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Improving Proton-Pump Inhibitor Adherence Intervention Between Primary Care and Community Pharmacies: A Pre-Post Intervention Study

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Purpose: Proton-pump inhibitor (PPI) therapy stands as the primary treatment for upper gastrointestinal symptoms, yet poor adherence often results in treatment failure. Given that patients experiencing these symptoms frequently seek assistance at community pharmacies, the development of collaborative tools with primary care is becoming imperative. The objective was to assess the effectiveness of a pharmaceutical intervention, as demonstrated by a collaborative model between primary care and community pharmacies, in enhancing adherence to PPI among patients experiencing upper gastrointestinal symptoms.

Patients and methods: A Pre-post intervention study was carried out in Spanish community pharmacies (June-October 2022). During the baseline visit, patients' sociodemographic and clinical variables were evaluated. Patients were categorized as adherent or non-adherent using the Morisky Medication Adherence Scale (MMAS-4). In the follow-up visit (14 days later), the impact of the intervention was measured by changes in the Gastroesophageal Reflux Disease Impact Scale (GIS).

Results: Of the 351 patients with an active PPI prescription, 178 (50.7%) were non-adherent. Nearly 70% of these patients (122, 68.5%) received an intervention to improve adherence. The overall GIS score improved after the intervention (mean 25.34, SD 5.66 vs mean 27.64, SD 5.63, $p < 0.001$). All GIS score items showed improvement after the intervention except for the item regarding the taking of additional medication different from that prescribed by the clinician ($p = 0.200$).

Conclusion: The pharmaceutical intervention had a positive impact on patients' symptom relief and overall quality of life, highlighting the significance and efficacy of a collaborative model between primary care and professional pharmaceutical services.

Clinical Trials Registry: Clinical Trial Registration (NCT05162079).

Keywords: community pharmacy, proton-pump inhibitors, primary care, upper gastrointestinal symptoms, collaborative model, treatment adherence

Introduction

Upper gastrointestinal symptoms are highly prevalent in the general population and varied significantly between countries ranging from 11% to 24%, socioeconomic factors, dietary habits and healthcare systems may influence in regional differences[1,2] Symptoms such as heartburn and/or regurgitation can be indicative of gastroesophageal reflux or gastrointestinal disorders affecting the retrosternal area.[3,4] Heartburn may also be manifest as functional heartburn[3] or be associated with other symptoms, such as dyspeptic, which affect the epigastric area.[5] Managing these symptoms is often challenging due to their heterogeneous nature and potential overlap.[6,7.]

When lifestyle interventions prove insufficient, the primary treatment approach, as outlined in clinical guidelines of gastroesophageal reflux disease and dyspepsia, involves Proton Pump Inhibitors (PPI) therapy.[8,9] According to the American Gastroenterological Association (AGA) guidelines, a trial of single-dose PPI therapy for 4 to 8-weeks is

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recommended for symptoms without alarm criteria. Persistent symptoms require revaluation of diagnosis and treatment, and clinicians should always emphasize the importance of educating patients on health habits related to symptom management.[10]

In Spain, PPIs rank among the most commonly prescribed therapies, according to the Spanish Agency of Medicines and Medical Devices (AEMPS). Over the past decade, PPI consumption increased by 13.4%, from 117.6 defined daily doses per 1000 inhabitants in 2010 to 133.4 defined daily doses per 1000 inhabitants in 2022.[11] Therefore, the use of these treatments is frequently prescribed.

When diagnosing gastrointestinal disorders, healthcare providers consider the severity, duration, and impact of the disease on patient's quality of life.[4,8,9] However, patients often delay seeking medical advice until symptoms cause significant discomfort.[12] Research indicates that a significant proportion of patients with reflux symptoms initially seek advice from community pharmacies and relief through over-the-counter (OTC) medications. According to a Spanish study, only 28% of patients with reflux symptoms visited their doctor.[13]

Therefore, the development of collaborative models between primary care and community pharmacies to treat upper gastrointestinal symptoms is crucial. Providing pharmacists with standardized tools to act as a filter to identify alarm symptoms and refer patients to primary care when necessary, will reduce the burden on primary care by providing guidance on treatment strategies, including health habits education, for mild symptoms.

To enable an integrated care system for the treatment of upper gastrointestinal symptoms, an interdisciplinary group comprising primary care, gastroenterology, and community pharmacy experts has devised an algorithm for comprehensive symptom management, endorsed by professional societies, the Spanish Society of Community Pharmacy (SEFAC) and the Spanish Society of Primary Care Clinicians (SEMERGEN).

This algorithm encompasses symptom assessment, screening for alarm symptoms, referral to primary care clinicians, health habits education, and non-prescription symptomatic pharmacological treatment.[14] Additionally, it addresses the optimization of prescribed pharmacotherapy, due to some studies have reported that poor adherence or compliance poses a risk of treatment failure or worsening symptoms.[15,16]

Since patients sometimes require re-evaluation of their treatment by their prescriber or non-adherence is one of the causes of treatment failure, the role of the pharmacist in prescribing PPi is crucial. Pharmacists can identify patients who need to be referred to primary care while implementing interventions to improve adherence (if applicable), ultimately reducing the burden on primary care services.

The aim of this study was to assess the impact of a pharmaceutical intervention reflected in a collaborative model to improve adherence to PPI among patients with upper-gastrointestinal symptoms in the community pharmacy, through real-world data.

Methods

Study Design

These results were part of a pre-post intervention study carried out in Spanish community pharmacies to evaluate the impact of an algorithm collaborative between community pharmacies and primary care on patients with upper gastrointestinal symptoms (Supplementary Figure 1). The protocol describing this algorithm was already published.[14] The study protocol was approved by the Ethics Committee of the Hospital de Sant Joan D'Alacant (code 19/335 Tut) and previously classified as NO-EPA by the Spanish Medicines Agency (AEMPS).

Study Population

Spanish community pharmacists who belong to the Spanish Society of Community Pharmacy (SEFAC) were invited to participate. We included patients older than 18 years who visited community pharmacies to seek advice or to request over-the-counter treatment for upper gastrointestinal symptoms. We excluded those patients with high-risk pregnancy or those requesting treatment for someone else were excluded from the study. The calculation of the sample size has been previously described in the protocol.[14]

We estimated the sample size needed to detect a 0.1-unit change on a 4-point Likert scale between two visits, with a standard deviation of 0.6. Assuming an alpha risk of 0.05, a two-sided test, and a beta risk of 0.20, we initially calculated a required sample size of 285 patients. We increase this size by considering the losses due to tracking by 20%. Therefore, we need to include a total of 342 patients.

Data Collection and Procedure

Data collection from patients was conducted between June - October 2022 and was divided in two visits: baseline visit and follow-up visit.

a) Baseline visit

Patients who fulfilled the inclusion criteria were invited to participate. The community pharmacist provided them with an information sheet explaining the study details. Before taking part, patients signed the informed consent and were assigned an anonymous identification code: CA-III-PN (CA: autonomous community code; III: researcher's initials; PN, and N: participant number).

The pharmacist then collected the following information from patients (the variables are detailed in Supplementary Data):

• Outcome variable: Adherence to PPIs (Proton Pump Inhibitors) was evaluated using the 4-item Morisky Medication Adherence Scale (MMAS-4)[17–19] which was recorded in a data collection notebook.

• Sociodemographic variables.

• Clinical variables.

• Patient's quality of life and the distribution of patient's symptoms through Gastroesophageal Reflux Disease Impact Scale (GIS) questionnaire.[20]

Intervention

If patients with an active PPI prescription had a non-compliant result in the Morisky Green test and the patient agreed, the pharmacist carried out an intervention to improve treatment adherence. The intervention was to reinforce and examine the items on the Morisky scale on which the patient was non-adherent. Then, the pharmacist explained how and when to take the medication and provided the patient with strategies to improve adherence.

b) Follow-up visit

After 14 days, the study monitor interviewed patients and collected the Gastroesophageal Reflux Disease Impact Scale (GIS) questionnaire. The impact of the interventions on adherence in improving the patient's gastrointestinal symptoms and quality of life was assessed by measuring the change in the GIS scale before and after the pharmaceutical interventions.

Data Analysis

Data were collected in the data collection notebook, only the principal investigator and study monitor had access to this information. The data collected in the pharmacy were entered into a platform designed for the study. The study monitor validated all information contained in the platform and transferred it to a database. Data analysis was performed using SPSS Statistics (IBM, version 27).

For the analysis of the adherence intervention, the patients included in this study were those who underwent the PPI adherence assessment test (4-item Morisky Medication Adherence Scale (MMAS-4)), so the analyses were conducted by classifying patients as: adherent and non-adherent. The test was performed on 392 patients, 41 were excluded because the results of the questions on adherence and the pharmacist's judgement of adherence did not coincide, so for the analysis we had a sample of 351 patients.

The data were analysed descriptively with specification of absolute and relative frequencies, with determination of the 95% confidence interval. The GIS scale score is measured on a Likert scale from 1 to 4, the higher the score, the better the patient's condition because the frequency of heartburn and/or reflux symptoms and their interference with the patient's quality of life is lower. Results were considered significant with a p-value <0.05.

Results

Clinical and Socio-Demographic Characteristics of Patients

Of the 1360 patients who consulted for heartburn and/or reflux in Spanish pharmacies during the study period, 351 (25%) were prescribed a PPI. Most patients (216, 61.5%) were female, with a mean age of 57.4 years (ds 15.5) and a BMI of 26.7 (ds 4.1). A request for over-the-counter medication was the most common reason for consultation (187, 53.3%), with antacids (140, 68.3%) being the most commonly requested. Most of patients had secondary/university education (197, 56.1%) and were retired (145, 41.3%). Regarding their lifestyle habits, 34.5% of the patients were daily physically active, 51.9% (182) of the patients never or once a year consume alcoholic beverages and 180 (51.3%) were never smokers. 27.6% once or twice a week, 51.3% of the patients had never smoked. On the other hand, 51.3% of the patients had previously been diagnosed with gastrointestinal disease and 82.6% had alarm criteria (Table 1).

Table 1 Clinical and Socio-Demographic Characteristics of Patients According to Their Adherence to Proton Pump Inhibitor Therapy

Variables N (%)	**Total (351)**	**Non Adherent (178, 50.7%)**	**Adherent (173, 49.3%)**	**p value**
Sex				0.021
Female	216(61.5)	99(55.6)	117(67.6)	
Male	135(38.5)	794.4)	56(32.4)	
Age (years) (mean, SD)	57.4(15.5)	55 (15)	60(15)	0.005
BMI (kg/m^2) (median, SD)	26.7(4.1)	26.6 (3.9)	26.8(4.3)	0.671
Reason for consultation				0.198
Seeking treatment advice for the symptoms	146(41.6)	71 (39.9)	75(43.4)	
Requesting over-the counter medication	187(53.3)	101(56.7)	86(49.7)	
Both	18(5.1)	6(3.4)	12(6.9)	
Requested over-the counter medication				0.358
Antiacid monotherapy	140(68.3)	73(68.2)	67(68.4)	
Alginates in combination with antiacids	27(13.2)	11(10.3)	16(16.3)	
PPIs	16(7.8)	11(10.3)	5(5.1)	
Non pharmacological treatment/others	22(10.7)	12(11.2)	10(10.2)	
Educational level				0.017
No studies/Primary education/NSNC	154(43.9)	67(37.6)	87(50.3)	
Secondary /university education	197(56.1)	111(62.4)	86(49.7)	
Employment status				0.007
Employee	114(32.5)	68(38.2)	46(26.6)	
Self-employed	29(8.3)	20(11.2)	9(5.2)	
Retired	145(41.3)	63(35.4)	82(47.4)	
Unemployed	63(17.9)	27(15.2)	36(20.8)	

(*Continued*)

Table 1 (Continued).

Variables N (%)	Total (351)	Non Adherent (178, 50.7%)	Adherent (173, 49.3%)	p value
Marital status				0.007
Single	65(18.5)	41(23.0)	24(13.9)	
Married	213(60.7)	103(57.9)	110(63.6)	
Divorced/separated	37(10.5)	23(12.9)	14(8.1)	
Widowed	36(10.3)	11(6.2)	25(14.5)	
Frequency of physical activity				0.072
Daily	121(34.5)	51(28.7)	70(40.5)	
Once or twice/a week	97(27.6)	55(30.9)	42(24.3)	
3–5 times/a month	62(17.7)	37(20.8)	25(14.5)	
Never	71(20.2)	35(19.7)	36(20.8)	
Smoking habits				0.259
Smokers/Ex smokers	171(48.7)	92(51.7)	79(45.7)	
Never smokers	180(51.3)	86(48.3)	94(54.3)	
Frequency of Alcohol intake				0.076
Daily or twice/a week	93(26.5)	51(28.7)	42(24.3)	
1–4 times/a month	76(21.7)	45(25.3)	31(17.9)	
Once a year/Never	182(51.9)	82(46.1)	100(57.8)	
Previous diagnosis of any gastrointestinal disease	180(51.3)	83(46.6)	97(56.1)	0.077
Alarm criteria	290(82.6)	142(79.8)	148(85.5)	0.154
Previous medication used before visiting the pharmacy:				0.803
Prescribed	150(50.3)	74(49.0)	76(51.7)	
Over the counter	93(31.2)	47(31.1)	46(31.3)	
Both	55(18.5)	30(19.9)	25(17.0)	
How the patient felt about the previous medication used				0.035
Well, it alleviated the symptoms	250(71.2)	120(67.4)	130(75.1)	
Fair-poor	48(13.7)	31(17.4)	17(9.8)	
PPi regimen				0.010
Breakfast	272(77.5)	139(78.1)	133(76.9)	
Lunch	11(3.1)	3(1.7)	8(4.6)	
Dinner	23(6.6)	10(5.6)	13(7.5)	
Breakfast and dinner	21(6.0)	7(3.9)	14(8.1)	

(*Continued*)

Table 1 (Continued).

Variables N (%)	Total (351)	Non Adherent (178, 50.7%)	Adherent (173, 49.3%)	p value
When the PPI prescription started?				0.682
1–4 weeks	35(10.0)	19(10.7)	16(9.2)	
1–6 months	52(14.8)	27(15.2)	25(14.5)	
1 year or more	264(75.2)	132(74.2)	132(76.3)	
Patient symptoms				0.024
Epigastric	47(13.4)	17(9.6)	30(17.3)	
Retroesternals	100(28.5)	46(25.8)	54(31.2)	
Both (overlapping)	204(58.1)	115(64.6)	89(51.4)	

Abbreviations: BMI, body mass index; PPi, Proton Pump Inhibitors.

Of the 351 patients who were on PPI treatment, 150 (50.3%) had an active prescription and 93 (31.2%) had received PPI dispensing as OTC medication, and 71.2% of the 351 patients reported feel alleviated from previously used treatment.

Most of patients took a PPI at breakfast (272, 77.5%) and had been prescribed it for more than a year (264, 75.2%). The predominant symptomatology was a combination of retrosternal and epigastric symptoms (overlapping) (204, 58.1%) (Table 1).

Patients' Characteristics Associated to Adherence to Treatment

Of the 351 patients included, 178 (50.7%) were considered as non-adherent to their PPI treatment and 173 (49.3%) as adherent to their treatment (Table 1).

Adherent patients were more likely to be women than those non adherent patients (117, 67.6% vs 99, 55.6%, p=0.021). Adherent patients were more likely to be older than non-adherent patients (mean 60 years, sd 15 vs mean 55 years, sd 15, p=0.005). Non-adherent patients were more likely to have secondary/university studies than adherent patients (111, 62.4% vs 86, 49.7%, p=0.017). Adherent patients were more likely to express that previous medication alleviated their symptoms than non-adherent patients (130, 75.1% vs 120, 67.4%, p=0.035). Non-adherent patients were more likely to be classified as overlapped symptoms than adherent patients (115, 64.6% vs 89, 51.4%, p=0.024).

In a multivariable analysis (adjusted by educational level, sex, age, educational level, employment status, marital status, how the patient felt about the previous medication used, PPI regimen and patient's symptoms), patients who felt that previous medication had had a fair poor impact on their symptoms were less likely to be adherent than those who felt that previous medication had alleviated their symptoms (RR 0.470, CI95%0.236–0.937, p=0.032). Those patients classified as having overlapping symptoms were less likely to be adherent than those with epigastric symptoms (RR 0.348, CI95%0.156–0.778, p=0.010) (data not shown).

Impact of Intervention to Improve Adherence to PPI Therapy

Of the 178 patients classified as non-adherent, 122 (68.5%) received a specific intervention to improve their adherence to treatment. There were no differences between those who received the intervention and those who did not.

Global score in the GIS scale before the implementation of the intervention was significantly different from the global score in the GIS scale after the intervention (mean 25.34, sd 5.66 vs mean 27.64, sd 5.63, p<0.001).

The number of patients who improved their symptoms after the intervention was statistically significative in all the different items of the GIS scale (Table 2). However, the intervention did not show a significant impact on the frequency that patients took additional medication other than what the physician told the patient before (p=0.200).

Table 2 Impact of the Pharmaceutical Intervention Related to Adherence to PPIs on GIS Scale Measured Through the Change in the Number of Patients Who Answered the Scale Before and After the Intervention

	Number of Patients in Each Category Before and After the Intervention			
	Pre-Intervention (n)	Post-Intervention (n)	% change	p value
1.How often have you had the following symptoms:				
a. Pain in your chest or behind your breastbone?				
Daily	4	2	−50	0.007
Often	14	9	−35,7	
Sometimes	20	10	−50	
Never	70	87	24,3	
b. Burning sensation in your chest or behind the breastbone				
Daily	10	2	−80	<0.001
Often	26	24	−7,7	
Sometimes	22	21	−4,5	
Never	50	61	22	
c. Regurgitation or acid taste in your mouth?				
Daily	12	3	−75	<0.001
Often	31	32	3,2	
Sometimes	30	33	10	
Never	35	40	14,3	
d. Pain or burning in your upper stomach?				
Daily	13	3	−76,9	<0.001
Often	39	36	−7,7	
Sometimes	29	25	−13,8	
Never	27	44	63,0	
e. Sore throat or hoarseness that is related to your heartburn or acid reflux?				
Daily	4	1	−75	<0.001
Often	20	15	−25	
Sometimes	14	19	35,7	
Never	70	73	4,3	

(*Continued*)

Table 2 (Continued).

	Number of Patients in Each Category Before and After the Intervention			
	Pre-Intervention (n)	**Post-Intervention (n)**	**% change**	**p value**
2.How often have you had difficulty getting a good night´s sleep because of your symptoms?				
Daily	4	2	−50	<0.001
Often	30	22	−26,7	
Sometimes	29	32	10,3	
Never	45	52	15,6	
3.How often have your symptoms prevented you from eating or drinking any of the foods you like?				
Daily	6	1	−83,3	0.001
Often	29	20	−31,0	
Sometimes	31	22	−29,0	
Never	42	65	54,8	
4.How frequently have your symptoms kept you from being fully productive in your job or daily activities?				
Daily	1	0	−100	0.028
Often	10	2	−80	
Sometimes	16	9	−43,8	
Never	81	97	19,8	
5.How often do you take additional medication other than what the physician told you to take?				
Daily	16	8	−50	0.200
Often	21	44	109,5	
Sometimes	20	32	60,0	
Never	51	24	−52,9	

Discussion

Main Findings

Our results showed that 50% of patients undergoing PPI treatment and receiving care at a community pharmacy were considered as non-adherent. In addition, patients experiencing both epigastric and retrosternal symptoms, as well as those who felt that their previous medication only moderately relieved their symptoms, were more prone to non-adherence. However, we found that the collaborative model intervention on adherence to PPIs led to a positive impact on patients' health.

Comparison with Existing Literature

Despite the fact that PPi treatment is one of the most prescribed in the healthcare system, according to a systematic review, a high percentage of patients, ranging between 17% and 32% in primary care trials and up to 45% in

observational studies, did not respond to treatment with PPI.[21] Additionally, other research indicates that symptoms persist in 40% of patients undergoing PPI therapy.[22] The literature extensively documents reasons behind poor treatment response, including inappropriate drug usage, non-adherence, incorrect dosage, and various clinical factors related to metabolism, acid release, and other physiological processes.[23,24] In our study, in which 50.7% of patients were identified as non-adherent, lack of treatment adherence may have been a potential factor contributing to treatment failure and may have led to more consultations in community pharmacies. This figure aligns closely with findings from a systematic review of observational studies, which reported non-adherence rates to PPI therapy ranging between 20% and 50%.[15]

Patients' variables such as age, marital status, educational level and sex have been assessed in other studies, which align with our findings.[15,25,26] Additionally, research highlights the importance of appropriate dosage timing related to symptom onset; for instance, nighttime intake may alleviate symptoms more effectively than taking medication with breakfast.[25,27] In our study we found that most patients who took their medication with breakfast exhibited lower adherence levels, emphasizing the need for patient education on optimal timing and dosage for treatment optimization. Another study evaluated adherence levels based on varying degrees of disease severity and reported that patients with more severe symptoms tended to exhibit lower adherence rates.[28] Our findings similarly show that patients with overlapping symptoms had lower treatment adherence compared to those with isolated epigastric or retrosternal symptoms. Additional research supports the correlation between symptom severity and treatment response.[24,26] Given that community pharmacies often serve as the primary point of entry into the healthcare system, implementing collaborative algorithms, such as the one used in our study, can enable pharmacists to assess patient symptomatology and develop personalized strategies to enhance treatment outcomes.

This study focuses on those patients who already have an active prescription but seek advice in community pharmacies because of persistent gastrointestinal symptoms. Following the intervention aimed at enhancing treatment adherence, we have observed positive changes in symptomatology and overall quality of life. As observed in previous studies, when symptoms persist, it is essential to address treatment adherence while also educating patients on hygiene and dietary measures to manage symptom occurrence.[23,29] Furthermore, it is noteworthy that the American Gastroenterology Association has established a policy regarding prescription discontinuation in cases where patients exhibit no response despite treatment measures. This policy emphasizes the need for physicians to re-evaluate chronic treatment and reconsider whether the patient really needs ongoing medication. Moreover, it suggests that doses should be minimized whenever possible.[30] Therefore, this algorithm can not only enhance treatment adherence but also, in collaboration with clinical referral, serves as a means of identifying patients in need of treatment reassessment. This, in turn, may lead to improvements in differences observed in GIS scores. Other collaborative models such as the MAS protocol, which includes treatment of minor symptoms, showed better results in terms of cost-effectiveness and optimization of primary care, while recognizing the importance of the pharmaceutical role.[31,32] So implementing these models had several benefits beyond symptoms and improving quality of life.

In this study, the use of additional medication outside of prescribed PPI treatment was explored as part of the patient's overall symptom management. Prior to the intervention, many patients reported using over-the-counter medications, such as antacids, to treat their gastrointestinal symptoms. The frequency with which patients used over-the-counter medications or other non-prescribed treatments suggests that further efforts are needed to address the use of additional medications, as it may indicate persistent symptoms or a lack of patient education about appropriate treatment options.

Strengths and Limitations

This study has several limitations. Primarily due to the COVID-19 pandemic, follow-up data collection after the 14-day intervention could not be conducted face-to-face. Nevertheless, all information was validated by the study monitor. Ten percent of the initially included patients were lost to follow-up. However, no significant differences were observed between patients who stayed in the study and those who were lost in follow-up. In addition, similar percentages were lost in all three patient groups classified according to symptoms. Although the patients agreed to participate in the study, more than 30% of them refused to receive the adherence interventions because they preferred to consult their clinician. However, there were no clinical and sociodemographic differences between the patients who accepted the intervention and those who did not. After the intervention, we did not reassess

treatment adherence using the Morisky Test. Instead, the evaluation of changes in the GIS score scale was deemed a reliable indicator of the improvement in patients' symptomatology and quality of life. After a follow-up period of 14 days we were able to assess the short-term outcomes of the intervention. Longer follow-up would therefore be necessary to assess sustained adherence and its implications for patient outcomes over time. The study was conducted in Spanish community pharmacies, where the population may have characteristics related to access to healthcare and pharmacy practices. Therefore, its generalisability to other settings will depend mainly on the accessibility of pharmacies in other settings.

Conclusion

This study represents the first attempt to evaluate the efficacy of an intervention aimed at improving adherence to PPI treatment in community pharmacies. It was observed that patients with poorer adherence tended to experience overlapping symptoms and felt that their previous medication only moderately relieved their symptoms. Pharmaceutical intervention to improve adherence produced positive results in terms of symptom relief and improved quality of life. This underlines the importance of integrating collaborative models between primary care and professional pharmaceutical services into clinical practice. Given that around 30% of patients did not accept the pharmaceutical intervention, it is essential to further explore aspects such as patients' acceptance of the role of community pharmacists and their integration of the healthcare system, as well as the long-term effects of the intervention. Addressing these areas will improve understanding and provide practical ideas for implementing collaborative care models, ultimately improving patient care and outcomes.

Abbreviations

PPI, Proton-pump inhibitor; MMAS-4, Morisky Medication Adherence Scale; GIS, Gastroesophageal Reflux Disease Impact Scale; OTC, over-the-counter medications; SEFAC, Spanish Society of Community Pharmacy; SEMERGEN, Spanish Society of Primary Care Clinicians; AEMPSSpanish Agency of Medicines and Medical Devices.

Data Sharing Statement

All data contained in this article can be made available upon reasonable request from the corresponding author.

Ethical Approval

The study protocol was approved by the Ethics Committee of the Hospital de Sant Joan D'Alacant (code 19/335 Tut) and previously classified as NO-EPA by the Spanish Medicines Agency (AEMPS). Participation of the research pharmacists in the study was free, voluntary and independent. The research pharmacist signed a researcher commitment to accurately record the data. The participant was informed by the pharmacist about his/her participation in the study verbally and with the participant information sheet and ensured that he/she had received and understood all information about the study before signing the informed consent. The data will be treated confidentially in accordance with the General Data Protection Regulation (Regulation 2016/679 of April 27). The study was conducted in accordance with the Declaration of Helsinki.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

Elsa López-Pintor is a member of the SEFAC Scientific Committee. ELP has previously worked as an external advisor for Reckitt. However, this has not influenced any aspect of this research or the work presented. All the authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; no financial relationships with any organizations that might have had an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

References

1. Haag S, Andrews JM, Gapasin J, et al. A 13-nation population survey of upper gastrointestinal symptoms: prevalence of symptoms and socioeconomic factors. *Aliment Pharmacol Ther*. 2011;33(6):722–729. doi:10.1111/j.1365-2036.2010.04564.x
2. Barberio B, Mahadeva S, Black CJ, et al. Systematic review with meta-analysis: global prevalence of uninvestigated dyspepsia according to the Rome criteria. *Aliment Pharmacol Ther*. 2020;52(5):762–773. doi:10.1111/apt.16006
3. Rome IVC. Rome Foundation. Available from: https://theromefoundation.org/rome-iv/rome-iv-criteria/. Accessed 15, may 2023.
4. Vakil N, van Zanten SV, Kahrilas P, et al. The Montreal definition and classification of gastroesophageal reflux disease: a global evidence-based consensus. *Am J Gastroenterol*. 2006;101(8):1900–1920. doi:10.1111/j.1572-0241.2006.00630.x
5. Savarino E, Pohl D, Zentilin P, et al. Functional heartburn has more in common with functional dyspepsia than with non-erosive reflux disease. *Gut*. 2009;58(9):1185–1191. doi:10.1136/gut.2008.175810
6. Choung RS, Locke GR, Schleck CD, et al. Overlap of dyspepsia and gastroesophageal reflux in the general population: one disease or distinct entities? *Neurogastroenterol Motil off J Eur Gastrointest Motil Soc*. 2012;24(3):229–34,e106. doi:10.1111/j.1365-2982.2011.01845.x
7. Geeraerts A, Van Houtte B, Clevers E, et al. Gastroesophageal reflux disease-functional dyspepsia overlap: do birds of a feather flock together? *Am J Gastroenterol*. 2020;115(8):1167–1182. doi:10.14309/ajg.0000000000000619
8. Black CJ, Paine PA, Agrawal A, et al. British Society of Gastroenterology guidelines on the management of functional dyspepsia. *Gut*. 2022;71(9):1697–1723. doi:10.1136/gutjnl-2022-327737
9. Katz PO, Dunbar K, Schnoll-Sussman FH, et al. ACG clinical guideline: guidelines for the diagnosis and management of gastroesophageal reflux disease. *Am J Gastroenterol*. 2022;117(1):27–56. doi:10.14309/ajg.0000000000001538
10. Yadlapati R, Gyawali CP, Pandolfino JE. AGA clinical practice update on the personalized approach to the evaluation and management of GERD: expert review. *Clin Gastroenterol Hepatol Off Clin Pract J Am Gastroenterol Assoc*. 2022;20(5):984–994.e1. doi:10.1016/j.cgh.2022.01.025
11. Agencia Española de Medicamentos y Productos Sanitarios. Informes publicados. 2019 Available from: https://www.aemps.gob.es/medicamentos-de-uso-humano/observatorio-de-uso-de-medicamentos/informes/. Accessed 6, February 2024.
12. Hungin APS, Hill C, Raghunath A. Systematic review: frequency and reasons for consultation for gastro-oesophageal reflux disease and dyspepsia. *Aliment Pharmacol Ther*. 2009;30(4):331–342. doi:10.1111/j.1365-2036.2009.04047.x
13. Rey E, Moreno-Elola-Olaso C, Rodriguez-Artalejo F, et al. Medical consultation for gastro-oesophageal reflux symptoms: reasons and associated factors. *Digestion*. 2004;70(3):173–177. doi:10.1159/000081626
14. López-Pintor E, Puig-Moltó M, Lumbreras B. EsReflux protocol: epidemiological study of heartburn and reflux-like symptoms in Spanish community pharmacies. *Int J Environ Res Public Health*. 2022;19(16):9807. doi:10.3390/ijerph19169807
15. Rettura F, Bronzini F, Campigotto M, et al. Refractory gastroesophageal reflux disease: a management update. *Front Med*. 2021;8:765061. doi:10.3389/fmed.2021.765061
16. Domingues G, Moraes-Filho JPP. Noncompliance is an impact factor in the treatment of gastroesophageal reflux disease. *Expert Rev Gastroenterol Hepatol*. 2014;8(7):761–765. doi:10.3389/fmed.2021.765061
17. Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. *Med Care*. 1986;24(1):67–74. doi:10.1097/00005650-198601000-00007
18. Morisky DE, Malotte CK, Choi P, et al. A patient education program to improve rate with antituberculosis drug regimens. *Health Educ Q*. 1990;17:253–268. doi:10.1177/109019819001700303
19. Morisky DE, DiMatteo MR. Improving the measurement of self-reported medication nonadherence: final response. *J Clin Epidemio*. 2011;64(3):262–263. doi:10.1016/j.jclinepi.2010.09.002
20. Nuevo J, Tafalla M, Zapardiel J. Validation of the reflux disease questionnaire (RDQ) and gastrointestinal impact scale (GIS) in patients with gastroesophageal reflux disease in the Spanish population. *Gastroenterol Hepatol*. 2009;32(4):264–273. doi:10.1016/j.gastrohep.2008.12.004
21. El-Serag H, Becher A, Jones R. Systematic review: persistent reflux symptoms on proton pump inhibitor therapy in primary care and community studies. *Aliment Pharmacol Ther*. 2010;32(6):720–737. doi:10.1111/j.1365-2036.2010.04406.x
22. Hillman L, Yadlapati R, Thuluvath AJ, et al. A review of medical therapy for proton pump inhibitor nonresponsive gastroesophageal reflux disease. *Dis Esophagus off J Int Soc Dis Esophagus*. 2017;30(9):1–15. doi:10.1093/dote/dox055
23. Azzam RS. Are the persistent symptoms to proton pump inhibitor therapy due to refractory gastroesophageal reflux disease or to other disorders? *Arq Gastroenterol*. 2018;55:85–91. doi:10.1590/S0004-2803.201800000-48

24. Cicala M, Emerenziani S, Guarino MPL, et al. Proton pump inhibitor resistance, the real challenge in gastro-esophageal reflux disease. *WJG*. 2013;19(39):6529–6535. doi:10.3748/wjg.v19.i39.6529
25. Castell D, Bagin R, Goldlust B, et al. Comparison of the effects of immediate-release omeprazole powder for oral suspension and pantoprazole delayed-release tablets on nocturnal acid breakthrough in patients with symptomatic gastro-oesophageal reflux disease. *Aliment Pharmacol Ther*. 2005;21(12):1467–1474. doi:10.1111/j.1365-2036.2005.02513.x
26. Fass R, Shapiro M, Dekel R, et al. Systematic review: proton-pump inhibitor failure in gastro-oesophageal reflux disease--where next? *Aliment Pharmacol Ther*. 2005;22(2):79–94. doi:10.1111/j.1365-2036.2005.02531.x
27. Hatlebakk JG, Katz PO, Kuo B, et al. Nocturnal gastric acidity and acid breakthrough on different regimens of omeprazole 40 mg daily. *Aliment Pharmacol Ther*. 1998;12(12):1235–1240. doi:10.1046/j.1365-2036.1998.00426.x
28. Mari A, Na'amnih W, Gahshan A, et al. Comparison in adherence to treatment between patients with mild–moderate and severe reflux esophagitis: a prospective study. *J Clin Med*. 2022;11(11):3196. doi:10.3390/jcm11113196
29. Meyer JC, MacBride-Stewart S, Fadare JO, et al. Key considerations from a health authority perspective when proton pump inhibitors are used to treat gastroesophageal reflux disease (GERD) and their implications. *Cureus*. 2022;14(11):e31918. doi:10.7759/cureus.31918
30. Targownik LE, Fisher DA, Saini SD. AGA clinical practice update on de-prescribing of proton pump inhibitors: expert review. *Gastroenterology*. 2022;162(4):1334–1342. doi:10.1053/j.gastro.2021.12.247
31. Dineen-Griffin S, Vargas C, Williams KA, et al. Cost utility of a pharmacist-led minor ailment service compared with usual pharmacist care. *Cost Eff Resour Alloc CE*. 2020;18:24. doi:10.1186/s12962-020-00220-0
32. Amador-Fernández N, Benrimoj SI, Olry de Labry Lima A, et al. Strengthening patients' triage in community pharmacies: a cluster randomised controlled trial to evaluate the clinical impact of a minor ailment service. *PLoS One*. 2022;17(10):e0275252. doi:10.1371/journal.pone.0275252