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Original Article

Multi-Faceted Intervention to Limit Over-Prescription of Proton Pump Inhibitors: A Quasi Experimental Study

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ABSTRACT

Objective: To assess knowledge and attitude regarding over-prescription of PPI, and to utilize multi-faceted educational interventions to reduce inappropriate and unwanted usage of PPIs.

Study Design: Quasi-experimental study.

Place and Duration of Study: Pak Emirates Military Hospital, and Combined Military Hospital Rawalpindi, Pakistan from Aug 2022 to Jan 2024.

Methodology: A total of 807 doctors were included in the study, 395 doctors as Group-A and 412 doctors were taken as Group-B. Group-A doctors were given questionnaires at start and end of intervention at PEMH, and doctors of Group-B were given questionnaires in CMH post-experimentally, as no educational intervention was done on them. Multifaceted intervention was used to find out the primary and secondary outcomes.

Results: Mean age of Group-A was 32.3±3.6 years, and Group-B was 30.2±2.5 years. Knowledge of the study groups was almost the same before intervention. Prescribing knowledge of PPI in Group-A (n=395) improved before and after educational intervention. Most common question which showed drastic change before and after intervention was "Duration of PPI prophylaxis is until no high-risk factors, or able to tolerate enteral feeding?" Before intervention 329(83.3%) vs after intervention 42 (10.6), with a *p*-value <0.001.

Conclusion: Prescribing knowledge of proton pump inhibitors (PPI) in study participants improved before and after educational intervention.

Keywords: Inappropriate Prescription, Multifaceted Intervention, Prescriptions, Proton Pump Inhibitors.

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INTRODUCTION

Proton pump inhibitors (PPIs) are acid-suppressing drugs, essential for treating gastric and duodenal diseases. Because of its safety profile and benefits, its over-consumption is significant, prompting concern about its long-term effects on the human body.[1,2] Omeprazole was the second-most utilized medicine in England in 2020, and in 2019 was among the commonest prescribed medicines in the US, with over 52 million prescriptions.[2] A study from Karachi, found 66.2% inpatients using it without indication, while only 33.8% inpatients received PPIs with appropriate need of use.[3]

PPIs are improperly administered by around 50% of doctors in both inpatient and outpatient settings, and misuse is particularly severe in elderly people.[4] PPIs are most commonly used inappropriately for gastro-protection for individuals, who don't utilise medication that are damaging to the digestive mucosa, prophylaxis for stress ulcers in low-risk patients, and other associated misdiagnoses.[5]

PPIs are safe in the short term, new evidence suggests that long-term use may pose risks, there is increasing proof of significant side effects with prolonged administration, like higher likelihood of pneumonia, intestinal illness, fractures of the bones, GI cancers, and diminished vitamin and mineral absorption.[6] Inappropriate drug prescription is linked to unnecessary medical expenses and the possibility of adverse reactions for patients.[7] There is a high prevalence of inappropriate medication prescriptions.[8]

Although inappropriate prescription of PPIs is common in Pakistan, not many interventions have been suggested by researchers or experts.[9] Hence, the present study was conducted to assess knowledge and attitude regarding over-prescription of PPI, and to utilize multi-faceted educational interventions to reduce inappropriate and unwanted usage of PPIs.

METHODOLOGY

This quasi-experimental study was conducted from August 2022 to January 2024 at the OPDs of Medicine, Surgery, Obstetrics and Gynaecology, Pediatrics, Rehab Departments of the Pak Emirates

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Military Hospital, Rawalpindi, Pakistan and all OPDs in Combined Military Hospital, Rawalpindi, Pakistan. Institutional Ethical Review Board permission was sought.

Inclusion Criteria: Doctors of either gender, and any age group, working in Pak Emirates Military Hospital (PEMH) and Combined Military Hospital (CMH) Rawalpindi, Pakistan were included.

Exclusion Criteria: Doctors working in the Emergency Department, Operation theatres and inpatients wards were excluded.

Sample size for the both groups was calculated using OpenEpi-software with response rate of 91.1% obtained from pilot testing. It came to 800. We included 807 doctors in our study. Three hundred and ninety-five doctors were included in Group-A and 412 doctors were taken as Group-B, after simple random sampling Figure. Informed consent was obtained. Questionnaire was pilot tested after peer-review from the two senior consultants, and its Cronbach Alpha was found to be 0.74. Group-A (n=395) doctors were given questionnaires at start and end of intervention in PEMH, and 412 doctors from Group-B were given questionnaires in CMH post-experimentally. The multifaceted intervention was carried out for the period of 17 months. The educational intervention included face-to-face feedbacks and meetings. Doctors were sensitized at different levels on the importance of i) making wise decisions in PPI prescription (sharing with patients information on risks about the medication and on evidence of over- and inappropriate prescriptions); ii) identifying patients in which PPIs are not indicated and/or are potentially dangerous; iii) withdrawing PPIs when not, or no longer indicated iv) promoting behavior changes by consulting the monitoring/benchmarking platform on new PPI prescriptions.

Educational meetings were held repeatedly in each department, where feedback and management guidelines on PPI prescriptions were discussed with all the doctors involved. These meetings were conducted by a group of experts composed of at least 2 clinicians (a specialist in general internal medicine and a specialist in medical pharmacology), and an expert in quality and patient safety.

Interventional strategies were applied in the PEMH, while the information of the other hospital was utilized as controls to additionally assess the effect of the methodology. Outcome measures of the study were to assess remarkable reduction in PPI over prescription in OPDs (primary outcome). Secondary outcome was to assess knowledge, attitude and behaviour before and after the intervention.

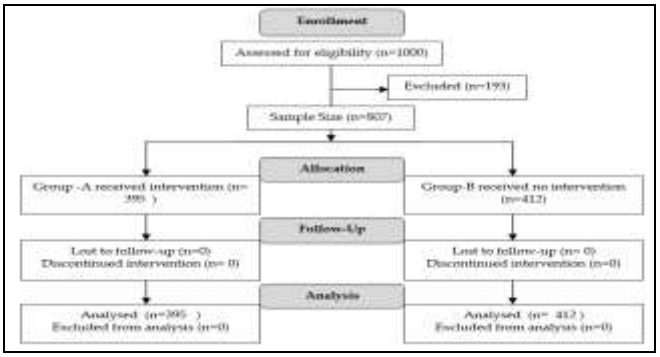

Figure: Patients Flow Diagram (n=807)

Statistical Package for Social Sciences (SPSS) version 26 was used for the data analysis. Quantitative variables with normal distribution were expressed as mean and standard deviation, and qualitative variables were expressed as frequency and percentages. Chi-square test was applied to explore the inferential statistics. A *p*-value ≤0.05 was taken as significant.

RESULTS

A total of 807 doctors were included in the study, 395 doctors as Group-A and 412 doctors were taken as Group-B. Mean age of Group-A was 32.3±3.6 years, and Group-B was 30.2±2.5 years. Age and gender distribution are shown in Table-I.

Table-I: Demographic details of Respondents (n=807)

Parameters		Groups	
Gender distribution		Group-A(n=395) n (%)	Group B(n=412) n (%)
	Male	231 (58.8)	240 (58.3)
	Female	164 (41.5)	172 (42.2)
Mean Age (in years)		32.3±3.6	30.2±2.5

Participants of both groups were asked questions through a structured questionnaire regarding knowledge related to PPIs, however Group-A (n=395) participants were asked the questions before and after the intervention, while in Group-B (n=412) questions were asked only once, as no educational intervention was done on them. Most common question which was answered 'yes' by participants [Group-A: n=348 (88.1%) vs. Group-B: n=356 (86.5%)] was "Followings are the PPIs: omeprazole, pantoprazole, lansoprazole, rabeprazole, esomeprazole, etc". The details of this comparison are shown in the Table-II.

The comparison of knowledge related to PPIs in Group-A before and after intervention showed

remarkable results. The knowledge of the doctors increased after the intervention, as per our 20 questions. Prescribing knowledge of PPI in Group-A (n=395) improved before and after educational intervention. Most common question which showed drastic change before and after intervention was "Duration of PPI prophylaxis is until no high-risk factors, or able to tolerate enteral feeding?' [Before intervention 329(83.3%) vs. After intervention 42(10.6%), p<0.001]. The details of this comparison are shown in the Table-III.

Table-II: Comparison of Knowledge related to Proton Pump Inhibitors (PPIs) across Groups (n=807)

Knowledge variables	Knowledge of Group-A (n=395)		Knowledge of Group-B(n=412)		*p*-value
	Yesn (%)	Non (%)	Yesn (%)	Non (%)	
PPI are inactive prodrugs or not	170 (43.0)	221 (57.0)	179 (43.5)	233 (56.5)	0.992
Followings are the PPIs (omeprazole, pantoprazole, lansoprazole, rabeprazole, esomeprazole, etc)	348(88.1)	47(11.9)	356(86.5)	56 (13.5)	0.471
PPI cure acid-related diseases by suppressing hydrochloric acid secretion or not?	237 (60.0)	158(40.0)	236 (57.3)	176 (42.7)	0.433
PPI can be used to prevent stress ulcer	209 (52.9)	186 (47.1)	215 (52.2)	197 (47.8)	0.836
PPI can be used to treat acute pancreatitis	199 (50.4)	196 (49.6)	216 (52.4)	196 (47.6)	0.560
Omeprazole has the largest individual difference compared with other PPIs	236 (59.7)	159 (40.3)	251 (60.9)	161 (39.1)	0.732
Omeprazole has the largest interaction compared with other PPIs	83 (21.0)	312 (79.0)	105 (25.4)	307 (74.5)	0.132
Esomeprazole has the longest acid inhibition time compared with other PPIs	134 (33.9)	261 (66.1)	148 (53.9)	262 (64.1)	0.518
Omeprazole should be selected for paediatric patients.	288 (72.9)	107 (27.1)	301 (73.1)	111 (26.9)	0.962
Rabeprazole should be selected for pregnant patients	347 (87.8)	48 (12.2)	357 (86.6)	55 (13.3)	0.610
New PPI or increased dosage will produce better and safer effect	251 (63.5)	144 (36.5)	265 (64.3)	147 (35.6)	0.818
PPI is usually available as enteric-coated capsules or tablets	192 (48.6)	203 (51.4)	201 (48.8)	211 (51.2)	0.694
PPI should usually be taken at breakfast	215 (54.4)	180 (45.6)	224 (54.4)	188 (45.6)	0.986
PPI can be taken after meal	316 (80.0)	79 (20.0)	329 (79.9)	83 (20.1)	0.958
PPI should be swallowed as whole piece?	345 (87.3)	50 (12.7)	359 (87.1)	53 (12.9)	0.930
It is advisable to increase the dose frequency rather than a single dose to improve effect	301 (76.2)	94 (23.8)	335 (81.3)	77 (18.7)	0.075
Patients should take PPI for only 7 days in the Helicobacter pylori eradication therapy	316 (80.0)	79 (20.0)	334 (81.2)	78 (18.8)	0.701
PPI treatment of gastric ulcer takes 2 weeks to 4 weeks	295 (74.7)	100 (25.3)	301 (73.1)	111 (26.9)	0.599
Duration of PPI prophylaxis is until no high-risk factors, or able to tolerate enteral feeding?	329 (83.3)	66 (16.7)	338 (82.1)	74 (17.9)	0.638
Long-term use of PPI may cause adverse reactions such as osteoporosis, pneumonia, etc	127 (32.2)	268 (67.8)	141 (34.2)	271(65.7)	0.532

The attitude of respondents regarding PPI use in Group-A before and after intervention was also assessed. The details of this comparison are shown in the Table-IV.

DISCUSSION

The present study concludes that PPI prescribing behaviour is prevailing in our country on a maximal level. More than 90% of the prevalence proved that doctors don't consider serious adverse reactions of the PPIs in mind, due to lack of awareness about the nature, dosage form, indication to be used and frequency of dosage of the medication. Multifaceted intervention produced large impacts for changing their knowledge related to their point of view. Moderate impact with pre- and post-reading difference of physician perception about safe prescription of PPI was noted with multifaceted intervention. Under 25% respondents thought that long-term use of PPI can cause ADRs in patients, which changed to positive response of over 75% in the Group-A. Previous studies showed a reduction in prescribing of PPI prophylactically to prevent Ulcer and gastrointestinal bleeding.[9] The referenced study has explained PPI is effective for stress ulcer prophylaxis in critically ill patients but prolong use can lead towards many issues, these include chronic as well as acute renal failure, C. difficile infection, a lack of magnesium, and fractured bones. Several multifaceted interventions have demonstrated safe and effective reductions in PPI use in the inpatient setting as reported by many authors before that support the results of the present study.[10,11] One study found a higher likelihood of cardiac diseases using PPIs for longer time, irrespective of other medications used combinations.[12]

Table-III: Comparison of Knowledge related to Proton Pump Inhibitors (PPIs) in Group-A Pre and Post Intervention (n=395)

Knowledge variables	Group-A(n=395)				*p*-value
	Before intervention		After intervention		
	Yes n(%)	No n(%)	Yes n(%)	No n(%)	
PPI are inactive prodrugs or not	170 (43)	221 (57)	389 (98.5)	6 (1.5)	0.178
Followings are the PPIs (omeprazole, pantoprazole, lansoprazole, rabeprazole, esomeprazole, etc)	348(88.1)	47(11.9)	378(95.7)	17(4.3)	0.002
PPI cure acid-related diseases by suppressing hydrochloric acid secretion or not?	237(60.0)	158(40.0)	371 (93.9)	24 (6.1)	<0.001
PPI can be used to prevent stress ulcer	209(52.9)	186 (47.1)	371 (93.9)	24 (6.1)	<0.001
PPI can be used to treat acute pancreatitis	199(50.4)	196 (49.6)	388 (98.2)	7 (1.8)	0.007
Omeprazole has the largest individual difference compared with other PPIs	236(59.7)	159 (40.3)	355 (89.9)	40 (10.1)	<0.001
Omeprazole has the largest interaction compared with other PPIs	83(21.0)	312 (79.0)	336 (85.1)	59 (14.0)	<0.001
Esomeprazole has the longest acid inhibition time compared with other PPIs	134(33.9)	261 (66.1)	314 (79.5)	81(20.5)	<0.001
Omeprazole should be selected for paediatric patients.	288(72.9)	107 (27.1)	84 (21.3)	311(78.7)	<0.001
Rabeprazole should be selected for pregnant patients	347(87.8)	48 (12.2)	84 (21.3)	311 (78.7)	<0.001
New PPI or increased dosage will produce better and safer effect	251(63.5)	144 (36.5)	353 (89.4)	42 (10.2)	<0.001
PPI is usually available as enteric-coated capsules or tablets	192(48.6)	203 (51.4)	314 (79.5)	81 (20.5)	<0.001
PPI should usually be taken at breakfast	215(54.4)	180 (45.6)	371 (93.9)	24 (6.1)	<0.001
PPI can be taken after meal	316(80.0)	79 (20.0)	62 (15.7)	333 (84.3)	<0.001
PPI should be swallowed as whole piece?	345(87.3)	50 (12.7)	395 (100)	00 (00)	<0.001
It is advisable to increase the dose frequency rather than a single dose to improve effect	301(76.2)	94 (23.8)	372 (94.2)	23 (5.8)	<0.001
Patients should take PPI for only 7 days in the Helicobacter pylori eradication therapy	316(80.0)	79 (20.0)	47 (11.9)	348 (88.1)	<0.001
PPI treatment of gastric ulcer takes 2 weeks to 4 weeks	295(74.7)	100 (25.3)	44 (11.1)	351 (88.9)	<0.001
Duration of PPI prophylaxis is until no high-risk factors, or able to tolerate enteral feeding?	329(83.3)	66 (16.7)	42 (10.6)	353 (89.4)	<0.001
Long-term use of PPI may cause adverse reactions such as osteoporosis, pneumonia, etc	127(32.2)	268 (67.8)	354 (89.6)	41 (10.4)	<0.001

Strategy of benchmarking showed a drastic decrease in prescribing behaviour of PPI in Group-A. After six months, controlled monitoring of prescription pattern of PPI in Group-A showed a drastic reduction from over 50% before intervention to below 25% after intervention. At national level no study is found related to physician's knowledge about the nature of PPI medication, whether it is a prodrug or active drug. Present study showed that under 50% of the Group-A thought that PPIs are inactive product. After multi-faceted intervention, the result moved to more than 90% of increase in knowledge about the nature of the proton pump inhibitors and Group-A were able to know that PPI are inactive prodrug and they need to be activated inside the body.

Table-IV: Attitude of Respondents Regarding use of Proton Pump Inhibitors (PPI) in Group-A Pre and Post Intervention (n=395)

Parameters	Before intervention n (%)	After intervention n (%)	*p*-value
Overuse of PPI is common at present in China			
Strongly agree	95 (24.1)	134 (33.9)	<0.001
Agree	284 (71.9)	243 (61.5)	
Disagree	16 (4.1)	18 (4.6)	
The main cause of PPI overuse is doctors' or patients' abuse of PPI.			<0.001
Strongly agree	136 (34.4)	256 (64.8)	
Agree	243 (61.5)	139 (35.2)	
Disagree	16 (4.1)	000	
The main purpose of PPI overuse is stress ulcer prophylaxis (SUP)2			
Strongly agree	23 (5.8)	292 (73.9)	<0.001
Agree	297 (75.2)	103 (26.1)	
Indifferent	59 (14.9)	000	
Disagree	16 (4.1)	000	
Overuse of PPI will cause an increase in adverse drug reaction and medical cost			
Strongly agree	23 (5.8)	124 (31.4)	<0.001
Agree	16 (4.1)	252 (63.8)	
Indifferent	154 (39.0)	19 (4.8)	
Disagree	202 (51.1)	000	
Necessary to carry out large scale education on rational use of PPI for medical staff and the public			
Strongly agree	23 (5.8)	308 (78.0)	<0.001
Agree	239 (60.5)	87 (22.0)	
Indifferent	133 (133.7)	000	
Necessary to strengthen the management of community pharmacy			
Strongly agree	23 (5.8)	268 (67.8)	<0.001
Agree	222 (56.2)	127 (32.2)	
Indifferent	101 (25.6)	000	
Disagree	49 (12.4)	000	

Researchers in China compared knowledge about PPI across different cadres of medical staff.[13] Pharmacists had substantially greater degrees of knowledge than nurses and physicians, and this was associated with age, gender, work nature, level of education, skilled title, nature of healthcare, and grade. Similarly, chemists outperformed doctors and nurses in terms of attitude regarding PPI utilisation. More than 25% of respondents of that study used a PPI during previous year, with omeprazole being most prevalent, which supports the results of the present study as well, (as our results showed that omeprazole is most taken drug). Pharmacists used PPI the least out of whole staff. The frequency of use was related to the profession and expert title. Nurses had significantly lower scores for PPI behaviour compared to doctors and pharmacists.[13] Although present study didn't compare knowledge, attitude and practices across cadres of medical staff, intra-difference of gender in Group-A showed that males consumed more PPIs in the previous years than females. Knowledge about the drug interaction of PPI was assessed by asking the Group-A about the drug interaction of omeprazole as compared to other PPIs. Their knowledge increased from below 25% to greater than 75% after multifaceted intervention. Doctors considered omeprazole as the safest PPI but multi-faceted intervention changed their knowledge and proved that omeprazole have higher interactions as compared to the other PPIs as reported by many authors before.[14,15]

Early studies reported that Proton pump inhibitors (PPIs) are widely used to treat gastrointestinal disorders, often for extended periods, raising the possibility of serious drug reactions in patients taking concomitant medicines. Lansoprazole and rabeprazole appear to possess lesser likelihood of drug interactions than omeprazole, though their interaction profiles, have been studied less thoroughly. One international study considered knowledge and attitude of high alert medications, not study regarding PPI was found yet to assess the knowledge about PPI among doctors.[16]

Knowledge of doctors about eradication therapy of Helicobacter Pylori infection was limited and over 75% of Group-A reported that PPI should only be given for 7 days in H. pylori infection. This improved after intervention. There have been few studies that assess physicians' knowledge and awareness of H. pylori, which showed that majority of the doctors knew about the first- and second-line antibiotics about H. pylori but no study has focused the role of PPI in the eradication therapy of it.[17-19]

Over 50% doctors thought that gastric ulcer regimen of PPI is 2-4 weeks but the actual time period is to 4-8 weeks. The current study is the first to assess knowledge, and attitudes towards stress ulcer prophylaxis in Pakistan. Two authors previously described physicians' awareness and attitudes towards

SUP, but the majority of the literature has focused solely on prescribing behaviour.[20,21] In our neighbouring country China, the SUP agent of choice was PPIs, ranging from 84 to 96%.[22,23] In the present study, the prescribing prevalence of PPI among Group-A was 93% in all aspects of diseases, and after multifaceted intervention, it reduced to 48% after benchmarking period of six months, which is the best outcome measure to assess the result of the intervention. Pakistan is not the only country with higher prevalence of PPI prescription similar results are seen in China 94% for SUP and Saudi Arabia (62.5% patients admitted to medical ward received PPIs).[24]

LIMITATIONS OF STUDY

Regardless of the helpful details gained from present research, several limitations should be noted. First, while these findings on PPI knowledge, attitude, and behaviour are limited to doctors, other medical staff could be included in future studies. Because this was a quasi-experimental study conducted in a single geographic location in Pakistan, the generalizability of the findings may be limited. Because only two settings were used in the study, additional research could be conducted using multiple settings across the country.

CONCLUSION

Prescribing knowledge of PPIs in the study participants improved before and after educational intervention. More than 90% frequency of inappropriate prescription proved that doctors don't consider serious adverse reactions of the PPIs in mind, due to lack of awareness about the nature, dosage form, indication to be used and frequency of dosage of the medication.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

RA & SN: Data acquisition, data analysis, critical review, approval of the final version to be published.

MK & TK: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

SL & FF: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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