knowledge score was computed by summing the correct responses from the three clinical scenarios, with one point assigned to each correct answer. Subsequently, participants were categorized into two groups: those with sufficient knowledge (scoring 2–3 points) and those with insufficient knowledge (scoring 0–1 point).

The study instrument can be found in the supplementary material 1.

Statistical analysis

In the case of a normal distribution, continuous variables were expressed as mean ± standard deviation (SD) while they were expressed as the median and interquartile range in a nonnormal distribution. Categorical variables as frequencies and proportions. A subgroup analysis was performed to assess the knowledge level on the following factors: the physician training level (trainee physicians vs. attending physician), number of years in practice (≤10 years vs >10 years), type of specialty (medical specialties vs surgical specialties), and time since the last review of PPIs indications (<5 years vs >5 years). Chi-square or 2-tailed Fisher's exact test were applied for categorical data. Statistical analyzes were calculated by using IBM® SPSS® Statistics 21.0

RESULTS

A total of 371 physicians took part in the survey, with the highest proportion practicing in Venezuela (70.9%), followed by Spain (23.5%) and Chile (5.7%). The mean age was 36.3±11.5 years. The majority of participants were residents (41.5%), followed by attending physicians (40.2%). Internal medicine (24.5%) and family medicine (13.5%) were the two most frequent specialties. The median number of years in practice was 10 years. The baseline features of the participants are summarized in TABLE 1.

TABLE 2 shows that 38.3% of the participants prescribe PPIs often. The majority of responders (57.9%) indicated that they prescribe this medication for prophylactic purposes in the inpatient set-

TABLE 1. Baseline characteristics of the physicians who answered the survey.

Variables	Values (n=371)
Age (years), mean (± SD)	36.3 (±11.5)
Sex, n (%)	
Female	243 (65.5)
Male	128 (34.5)
Country, n (%)	
Venezuela	263 (70.9)
Spain	87 (23.5)
Chile	21 (5.7)
Physician training level, n (%)	
Attending	149 (40.2)
Resident	154 (41.5)
Intern	68 (18.3)
Specialty, n (%)	
Internal medicine	91 (24.5)
Family Medicine	50 (13.5)
General surgery	46 (12.4)
Traumatology and orthopedic surgery	31 (8.4)
Anesthesiology	19 (5.1)
Cardiology	18 (4.9)
Nephrology	14 (3.8)
Psychiatry	14 (3.8)
Neurology	13 (3.5)
Gastroenterology	12 (3.2)
Others	46 (12.4)
Number of years in practice, median (IQR)	10 (3–23)
Patients seen per week, (n) (%)	
1–20	112 (30.2)
21–50	139 (37.5)
51–100	80 (21.6)
>100	40 (10.8)

TABLE 2. Prescription patterns of proton pump inhibitors.

Variables	Values (n=371)
Prescription frequency, n (%)	
Always	28 (7.5)
Very often	112 (30.2)
Often	142 (38.3)
Rarely	89 (23.9)
Patient care setting for prescriptions, n (%)	
Inpatient setting	209 (56.3)
Outpatient setting	162 (43.6)
Intent of prescription	
Prophylactic	215 (57.9)
Therapeutic	156 (42.0)
Most used route of administration, n (%)	
Intravenous	205 (55.3)
Oral	166 (44.7)
Review frequency of the ongoing indication of patients taking a PPI, n (%)	
Always	24 (6.5)
Often	115 (31.0)
Rarely	202 (54.4)
Very rarely	30 (8.1)

ting (56.3%), with the intravenous route being the most commonly employed mode of administration (55.3%). Eighty percent answered that they did not know strategies for deprescribing PPIs. Additionally, the majority of participants (54.4%) reported that they rarely review the ongoing indication of patients taking a PPI.

Regarding the latest literature review on PPI indications, 39.9% of physicians reported having conducted such a review a few months ago, while 39.6% indicated that their most recent review was between 1 and 5 years ago. On the other hand, when asked about their most recent literature review concerning the adverse effects of PPIs, 43.4% of participants indicated that their last review had taken place between 1 and 5 years ago. FIGURE 1 offers a visual summary of these results.

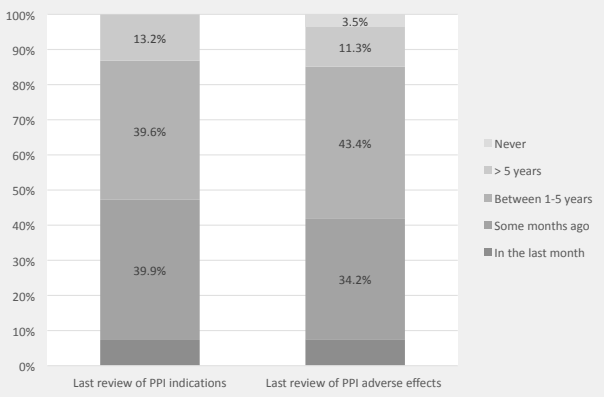

FIGURE 1. Latest review of literature on indications and adverse effects of proton pump inhibitors.

The use of nonsteroidal anti-inflammatory drugs (NSAIDs)/aspirin in patients >65 years was the prophylactic indication of PPIs that participants chose most frequently (52.3%), followed by NSAIDs/aspirin in combination with steroids (45.2%), stress ulcer prophylaxis (SUP) in non-critically ill patients (44.7%), and antibiotic users (38.9%). (FIGURE 2).

Two hundred forty respondents surveyed (64.7%) had sufficient knowledge, achieving scores ranging from 2 to 3 points based on their responses to the hypothetical clinical scenarios. According to the results of the chi-square test, the variables significantly associated with sufficient knowledge were type of specialty (medical specialty vs surgical specialty: 69.4% vs 46.8%, $P<0.001$) and timing of the last review of PPI indications (<5 years vs >5 years: 71.4% vs 58.7%, $P=0.010$). However, no significant associations were found with physician training level or years in practice (TABLE 3).

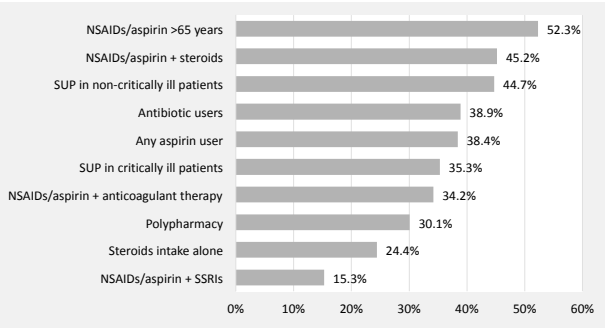

FIGURE 2. Physician responses regarding prophylactic indication of proton pump inhibitors.
NSAIDs: nonsteroidal anti-inflammatory drugs; SUP: stress ulcer prophylaxis; SSRIs: selective serotonin reuptake inhibitors.

TABLE 3. Analysis of factors associated with knowledge level in proton pump inhibitors prescription.

Variables	Sufficient knowledge (n=240)	Insufficient knowledge (n=131)	*P* value
Physician training level, n (%)			0.092
Attending physician	104 (69.8)	45 (30.2)	
Trainee physician	136 (61.3)	86 (38.7)	
Number of years in practice, n (%)			0.759
>10 years	191 (64.3)	106 (35.7)	
<10 years	49 (66.2)	25 (33.8)	
Type of specialty, n (%)			<0.001
Medical specialty	204 (69.4)	90 (30.6)	
Surgical specialty	36 (46.8)	41 (53.2)	
Last review of PPIs prophylactic indications, n (%)			0.010
>5 years	115 (58.7)	81 (41.3)	
<5 years	125 (71.4)	50 (28.6)	

DISCUSSION

Omeprazole was the first PPI, released in 1989[21]. Since then, PPIs have gained a prominent position among the most extensively prescribed medications globally. It is noteworthy that omeprazole is currently included in the WHO list of essential medications[22]. Paradoxically, their good profile and wide availability without prescription have contributed to the pre-

valent issue of overprescription[6]. PPIs are considered to be overprescribed when they are prescribed outside of guideline recommendations, or when their usage continues without the necessary reevaluation for persistent conditions[23]. According to numerous studies conducted worldwide, the rate of overprescription of PPIs ranges from 35% to 82%[24-28]. These numbers highlight the magnitude of the issue and its potential impact on healthcare expenses, as well as the potential adverse effects related to long-term use. Given these considerations, it is important to identify the factors contributing to overprescribing, which may include the pattern of PPIs usage and the level of knowledge of the physicians.

Based on the findings of the current survey, a majority of respondents prescribe PPIs routinely, in an inpatient setting, and for prophylactic purposes. The intravenous route was the most frequently chosen method for administering PPIs. This trend has been documented in numerous earlier studies that found intravenous PPIs are widely utilized in hospital practice, frequently in contexts where their usage is inappropriate[29-32]. Opting for intravenous administration, like any other drug administered this route, may expose patients to unnecessary risks compared to the oral route, including susceptibility to infections, phlebitis, and even the potential for air embolism. Consequently, employing the intravenous route should be reserved for specific scenarios, such as the treatment of upper gastrointestinal bleeding, stress ulcer prophylaxis (SUP), gastric hypersecretion syndromes, and situations where oral intake is not feasible[32]. In cases where patients are not allowed to consume anything orally or experience dysphagia, the administration of oral dispersible tablets emerges as a viable substitute that merits thoughtful consideration[33].

Regarding the prophylactic indications of PPIs, most physicians answered that the use of NSAIDs/aspirin in patients older than 65 years (52.3%) and the use of such medications in combination with steroids (45.2%) are prophylactic indications. These indications are well-established and supported by guidelines. On the other hand, it is noteworthy that a significant number of respondents indicated that SUP in non-critically ill patients, antibiotic use, any use of NSAIDs/aspirin, polypharmacy, and the use of steroids alone are prophylactic indications for PPIs. These reasons do not align with current guidelines, which is consistent with the findings of previous studies identifying these prophylactic indications as frequent contributors to the overprescribing of PPIs[25,28,34,35].

One key factor that emerges as a possible explanation for this trend is the frequency of professional reviews. In the current survey, almost 40% of the respondents reported that their most recent review of the literature on indications for PPIs had taken place within the past one to five years, while 13% had not conducted such a review in over five years. Additionally, the chi-square test revealed that the timing of the last review of indications more than 5 years ago was associated with insufficient knowledge about the use of PPIs in clinical scenarios. These findings emphasize the need for continuous medical education to ensure that physicians remain up-to-date with current guidelines.

An interesting finding in the current study was the correlation between the type of specialty and the level of knowledge regarding PPIs. In most cases, medical specialties exhibited sufficient knowledge in the proposed clinical scenarios, possibly owing to their continuous contact with patients with chronic conditions that require prophylactic PPI treatments. In contrast, surgical specialties, which primarily focus on surgical interventions, might place relatively less emphasis on clinical pharmacotherapy, resulting in a less detailed knowledge of PPIs. The discrepancy in clinical pharmacotherapy knowledge between medical and surgical specialties has been previously highlighted in a study conducted by van den Hanenberg et al. Their research reported that medical doctors achieved higher test scores in pharmacotherapy and polypharmacy knowledge compared to their surgical counterparts[36]. In light of these findings, it is recommended that surgical training programs contemplate the integration of more comprehensive pharmacotherapy education. This could involve the incorporation of pharmacological coursework or clinical rotations that concentrate on medications frequently encountered in surgical practice such as PPIs.

In the present study, it was found that more than half of the participants (54%) reported that they rarely reviewed the indications for the use of PPIs in patients prescribed such medications. These results

underscore the importance of adhering to current guidelines, which recommend regular reviews of PPI indications, along with considering deprescribing trials for patients without a definitive indication for their long-term use[18]. Additionally, a significant majority of participants indicated that they were not familiar with strategies for deprescribing PPIs. Both factors may lead to overprescription of PPIs.

There are several limitations in the present study that should be taken into consideration. First, there is the potential for voluntary response bias, as participants who voluntarily completed the survey may have had a heightened interest in their knowledge of PPIs. Second, the presence of social desirability bias is another concern, as participants may have provided responses that they believed were socially acceptable, potentially impacting the reliability of our findings. Finally, the current survey administration method limits direct interviews with participants for clarifications on survey questions, possibly introducing a comprehension bias.

In conclusion, the current study illustrates that the majority of participants routinely prescribe PPIs, often in inpatient settings and for prophylactic purposes. It was found that the timing of the last review of PPI indications less than 5 years and belonging to medical specialties were associated with sufficient knowledge regarding PPI prescriptions. Another significant finding was that a considerable number of participants rarely review the ongoing indications of patients taking a PPI and are unfamiliar with deprescribing strategies. These results underscore the need to address the issue of PPI overprescription through improved physician education, frequent guideline reviews, and enhanced awareness of deprescribing strategies. Such measures are crucial not only for ensuring the appropriate and cost-effective use of PPIs but also for avoiding potential adverse effects related to their long-term use.

Authors' contribution

Involved in the conception, analysis of data and draft of the manuscript: Piñerúa-Gonsálvez JF and Zambrano-Infantino RC. Involved in the acquisition of data: Albornoz-Sandoval JC, Tong-Morao PW, León-Hernández MN, Matheus-Alonso BD, Suárez-López F, Flores Y, Higuera SN, Ruiz-Rebollo ML and Sulbaran M: Revised manuscript critically for important intellectual content: MS. All authors contributed to the article and approved the submitted version.

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Supplementary material 1

We thank you for dedicating your time and demonstrating your willingness to participate in this survey focused on assessing the prescription patterns of Proton Pump Inhibitors (PPIs). Your input is highly valuable to our research.

Section I: Demographic and professional information

1) Age _____

2) Gender: M___ F___

3) Physician training level
- a. Internship
- b. Resident
- c. Attending

4) How many years of professional experience do you have?

5) Which medical specialty do you belong to?
- a. Internal Medicine
- b. General Surgery
- c. Cardiology
- d. Nephrology
- e. Rheumatology
- f. Traumatology
- g. Family Medicine
- h. Other: _____

6) Approximately how many patients do you typically evaluate each week in your medical practice?
- a. 1–20
- b. 21–50
- c. 51–100
- d. >100

Section II: Patterns of PPI usage in your practice and familiarity with published evidence regarding PPI

7) In general, how often do you prescribe proton pump inhibitors to your patients?
- a. Always
- b. Very often
- c. Often
- d. Rarely

8) When you prescribe PPIs, is it most commonly for:
- a. Therapeutic purposes
- b. Prophylactic purposes

9) In which type of patients do you most frequently prescribe PPIs?
- a. Hospitalized patients
- b. Outpatient clinic patients

10) What is the most common route of administration for PPIs that you prescribe?
- a. Intravenous
- b. Oral

11) How long has it been since you last reviewed the scientific literature regarding indications for proton pump inhibitors?
- a. More than 5 years ago.
- b. Between 1 and 5 years ago.
- c. A few months ago.
- d. In the last month.
- e. Never

12) According to the information you have, which of the following are indications for the prophylactic use of PPIs (you may select multiple answers):
- a. Polypharmacy in elderly patients.
- b. Stress ulcers in non-critically ill patients.
- c. Patients >65 years using aspirin/NSAIDs chronically.
- d. Patients on antibiotic treatment.
- e. steroid treatment.
- f. Users of aspirin/NSAIDs in combination with steroids.
- g. Users of aspirin/NSAIDs in combination with oral anticoagulants.
- h. Users of aspirin/NSAIDs in combination with Selective Serotonin Reuptake Inhibitors (SSRIs).
- i. Stress ulcers in critically ill patients.
- j. Any user of aspirin/NSAIDs.

13) How long has it been since you last reviewed the scientific literature on possible adverse effects associated with proton pump inhibitors?
- a. More than 5 years ago.
- b. Between 1 and 5 years ago.
- c. A few months ago.
- d. In the last month.
- e. Never

14) How often do you review the indication for the use of PPIs in patients who regularly take this medication?
- a. Always
- b. Often
- c. Rarely
- d. Very rarely

15) Are you familiar with any strategies for discontinuing PPIs?
- a. Yes
- b. No

Section III: Clinical scenarios

16) A 56-year-old patient with mechanical low back pain due to recent physical exertion was prescribed ibuprofen every 8 hours for one week. The patient has a significant history of smoking. They present to the emergency department with melena without hemodynamic instability. Laboratory findings reveal a hemoglobin level of 10 g/dL. Upper gastrointestinal endoscopy shows a Forrest III gastric ulcer (no signs of active bleeding). Omeprazole is prescribed during their hospital stay. How long would you prescribe outpatient PPI therapy for this patient:
- a. 1 week
- b. 4–8 weeks
- c. >8 weeks
- d. Indefinitely.

17) A 45-year-old patient diagnosed with Systemic Lupus Erythematosus with joint involvement is receiving low-dose prednisone therapy with a good response. During a follow-up appointment, the patient inquiries about “gastric protectors” as they are concerned about potential gastric side effects from their baseline treatment. The patient has no digestive symptoms, normal laboratory results, and no other relevant medical history. Choose one of the following options:
- a. PPI use is not indicated.
- b. Prophylactic omeprazole 20 mg/day for 1 month would be indicated.
- c. Prophylactic omeprazole 20 mg/day for the duration of corticosteroid treatment would be indicated.
- d. Prophylactic omeprazole 20 mg every 12 hours for the duration of corticosteroid treatment would be indicated.

18) 50-year-old patient experiences frequent episodes of heartburn and acid regurgitation throughout the day, which disrupt their sleep, for the past 6 months. They initiate therapy with daily morning omeprazole. Endoscopic examination reveals no significant findings. After 2 months of treatment, the patient reports significant improvement in symptoms, with isolated episodes of heartburn occurring 1-2 times per month. What management strategy would you apply in this patient’s case:
- a. Maintain the same dose of PPI for an additional 8 weeks.
- b. Prescribe PPI only when symptomatic (on-demand) instead of daily doses.
- c. Double the dose of PPI and continue for 8 weeks.
- d. Combine the PPI with an H2 blocker like Ranitidine.

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RESUMO –Contexto – Os inibidores da bomba de prótons (IBPs) são amplamente prescritos em todo o mundo, muitas vezes resultando em seu uso excessivo. Consequentemente, é essencial identificar as prováveis causas desse uso excessivo para facilitar sua prescrição adequada. **Objetivo** – Este estudo tem como objetivo avaliar o padrão de prescrição dos médicos, seu conhecimento sobre IBPs e fatores que afetam seu conhecimento. **Métodos** – Uma pesquisa on-line foi conduzida entre médicos latino-americanos e espanhóis, coletando os seguintes dados: informações profissionais, padrões de uso de IBP, familiaridade com evidências publicadas e abordagem de manejo em três casos-cenários hipotéticos. O conhecimento dos participantes foi categorizado em suficiente ou insuficiente com base nos resultados dos cenários de caso. Posteriormente, a análise de subgrupos foi realizada com base no nível de formação do médico, anos de prática, especialidade e tempo desde a última revisão da literatura dos IBPs. **Resultados** – Um total de 371 médicos participaram da pesquisa. Trinta e oito por cento prescrevem frequentemente IBP, principalmente para fins profiláticos (57,9%). Oitenta por cento não estavam familiarizados com as estratégias de prescrição de IBP, e 54,4% raramente revisaram a indicação contínua de pacientes em uso de IBP. Sessenta e quatro por cento demonstraram conhecimento suficiente nos cenários-caso. Observou-se associação significativa entre o tipo de especialidade (médica vs cirúrgica: 69,4% vs 46,8%, *P*<0,001), o momento da revisão da literatura de indicação do IBP (<5 anos vs >5 anos: 71,4% vs 58,7%, *P*=0,010) e conhecimento suficiente. **Conclusão** – Embora a maioria dos participantes prescrevesse IBPs regularmente e para fins de profilaxia, no entanto, não estava familiarizada com estratégias de prescrição e raramente revisava as indicações em andamento. O conhecimento suficiente está correlacionado com revisões recentes da literatura e afiliação à especialidade médica.

Palavras-chave – Inibidores da bomba de prótons; terapia medicamentosa; prescrição inadequada.

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