

KNOWLEDGE, ATTITUDE AND AWARENESS OF FAMILY MEDICINE RESIDENTS ABOUT PROTON PUMP INHIBITORS

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ABSTRACT

Aim: In this Study, we aimed to determine the knowledge, attitude, and awareness of family medicine residents about Proton Pump Inhibitors (PPIs).

Methods: An online questionnaire with 33 questions was sent to the 142 residents of the Family Medicine Clinics of Prof. Dr. Cemil Tascioglu City Hospital, Gaziosmanpasa Training and Research Hospital, Sisli Etfal Training and Research Hospital, and Haseki Training and Research Hospital.

Results: When the participants' answers to the true/false questions about PPIs were analyzed, almost all physicians answered the question about the ideal intake of PPIs 30-60 minutes before breakfast correctly (97%). 93% of them indicated various recommendation options they preferred for the patient, including avoiding heavy meals / fatty foods, avoiding alcoholic and acidic/carbonated drinks, smoking cessation, and diet. Participating physicians also answered correctly with a high percentage that pantoprazole is the proton pump inhibitor with the lowest likelihood of drug interactions; that PPIs alter the effectiveness of ketoconazole, levothyroxine, and clopidogrel; and that omeprazole affects the concentration of diazepam, warfarin, and phenytoin. It was also found that a high percentage of physicians (69%) were correctly informed about the need for cautious use of PPIs in patients with renal insufficiency. The question about the use of PPIs in pregnancy was the question most frequently answered incorrectly by physicians, by almost half. The preferred source of information for the participants was training in the clinics (70%).

Conclusions: Physicians should refresh their knowledge by receiving the necessary up-to-date training. Trainings to improve the knowledge, attitudes, and awareness of doctors should be continued regularly.

Keywords: Education, family physician, knowledge, primary care, proton pump inhibitors

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INTRODUCTION

Proton pump inhibitors (PPIs) are benzimidazole derivatives that strongly block gastric acid secretion and are among the most commonly used groups of drugs worldwide. The indications for proton pump inhibitors, which are safe and effective in the treatment of acid-related diseases such as for controlling dyspeptic symptoms, reducing the recurrence of erosive diseases, and protecting gastric structures, are clearly defined in the guidelines. However, long-term use is common and can lead to complications such as *Clostridium difficile* infection, pneumonia, bone fractures, B12 deficiency, anemia, and renal failure [1].

An estimated 20-80% of people worldwide who take proton pump inhibitors do so without an approved indication [2]. In addition, the overuse of proton pump inhibitors represents an economic burden on the healthcare system. Physicians' awareness and knowledge of PPIs are believed to play a very important role in regulating the use of these drugs and avoiding side effects, drug-drug interactions, and inappropriate use of PPIs. Taking all these into consideration, this study was planned to determine the knowledge, attitude, and awareness of family medicine residents about PPIs.

METHODS

This study was conducted after the approval of Prof. Dr. Cemil Tascioglu City Hospital Clinical Research Ethics Committee, dated 19/09/2022 and numbered E-48670771-514.99. An online

questionnaire with 33 questions was sent to the 142 residents of the Family Medicine Clinics of Prof. Dr. Cemil Tascioglu City Hospital, Gaziosmanpasa Training and Research Hospital, Sisli Etfal Training and Research Hospital, and Haseki Training and Research Hospital.

Statistical Analysis:

We utilized the SPSS 15.0 (Statistical Package for the Social Sciences, version 21) statistical software to analyze our research outcomes. The normal distribution was assessed using the Kolmogorov-Smirnov test. Descriptive statistics were provided for numerical variables, including minimum, maximum, median, mean, and standard deviation, while categorical variables were presented in terms of frequency and percentage. For numerical variables that did not meet the criteria of a normal distribution, median and interquartile ranges were provided. For comparing qualitative data, Pearson's Chi-Square Test was applied. We considered a p-value less than 0.05 to be statistically significant when interpreting our results.

RESULTS

Among the participants, 69% were female, 45% were married, the median age was 29 (IQR:4) years, and the median duration of employment was 3 (IQR:3) years. In addition, 88% were family medicine residents and 37% had been working in their profession for 5 or more years.

Although 71% of the participants stated that they had no known history of disease, 7% of them

stated that they had experienced gastritis/gastroenteritis. Regarding the use of PPIs for themselves as a physician, 43% of physicians stated that they use PPIs for some indications in their lives, and 86% of the users stated that they use PPIs only "when symptoms are present".

In the study, 50% of physicians responded to the question "On average, how often do you prescribe PPIs in your daily routine outpatient clinic?" as "often" (Figure 1). Again, physicians indicated that they most frequently prescribe PPIs for "gastroesophageal reflux disease" (87%), followed by "acute/chronic gastritis" (60%) and "for gastroprotective purposes in addition to other medications" (47%) (Figure 2). Among the medication groups for which PPIs were prescribed in addition to other medications for gastroprotective purposes, "NSAIDs" had the highest rate, followed by "steroids" in second place (Figure 3).

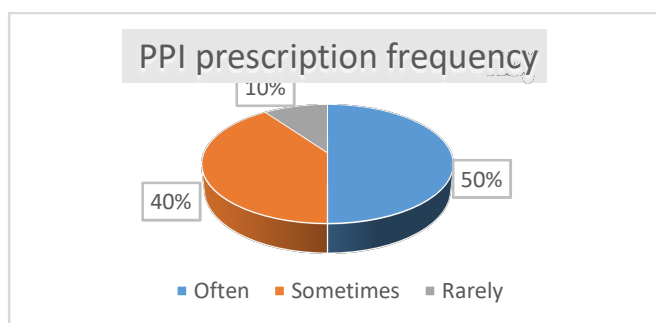


Figure 1: Participants' PPI prescription frequency

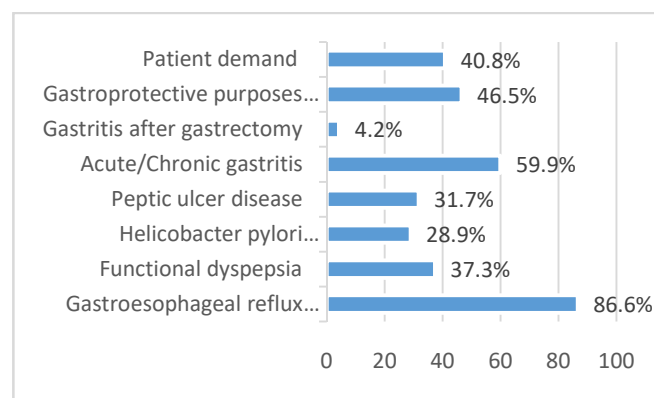


Figure 2: Frequency of PPI prescribing indications among participants

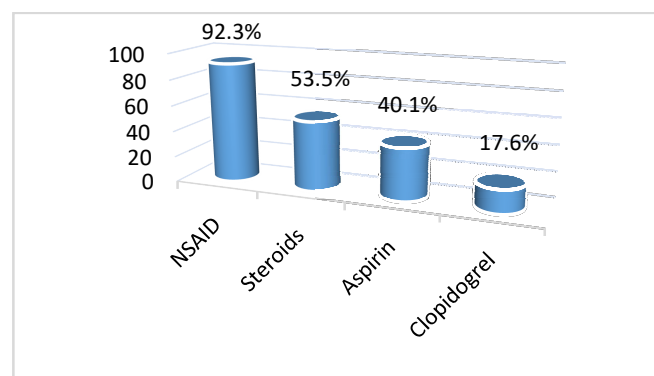


Figure 3: Participants' concomitant PPI prescriptions for gastroprotective purposes

The active ingredients most preferred by doctors were pantoprazole with 83% and lansoprazole with 53%. Omeprazole was in last place with 10%. In addition, esomeprazole and rabeprazole were significantly more commonly preferred by physicians with 5 or more years of experience than by physicians with 0-4 years of experience ($p=0.041$ and $p<0.001$ respectively) (Table 1).

Table 1. Evaluation of the PPI preparations preferred by the participants according to the year of profession

		Time spent in the profession (years)				
		0-4 years		5 years and more		
		n	%	n	%	p-value
Which active substance(s) of PPIs do you prescribe most often?	Esomeprazole	14	15.7	16	30.2	0.041
	Lansoprazole	47	52.8	31	58.5	0.510
	Omeprazole	6	6.7	8	15.1	0.106
	Pantoprazole	77	86.5	41	77.4	0.159
	Rabeprazole	10	11.2	19	35.8	<0.001
Pearson Chi-Square test						

The active ingredients esomeprazole and rabeprazole are preferred at a significantly higher level among the participants who chose medical books and journals as a source of information compared to those who did not ($p=0.002$; $p=0.009$ respectively). In addition, those who chose this

source of information were significantly more likely to warn their patients about side effects when prescribing PPIs and were significantly more likely to respond positively to the question regarding "Acute interstitial nephritis/chronic kidney disease" as a possible side effect ($p=0.047$ and $p=0.015$ respectively) (Table 2).

Table 2. Evaluation of the knowledge, awareness, and attitudes of the participants who chose medical books and journals as sources of information about PPIs

		Source of Information medical books and journals				
		Yes		No		
		n	%	n	%	
Which active substance(s) of PPIs do you prescribe most often?	Esomeprazole	3	22.4	17	20.2	0.755
	Lansoprazole	1	53.4	47	56.0	0.768
	Omeprazole	1	19.0	3	3.6	0.002
	Pantoprazole	0	86.2	68	81.0	0.411
	Rabeprazole	8	31.0	11	13.1	0.009
How often do you warn your patients about side effects when prescribing PPIs?	Often	1	19.0	14	16.7	0.047
	Sometimes	1	53.4	30	35.7	
	Rarely	6	27.6	40	47.6	

What side effects do you inform your patients about when taking PPIs?	Decreased absorption of vitamin B12	4	75.9	52	61.9	0.081
	Decreased absorption of iron	4	58.6	47	56.0	0.752
	Hypomagnesemia	9	15.5	7	8.3	0.183
	Acute interstitial nephritis/chronic kidney disease	9	15.5	3	3.6	0.015
	Bone loss/fracture	3	39.7	28	33.3	0.440
	Fundus polyps	8	13.8	8	9.5	0.429
	Clostridium difficile infection	3	5.2	2	2.4	0.399
	Pneumonia	2	3.4	1	1.2	0.567
	Dementia	0	0.0	1	1.2	1.000
Pearson Chi-Square test						

Among the participating physicians, those with a history of gastritis/gastrointestinal disease were significantly more likely to prescribe PPIs for

gastroprotective purposes in addition to other medications and to inform their patients to avoid alcoholic and acidic/carbonated beverages than physicians without a history of known disease (Table 3).

Table 3. Knowledge, awareness, and attitudes about PPI among participants with chronic diseases

		History of known disease						
		No		Gastritis/Gastro-esophageal reflux disease		Others		
		n	%	n	%	n	%	p-value
How often do you prescribe PPIs in your daily routine outpatient clinic?	Often	55	54.5	6	54.5	10	33.3	0.057
	Sometimes	34	33.7	4	36.4	19	63.3	
	Rarely	12	11.9	1	9.1	1	3.3	
In which cases are PPIs most commonly prescribed?	Gastro-esophageal reflux disease	88	87.1	9	81.8	26	86.7	0.767
	Functional dyspepsia	38	37.6	4	36.4	11	36.7	1
	Helicobacter pylori eradication treatment	24	23.8	4	36.4	13	43.3	0.098

	Peptic ulcer disease	33	32.7	3	27.3	9	30	0.912
	Acute/Chronic gastritis	58	57.4	7	63.6	20	66.7	0.64
	Post-gastrectomy gastritis	4	4	1	9.1	1	3.3	0.596
	In addition to other drugs for gastroprotective purposes	45	44.6	9	81.8	12	40	0.046
	Due to patient demand	41	40.6	5	45.5	12	40	0.947
Do you advise your patients on lifestyle changes when prescribing PPIs?	I don't make suggestions	6	5.9	1	9.1	3	10	0.441
	Dietary advice	63	62.4	9	81.8	23	76.7	0.189
	Losing weight	31	30.7	4	36.4	13	43.3	0.43
	Avoiding heavy meals/fatty foods	85	84.2	11	10.0	26	86.7	0.544
	Avoiding alcoholic and acidic/gas drinks	61	60.4	10	90.9	25	83.3	0.014
	Avoiding coffee	71	70.3	10	90.9	25	83.3	0.154
	Quitting smoking	60	59.4	9	81.8	24	80	0.057

In addition, physicians with a history of gastritis/gastrointestinal disease were significantly more likely to correctly answer the question "PPI/misoprostol should be prescribed for chronic use of NSAIDs in the elderly, even in the absence of concomitant risk factors such as peptic ulcers or dyspepsia/gastrointestinal symptoms" than physicians without a history of known disease.

In this study, more than half of the physicians stated that they informed patients about the side effects, particularly the reduced absorption of vitamin B12 and iron. In addition, bone loss/fractures, hypomagnesemia, fundus polyps, acute interstitial nephritis/chronic kidney disease, clostridium difficile infection, pneumonia, and dementia were also reported, albeit to a lesser extent (Table 4).

Table 4. Evaluation of the frequency of PPI prescription status of the participants

		n	%
Frequency of warning patients about side effects when prescribing PPIs	Often	25	17.6
	Sometimes	61	43.0
	Rarely	56	39.4
Frequency of side effects for which information on PPI use was provided	Decreased absorption of vitamin B12	96	67.6
	Decreased iron absorption	81	57.0
	Bone loss/fracture	51	35.9
	Hypomagnesemia	16	11.3
	Fundus polyps	16	11.3
	Acute interstitial nephritis/chronic kidney disease	12	8.5
	Clostridium difficile infection	5	3.5
	Pneumonia	3	2.1
	Dementia	1	0.7

When the participants' answers to the true/false questions about PPIs were analyzed, almost all physicians answered the question about the ideal intake of PPIs 30-60 minutes before breakfast correctly (97%). 93% of them indicated various recommendation options they preferred for the patient, including avoiding heavy meals / fatty foods, avoiding alcoholic and acidic/carbonated drinks, smoking cessation, and diet.

Participating physicians also answered correctly with a high percentage that pantoprazole is the proton pump inhibitor with the lowest likelihood of drug interactions; that PPIs alter the effectiveness of ketoconazole, levothyroxine, and clopidogrel; and that omeprazole affects the concentration of diazepam, warfarin, and phenytoin. It was also found that a high percentage of physicians (69%) were correctly

informed about the need for cautious use of PPIs in patients with renal insufficiency (Table 5). The question about the use of PPIs in pregnancy was the question most frequently answered incorrectly by physicians, by almost half (Table 5). The preferred source of information for the participants was training in the clinics (70%) (Figure 5).

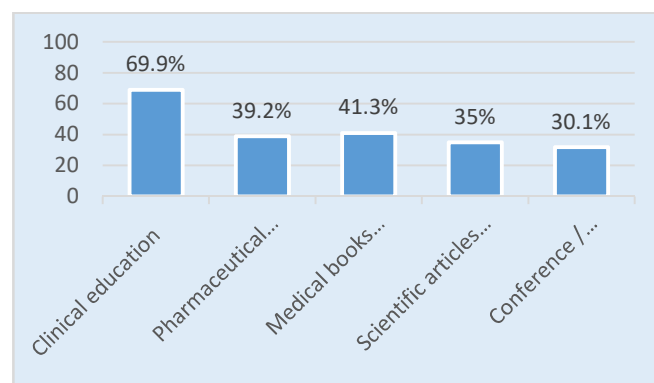
**Figure 5: Participants' preferred sources of information**

Table 5. Evaluation of participants' true-false questions and answers about PPIs

Questions		n	%
PPIs are prodrugs activated in the acid environment of the stomach that suppress gastric acid secretion through irreversible inhibition of H ⁺ /K ⁺ ATPase in gastric parietal cells (True)	True	118	83.1
	False	22	15.5
	I don't know	2	1.4
In the treatment of uncomplicated peptic ulcer or erosive peptic esophagitis, the use of PPIs at full therapeutic dose for more than 8-12 weeks is not appropriate and there is an indication for dose reduction or discontinuation in a shorter time (True)	True	89	62.7
	False	29	20.4
	I don't know	24	16.9
Although there are challenges in the eradication of Helicobacter pylori, PPIs are used as a component of all treatment regimens (2 times a day for an average of 10-14 days) (True)	True	99	69.7
	False	26	18.3
	I don't know	17	12.0
Aspirin, Clopidogrel, NSAIDs, or Steroids are appropriate without PPI in patients with a history of ulcers or symptoms of dyspepsia-OR (False)	True	13	9.2
	False	127	89.4
	I don't know	2	1.4
In chronic use of NSAIDs in the elderly, PPI/misoprostol should be given, even in the absence of concomitant risk factors such as a history of ulcer or dyspepsia-OR symptoms	True	108	76.1
	False	23	16.2
	I don't know	11	7.7
In case of non-response to empirical treatment, alarm symptoms, and the presence of new-onset symptoms in patients older than 50 years of age, the patient should be referred to the relevant specialist for further investigations such as endoscopy, etc. (True)	True	138	97.2
	False	2	1.4
	I don't know	2	1.4
PPI should be used with caution in patients with renal insufficiency (True)	True	98	69.0
	False	20	14.1
	I don't know	24	16.9
PPIs should ideally be taken 30-60 minutes before breakfast (True)	True	138	97.2
	False	3	2.1
	I don't know	1	0.7

The absorption of most PPIs is reduced by an average of 50% when taken with a meal. However, Rabeprazole and Pantoprazole can be taken after a meal (True)	True	67	47.2
	False	14	9.9
	I don't know	61	43.0
In cases such as prophylaxis of NSAID-induced gastropathy, Barret's esophagus, and Zollinger-Ellison syndrome, we assess the need for chronic PPI therapy and generally do not stop treatment (True)	True	94	66.2
	False	23	16.2
	I don't know	25	17.6
PPIs do not alter the efficacy of ketoconazole, levothyroxine, and clopidogrel (False)	True	12	8.5
	False	97	68.3
	I don't know	33	23.2
Omeprazole may increase the concentration of diazepam, warfarin, and phenytoin. If there is an indication for PPI use in patients on warfarin, a PPI other than omeprazole should be preferred (True)	True	92	64.8
	False	4	2.8
	I don't know	46	32.4
Pantoprazole is the proton pump inhibitor with the lowest probability of drug-drug interaction (True)	True	103	72.5
	False	16	11.3
	I don't know	23	16.2
A step-by-step approach is supported in the treatment of GERD in pregnancy. Initially, it can be treated by changing diet and lifestyle. Antacids, including alginic acid, are recommended if necessary. PPI cannot be given if there is no response (False)	True	68	47.9
	False	55	38.7
	I don't know	19	13.4
Esomeprazole, Lansoprazole, Pantoprazole, and Rabeprazole have pregnancy category B. However, there are insufficient studies on their safety in pregnant women (True)	True	97	68.3
	False	12	8.5
	I don't know	33	23.2
Omeprazole has a risk category of C in pregnant women, but this drug has the most studies on safety (True)	True	45	31.7
	False	13	9.2
	I don't know	84	59.2
GERD: Gastro Esophageal Reflux Disease NSAID: Non-steroidal anti-inflammatory drug PPI: Proton pump inhibitor			

DISCUSSION

Comparing the data of our study with the available data, there are mostly similarities in terms of frequency of PPIs prescribing and indications, but the proportion of PPIs prescribing for gastroprotective purposes in addition to other drugs, especially NSAIDs, is significantly higher.

In a study conducted abroad, omeprazole was the most commonly used PPIs until 2012, after which its use gradually declined. During the same period, the use of pantoprazole increased significantly and it became the leading PPIs in 2020 [3].

It is assumed that physicians' experience, individual preferences, drug costs, and companies' promotional activities and, in particular, interactions between PPIs and drugs influence preferences for an active substance [4-8]. Previous studies showed that physician education is an effective way to reduce the number of inappropriately prescribed PPIs [9-12]. Among other studies, a review conducted in the United States of America emphasized the clarity and simplicity of treatment reduction protocols given to patients and the education of physicians responsible for prescribing for a successful strategy, particularly regarding actions to take in the event of symptom recurrence [13]. Comparing the data from different studies, the level of knowledge of physicians in our study about the side effects of PPIs and the rate of education of their patients is significantly higher.

A review of the existing studies shows that most of the studies focused on the patients in our country [14-18] and only a few studies examined the awareness of physicians about PPIs [19, 20]. Future studies can make an important contribution to

preventing inappropriate PPIs use and potential adverse drug interactions by educating and raising awareness among patients as well as physicians and other healthcare professionals [21, 22].

In conclusion, PPIs are among the most commonly prescribed medications today and studies have reported potentially harmful side effects associated with PPIs. Although some of the results of these studies are controversial, they are important. Furthermore, over-prescribing of PPIs creates economic costs and contributes to polypharmacy. With the increasing number of observational studies showing an association between PPIs and numerous side effects, a holistic, comprehensive and multifaceted approach is needed to prevent misuse and not to overlook the potentially life-saving benefits of PPIs. In addition, prescribing guidelines for re-evaluation of PPIs should be developed to ensure rational drug use and tapering strategies in maintenance therapy. Physicians should refresh their knowledge by receiving the necessary up-to-date training. Meeting patients' expectations, educating them about reported side effects, and listening to them patiently based on empathy are invaluable for a good doctor-patient relationship and an effective treatment process. Trainings to improve the knowledge, attitudes, and awareness of doctors should be continued regularly.

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References

1. Turshudzhyan, A., Samuel, S., Tawfik, A., & Tadros, M. (2022). Rebuilding trust in proton pump inhibitor therapy. *World Journal of Gastroenterology*, 28(24), 2667.
2. Del-Pino, M., & Sanz, E. J. (2023). Analysis of deprescription strategies of proton pump inhibitors in primary care: a narrative review. *Primary Health Care Research & Development*, 24, e14.
3. Stojaković, N., Golić Jelić, A., Stoisavljević Šatara, S., Bednarčuk, N., Stojiljković, M. P., & Škrbić, R. (2022). Characteristics and patterns of proton pump inhibitors prescribing at the primary health care. *Medicina*, 58(11), 1622.
4. Joyce, G. F., Carrera, M., Goldman, D. P., & Sood, N. (2011). Physician prescribing behavior and its impact on patient-level outcomes. *The American journal of managed care*, 17(12), e462.
5. Burns, L. R., Housman, M. G., Booth, R. E., & Koenig, A. M. (2018). Physician preference items: what factors matter to surgeons? Does the vendor matter?. *Medical Devices: Evidence and Research*, 39-49.
6. Murshid, M. A., & Mohaidin, Z. (2017). A systematic review of the influence of medical representatives and promotional tools on prescribing: A comparison between developed and developing countries. *International Journal of Pharmaceutical and Healthcare Marketing*, 11(4), 361-394.
7. Murshid, M. A., & Mohaidin, Z. (2018). The influence of information, brand, medical representatives and sales promotion on physician prescribing decision. *Journal of Pharmaceutical Health Services Research*, 9(3), 259-269.
8. Sullivan, H. W., Squire, C., Aikin, K. J., Tzeng, J., Ferriola-Bruckenstein, K., Brodsky, E., ... & Johnson, M. (2022). Physicians' use of and preferences for FDA-approved prescribing information. *Research in Social and Administrative Pharmacy*, 18(6), 3027-3037.
9. Batuwitage, B. T., Kingham, J. G., Morgan, N. E., & Bartlett, R. L. (2007). Inappropriate prescribing of proton pump inhibitors in primary care. *Postgraduate medical journal*, 83(975), 66-68.
10. McDonald, E. G., Jones, J., Green, L., Jayaraman, D., & Lee, T. C. (2015). Reduction of inappropriate exit prescriptions for proton pump inhibitors: A before-after study using education paired with a web-based quality-improvement tool. *Journal of hospital medicine*, 10(5), 281-286.
11. Hamzat, H., Sun, H., Ford, J. C., MacLeod, J., Soiza, R. L., & Mangoni, A. A. (2012). Inappropriate prescribing of proton pump inhibitors in older patients: effects of an educational strategy. *Drugs & aging*, 29, 681-690.
12. Lin, D., Eke, C., Cai, C., Thrift, A. P., & Shukla, R. (2020). Decreasing overall and inappropriate proton pump inhibitor use: perspective from a large safety-net healthcare system. *Clinical Gastroenterology and Hepatology*, 18(4), 763-766.
13. Targownik, L. E., Fisher, D. A., & Saini, S. D. (2022). AGA clinical practice update on de-prescribing of proton pump inhibitors: expert review. *Gastroenterology*, 162(4), 1334-1342.

14. Çalışkan, H. M., & Çelik, B. (2021). Evaluation of management of patients who apply to emergency service with dyspeptic complaints. *Journal of Contemporary Medicine*, 11(5), 640-646.
15. DEMİRCAN, C., HASANZADE, U., TATAR, M., & BÜYÜKUYSAL, M. (2023). EVALUATING POTENTIALLY INAPPROPRIATE MEDICATIONS IN THE ELDERLY WITH SEVEN DIFFERENT SCREENING TOOLS. *TURKISH JOURNAL OF GERIATRICS-TURK GERIATRI DERGISI*, 26(4).
16. Polat, Ö., Çırak, M., Polat, H., & Yürüyen, M. (2020). Medication Adherence and Related Factors in Elderly Patients. *European Journal of Geriatrics & Gerontology*, 2(3).
17. Koçak, F. Ö. K., Taşkıran, E., Öztürk, Z. K., & Şahin, S. (2022). Potentially inappropriate medication use among nursing home residents: Medication errors associated with pro re nata medications and the importance of pill burden. *Annals of Geriatric Medicine and Research*, 26(3), 233.
18. Albayrak, A., & Demirbaş, H. (2023). Evaluation of potentially inappropriate medications use and medication complexity in elderly patients applying to community pharmacy in Turkey. *BMC geriatrics*, 23(1), 655.
19. Hamurtekin, E., Boşnak, A. S., Azarbad, A., Moghaddamshahabi, R., Hamurtekin, Y., & Naser, R. B. (2023). Knowledge, attitude, and practices regarding proton pump inhibitors among community pharmacists and pharmacy students. *Nigerian Journal of Clinical Practice*, 26(2).
20. Eryilmaz, A., Basal, Y., Gunel, C., Basak, S., Ture, M., Elatik, H., & Basak, O. (2016). Awareness and daily practices of family physicians and trainees towards laryngopharyngeal reflux. *European Archives of Oto-Rhino-Laryngology*, 273(12), 4377-4384.
21. Simadibrata, D. M., Syam, A. F., & Lee, Y. Y. (2022). A comparison of efficacy and safety of potassium-competitive acid blocker and proton pump inhibitor in gastric acid-related diseases: A systematic review and meta-analysis. *Journal of Gastroenterology and Hepatology*, 37(12), 2217-2228.
22. Alnabulsi, R. K., Jambi, R. O., Dhabab, N., Alsubahi, T., Basheikh, M. A., Kamel, F. O., & Magadmi, R. M. (2018). Physician's practice toward and knowledge about proton pump inhibitor prescription in Jeddah, Saudi Arabia. *Int Ann Med*, 2(6).