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Investigation of Risk Factors Related to The Use of Non-Prescription Proton Pump Inhibitors in Patients Referred to A Tertiary Health Care Institution

Üçüncü Basamak Sağlık Kuruluşuna Başvuran Hastalarda Reçetesiz Proton Pompa İnhibitörü Kullanımına Ait Risk Faktörlerin İncelenmesi

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ABSTRACT

Introduction: Proton pump inhibitors are benzamidazole derivative drugs that act by inhibiting gastric acid secretion controlled by parietal cells in the gastric epithelium through neuroendocrine pathways. Today, they are widely used worldwide for the treatment of all gastric acid-related diseases, especially gastroesophageal reflux disease.
Objective: It is known that proton pump inhibitors, which are most commonly prescribed to patients in our society, have recently been prescribed for inappropriate and unnecessary indications as well as being used without a prescription. Within the scope of rational drug use, correct and effective use of drugs in this group is important. The aim of this study was to investigate the risk factors for the use of non-prescription proton pump inhibitors in outpatients admitted to a tertiary health care institution.
Method: In this cross-sectional and analytical study, a questionnaire was administered face-to-face by the investigators to 300 volunteer patients who applied to the Internal and Surgical Outpatient Clinics of Balıkesir Atatürk City Hospital.
Results: It was found that 115 (38.3%) and 26 (8.7%) of the participants were male. It was found that 283 (94.3%) of the cases were prescription drugs, and when the reasons for use were analysed, it was determined that 116 (38.7%) were multiple drug use and 125 (41.7%) were dyspepsia in the first two. It was determined that an increase in age decreased the risk of using non-prescription proton pump inhibitors at a statistically significant level, and a higher level of education increased the risk of using non-prescription proton pump inhibitors 5.791 times at a statistically significant level.
Conclusion: In this study, it was observed that the use of proton pump inhibitors was extremely common in outpatients admitted to tertiary health care institutions. Off-label prescription use of these drugs as well as over-the-counter use was found to be high. For this reason, it is obvious that new multicenter studies should be conducted in order to examine the factors affecting the use of over-the-counter medication within the scope of rational drug use.

Keyswords: Proton Pump Inhibitor, Use Of Non-Prescription Drugs, Rational Drug Use.

ÖZET

Giriş: Proton pompa inhibitörleri mide epitelindeki parietal hücreler tarafından nöroendokrin yollarla kontrol edilen gastrik asit salınımını inhibe ederek etki eden benzamidazol türevi ilaçlardır. Günümüzde tüm dünyada, başta gastroözofageal reflü hastalığı olmak üzere gastrik asitle ilişkili tüm hastalıklarda yaygın olarak tedavi amaçlı kullanılmaktadır.
Amaç: Toplumuzda hastalara en çok reçete edilen proton pompa inhibitörlerin son zamanlarda uygun olmayan gereksiz endikasyonlar nedeniyle reçete edildiği gibi reçetesiz de kullanımının olduğu bilinmektedir. Akılcı ilaç kullanımı kapsamında bu gruptaki ilaçlarının doğru ve etkin kullanımı önem arz etmektedir. Bu çalışmada üçüncü basamak sağlık kuruluşuna ayaktan başvuran hastalardaki reçetesiz proton pompa inhibitörü kullanımına ait risk faktörlerin incelenmesi amaçlanmıştır.
Yöntem: Kesitsel ve analitik tipte olan bu çalışmada Balıkesir Atatürk Şehir Hastanesi dahili ve cerrahi polikliniklerine başvuran gönüllü 300 hasta katılım sağlanmış ve araştırıcılar tarafından yüz yüze soru-cevap şeklinde anket uygulanmıştır.
Bulgular: Çalışmaya katılanların 115'inin (%38,3) erkek olduğu, 26'sının (%8,7) olduğu bulundu. Vakaların 283'ünün (%94,3) ilaçların reçeteli olduğu, kullanım nedenlerine bakıldığında da 116'sının (%38,7) çoklu ilaç kullanımı, 125'inin (%41,7) dispepsi olarak ilk ikide tespit edildi. Yaş değerlerindeki artışın istatistiksel açıdan anlamlı seviyede reçetesiz proton pompa inhibitörü kullanma riskini azalttığı, eğitim seviyesinin yüksekliği istatistiksel açıdan anlamlı seviyede reçetesiz proton pompa inhibitörü kullanma riskini 5,791 kat arttırdığı tespit edilmiştir.
Sonuç: Yapılan bu çalışma ile üçüncü basamak sağlık kuruluşuna ayaktan başvuran hastalarda proton pompa inhibitör kullanımının son derece yaygın olduğu görülmüştür. Bu ilaçların endikasyon dışı reçeteli kullanımı olduğu gibi reçetesiz kullanımınında fazlaca olduğu tespit edilmiştir. Bu sebeple akılcı ilaç kullanımı kapsamında ileriye yönelik reçetesiz ilaç kullanımına etki eden faktörlerin incelenmesi amacıyla çok merkezli yeni çalışmaların yapılma zorunluluğu aşikadır.

Anahtar Kelimeler: Proton Pompa İnhibitörü, Reçetesiz İlaç Kullanımı, Akılcı İlaç Kullanımı.

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INTRODUCTION

Proton pump inhibitors (PPIs) are benzamidazole derivative drugs that act by inhibiting gastric acid secretion controlled by neuroendocrine pathways in the parietal cells of the gastric epithelium. Currently, these widely used drugs are the most commonly prescribed group for the treatment of conditions such as peptic ulcer, gastroesophageal reflux disease, esophagitis, and functional dyspepsia (1). While their use is generally considered safe due to correct indications, long-term use of these drugs can lead to complications such as pneumonia, bone fractures, vitamin B12 and iron deficiency, gastric polyp development, and enterocolitis. Their use has further increased due to their strong effects in preventing gastrointestinal side effects of non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, and other drugs used in the treatment of diseases such as atherosclerotic heart disease, osteoarthritis, and rheumatoid arthritis (2,3). Studies have reported that PPIs are among the most frequently prescribed medications in many health institutions and that their use without a prescription has also increased recently. Often, they are prescribed by various specialties for inappropriate and unnecessary indications (4). It has been observed that PPIs, which are used in an uncontrolled and increasingly frequent manner, can be obtained without a prescription by patients themselves, their relatives, or through other means. Therefore, the widespread use of over-the-counter PPIs has been noted, and few studies have examined the risk factors contributing to this situation. This widespread use is contrary to rational drug use principles, posing a significant economic burden on healthcare institutions and potential long-term adverse effects for patients. This study aims to analyze the main risk factors influencing the use of over-the-counter PPIs and ensure the correct and effective use of this drug group. The development of advanced methods to prevent the extensive prescription of PPIs, raising awareness among physicians regarding prescription practices, and increasing awareness were planned with this study.

METHODS

This cross-sectional and analytical study included 300 voluntary patients, aged between 18 and 80 years, of both genders who visited the internal medicine and surgical outpatient clinics of Balıkesir Atatürk City Hospital. The sample of the study consisted of patients using PPIs between December 2023 and February 2024. Informed consent forms were prepared in advance and provided to the patients, who were then informed about the study. The evaluation questionnaire, pre-determined for this study, was administered face-to-face in a question-and-answer format to patients who were mentally competent and consented to participate.

The survey collected demographic data (age, gender, marital status, education level, etc.), information on chronic diseases, the regularity of PPIs usage (in our study, appropriate use was defined as taking the medication approximately 30 minutes before meals and regularly once a day before symptoms began), whether the medication was prescribed by a physician, the specialty of the prescribing physician, the duration and indication for use, and the effectiveness of usage. The responses were recorded through the questionnaire form.

Statistical Analysis

The demographic and clinical characteristics of the cases evaluated in the study were examined using descriptive statistical analyses (e.g., numbers, percentages). Factors influencing the risk of using PPIs without a prescription or unnecessarily were analyzed using univariate and multivariate binary logistic regression analyses. The significance level for all analyses was set at $p<0.05$. The normal distribution of the data was checked using kurtosis and skewness values (±1.5). IBM SPSS 26.0 software was used to perform the analyses.

Ethics Committee Approval

Our study was approved by the Scientific Research Ethics Committee of Balıkesir Atatürk City Hospital with the decision dated 23/11/2023 and number 2023/11/75.

RESULTS

In the study, it was found that 115 (38.3%) of the patients using PPIs were male, 26 (8.7%) were single, 43 (14.3%) had deceased spouses, and 231 (77%) were married. Additionally, 16 (5.3%) were illiterate, 41 (13.7%) were literate, 86 (28.7%) had primary education, 40 (13.3%) had secondary education, 51 (17%) had high school education, and 66 (22%) had a university education. Regarding economic status, 3 (1%) were very well-off, 71 (23.7%) were well-off, 201 (67%) were average, and 25 (8.3%) were poor (Table 1).

Table 1. Demographic Characteristics of Cases Using PPIs

		n	%
Sex	Male	115	38.3
	Female	185	61.7
Marriage Status	Single	26	8.7
	Wife passed away	43	14.3
	Married	231	77.0
Education Status	No Literate	16	5.3
	Literate	41	13.7
	Primary School	86	28.7
	Middle School	40	13.3
	High School	51	17.0
	University	66	22.0
Economic Situation	Very good	3	1.0
	Good	71	23.7
	Little	201	67.0
	Bad	25	8.3
Smoker	Yes	74	24.7
	Nok	226	75.3
Alcohol Consumption	Yes	21	7.0
	No	279	93.0

It was found that 283 (94.3%) of the patients had PPIs prescribed. The reasons for PPIs use included polypharmacy in 116 (38.7%), dyspepsia in 125 (41.7%), gastritis in 4 (1.3%), peptic ulcer in 12 (4%), reflux in 27 (9%), gallstones in 1 (0.3%), and irritable bowel syndrome in 15 (5%). Among the patients, 163 (54.3%) occasionally paid attention to PPIs use, 105 (35%) paid attention, and 32 (10.7%) did not pay attention. It was found that 30 (10%) had previously been informed about PPIs use, and 5 (1.7%) experienced side effects from PPIs use.

Table 2. Factors Affecting The Risk of Over The Counter PPIs Use

				95%CI					95%CI	
	βa	p	OR	LL	UL	βb	p	OR	LL	UL
Age	**0.088**	**<0.001**	**0.916**	**0.880**	**0.953**	**-0.098**	**0.003**	**0.907**	**0.850**	**0.968**
Marriage Status	0.031	0.957	0.969	0.305	3.074	1.401	0.094	4.060	0.788	20.917
Education	**1.756**	**0.001**	**5.791**	**2.111**	**15.886**	0.325	0.626	1.385	0.374	5.132
Economic Situation	**1.328**	**0.009**	**3.773**	**1.399**	**10.173**	0.849	0.173	2.338	0.689	7.934
Smoker	0.545	0.300	1.725	0.615	4.838	-0.461	0.439	0.630	0.196	2.028
Alcohol Consumption	0.617	0.435	1.853	0.394	8.703	-0.002	0.998	0.998	0.180	5.532
Chronic Disease	**2.836**	**0.006**	**17.051**	**2.231**	**130.309**	1.660	0.128	5.260	0.620	44.612

a=Univariate Binary Logistic Regression Analysis, b= Multivariate Binary Logistic Regression Analysis.

Regarding the prescribing departments, it was found that 2 (0.7%) prescriptions came from emergency medicine, 45 (15%) from family medicine, 1 (0.3%) from neurosurgery, 1 (0.3%) from physical therapy, 15 (5%) from gastroenterology, 9 (3%) from general surgery, 6 (2%) from pulmonary diseases, 1 (0.3%) from ophthalmology, 148 (49.3%) from internal medicine, 37 (12.3%) from cardiology, 2 (0.7%) from otolaryngology, 4 (1.3%) from neurology, 1 (0.3%) from oncology, 12 (4%) from orthopedics, and 1 (0.3%) from psychiatry. It was found that 3 (1%) had asthma, 4 (1.3%) had COPD, 50 (16.7%) had diabetes, 78 (26%) had hypertension, 9 (3%) had hypothyroidism, 23 (7.7%) had coronary heart disease, and 6 (2%) had other clinical conditions.

According to univariate binary logistic regression analysis, an increase in age was found to statistically significantly reduce the risk of using PPIs without a prescription (p<0.001). Higher education level was found to statistically significantly increase the risk of using PPIs without a prescription by 5.791 times (p=0.001). Better economic status was found to statistically significantly increase the risk of using PPIs without a prescription by 3.773 times (p=0.009). Additionally, the absence of comorbidities was found to statistically significantly increase the risk of using PPIs without a prescription by 17.051 times (p=0.006) (Table 2).

Table 3. Factors Affecting The Risk of PPIs Use for Unnecessary Indication

				95%CI					95%CI	
	βa	p	OR	LL	UL	βb	p	OR	LL	UL
Age	**0.072**	**<0.001**	**1.074**	**1.053**	**1.095**	**0.050**	**<0.001**	**1.052**	1.027	1.077
Marriage Status	0.337	0.225	0.714	0.414	1.230	0.134	0.717	0.875	0.424	1.803
Education	**1.534**	**<0.001**	**0.216**	**0.105**	**0.443**	0.049	0.926	0.952	0.337	2.686
Economic Situation	0.690	0.019	0.502	0.282	0.893	0.401	0.306	0.670	0.311	1.444
Smoker	**1.483**	**<0.001**	**0.227**	**0.116**	**0.444**	0.997	0.029	0.369	0.151	1.902
Alcohol Consumption	0.749	0.155	0.473	0.168	1.328	0.982	0.157	2.669	0.686	10.393
Chronic Disease	**1.825**	**<0.001**	**0.161**	**0.096**	**0.272**	**1.365**	**<0.001**	**0.255**	0.143	0.457

a=Univariate Binary Logistic Regression Analysis, b= Multivariate Binary Logistic Regression Analysis.

According to univariate binary logistic regression analysis, an increase in age was found to statistically significantly increase the risk of unnecessary PPIs use by 1.074 times (p<0.001). Higher education level was found to statistically significantly reduce the risk of unnecessary PPIs use (p<0.001). The absence of comorbidities was found to statistically significantly increase the risk of unnecessary PPIs use (p<0.001). According to multivariate binary logistic regression analysis, an increase in age was found to statistically significantly increase the risk of unnecessary PPIs use by 1.052 times, while the absence of comorbidities was found to statistically significantly decrease the risk (p<0.001) (Table 3).

DISCUSSION

The frequency of PPIs usage is increasing, and numerous studies have been conducted on this topic. When examining the demographic data of our cross-sectional study, it was shown that the rate of PPIs usage was higher in women at 61.7%. A study conducted by Susanna et al. in Sweden also demonstrated a higher rate of PPIs usage among women (5). Similarly, another study in the literature reported a higher proportion of PPIs usage in women (6). Thus, it is evident that the publications support our study in this regard.

When examining the clinical characteristics of patients using PPIs, it was found that 94.3% of the medications were prescribed, while 5.7% were obtained without a prescription. Many studies have shown that numerous medications are excessively and inappropriately prescribed for incorrect indications (4). PPIs are known to be among these medications. Despite various activities, announcements, and other efforts to reduce unnecessary PPIs usage and prescriptions in many communities, the prescription rates remain high. Therefore, various announcements and measures have been emphasized in our country regarding the importance of rational drug use, similar to antibiotics. Another study reported that the rate of PPIs usage without a physician's prescription was 14%. In a randomized cross-sectional study related to rational drug use conducted by Ozdinç et al., it was shown that 54% of participants used medication without any physician's prescription, and 26.5% consulted a family member, neighbor, or relative (7). In our study, the rate of PPIs usage without a physician's prescription was found to be 5.7%, which does not support the results of other studies. It is thought that the measures and practices organized in our society to prevent the use of non-prescription drugs within the scope of rational drug use may be related to our findings. Moreover, in our study, the increase in age was found to decrease non-prescription PPIs usage, while higher education level and better economic status were found to significantly increase non-prescription PPIs usage. The literature does not report studies showing the effect of better economic status and higher education level on PPIs usage. The notable finding in our study may be related to patients having both physician supervision and easy access to healthcare facilities. As in most studies, the rate of prescribed PPIs usage is high. A study by Ozdemir et al. reported a high rate of prescribed PPIs usage among elderly individuals, but it did not examine non-prescription PPIs usage (6).

It is known that many medications are inappropriately and unnecessarily prescribed for indications that are not suitable. PPIs are among these medications, as evidenced by their widespread prescription by various specialties. When examining the findings of our study, it was found that the prescription status of PPIs by specialty was in line with other studies, with internal medicine being the most common at 49.3%. Regarding the indications for use, it was shown that 41.7% of the usage was for dyspepsia and 38.7% for polypharmacy. According to current information, using PPIs for polypharmacy without gastrointestinal risk factors is an unnecessary indication and not a correct approach. However, the literature shows the widespread prevalence of inappropriate and unnecessary PPIs usage (8-12). Supporting our study, the findings of a randomized study by Chia et al. showed that the rate of off-label usage was 54.1%.

Other findings from our study showed that an increase in age was associated with an increase in unnecessary PPIs usage. Similarly, higher education level was found to reduce unnecessary PPIs usage. This can be explained by patients being more conscious and rational in their medication usage and remaining under physician supervision. Additionally, the absence of comorbidities was found to increase the risk of unnecessary PPIs usage.

In our study, the excessive use of PPIs due to unnecessary indications, and the increase in non-prescription PPIs usage associated with higher education level and better economic status, were found to be significant. To prevent this situation, individuals can be encouraged through accessible, easy, and up-to-date information campaigns within the scope of rational drug use. Since our study was single-centered and conducted with patients visiting outpatient clinics, it may not reflect the true values of non-prescription drug usage.

CONCLUSION

As a result, it is evident that PPIs therapy is frequently initiated for both necessary and unnecessary indications, followed by a significant amount of usage without physician supervision and without a prescription. This study demonstrated that the prevalence and inappropriate usage rate of these medications are in line with the results of other studies in the literature. However, there is a clear need for new multicenter studies to investigate the non-prescription use of PPIs and the factors influencing this behavior. Therefore, we believe that encouraging contributions to other actions within the scope of rational drug use are important.

DESCRIPTIONS

No financial support.

No conflict of interest.

Ethical Declaration: All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. Ethics committee approval has been granted from our institution. Informed consent was obtained from all participants.

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