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A CLINICAL COMPARATIVE OBSERVATIONAL STUDY ON IRRATIONAL USE OF PROTON PUMP INHIBITORS AND H2 RECEPTOR BLOCKERS

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Abstract

Background: PPIs and H2 Blockers are the most commonly used drugs in clinical practice. Inappropriate prescribing that is, PPIs and H2 Receptor Antagonists that are prescribed without detecting any FDA Approved indications may result in increased therapeutic load and cause pill burden to patients. Hence, a study was conducted to determine the prescribing pattern (rationality and irrationality) of both IV and oral PPIs and H2 Receptor Antagonists in the in-patient department of General Medicine [GM] to create awareness on appropriate prescribing of drugs.

Aim and Objective: The primary objective of this study is to assess the rationality of prescribing oral and IV Proton pump inhibitors and H2 Receptor Antagonists.

The other objective is to reduce pill burden

Methodology: A clinical comparative observational study was carried out in the in-patient department of General Medicine in ESI hospital, Ayanavaram, Chennai for six months of duration.

Results: A total of 152 patients who were prescribed with oral and IV PPIs and H2 Receptor Antagonists were gathered during the research period to assess the rationality of drug use and the result constituted that about 94 patients received rational therapy and 58 patients received Irrational therapy based on various aspects such as the duration of drug use and justified indications.

Conclusion: Based on the results, a significant irrationality in the use of PPIs and H2 Receptor Antagonists were found. In addition, utmost care should be taken while administering PPIs in patients receiving multiple drugs and other elder patients prone to take combination of drugs to attain a rational therapy. PPIs proven to have lower risks of drug interaction would be the favourable choice in those occasions.

Keywords: Proton pump inhibitors, Receptor Antagonists, gastroesophageal reflux disease

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INTRODUCTION

In the primary care, proton pump inhibitors (PPIs) are one of the most often given classes of drugs and are regarded as a significant advancement in the treatment of acid-peptic illnesses.. Omeprazole, Lansoprazole, and Rabeprazole, three proton pump inhibitors, seem to be equally effective along with Histamine type 2 receptor antagonists (H2RAs), which inhibit the histamine receptor on parietal cells in order to cure acid-related illnesses.[1] "Proton Pump Inhibitors: U.S. Food and Drug Administration-Approved Indications and Dosages for Use in Adults" states the approved indications for PPIs use that is managed by U.S. Centres for Medicare & Medicaid Services.[2]

PPIs may be violated in hospital and ambulatory care settings, according to several reports.[3] Before recommending a proton pump inhibitor, a number of factors should be considered, such as the following: (i) dosages, length of therapy, and clinical justifications for using a PPI, along with an evaluation of the appropriateness of the course of action; (ii) whether the use of H2-receptor antagonists is appropriate prior to recommending a proton pump inhibitor; and (iii) how frequently patients receiving a proton pump inhibitor for gastroesophageal reflux disease. Whereas, H2RAs are FDA-approved for short-term use in treating uncomplicated gastroesophageal reflux disease (GERD), gastric or duodenal ulcers, gastric hyper secretion, and mild to infrequent heartburn or indigestion.[4]

It is known that rational prescribing of medication is assurance that the patient receives the appropriate medication according to his/her medical needs in a dose and route of administration meet the condition requirement for adequate period of time.[5] To assess the rationality of use of oral & iv PPIs and H2RAs, a comparative observational study to investigate prescribing patterns, followed by input to clinicians in the establishment of recommendations, and the development of a fresh approach to evidence-based decision making to demonstrate prudent use of medications.

The effect of pharmaceutical interventions on the prudent use of PPIs and H2RAs show s that the medication therapy interventions enhanced the proportion of patients with logical justification and increased the accuracy rate of administration method. According to various therapeutic situations, research have shown that patients utilise PPIs at a high rate of irrational usage.[6]

Over prescribing of PPIs and H2RAs are increased in hospitals which leads to therapeutic burden, increased frequency of adverse effects and pill burden for patients.[7]

As a result, the prescription pattern varies from patient to patient and from physician to physician. The rationale for this difference in prescribing patterns is a physician's conflict of interest. Thus, by definition, such studies provide a logical foundation for establishing the rationality of medication usage as well as evidence-based recommendations for policy decisions at various levels of healthcare. There is usually variance in medication use among nations and even within countries and occasionally within the same institute at various points in time, most likely due to changing illness patterns throughout time.[8]

A clinical observational research was conducted for a period of six months in in-patient department of General Medicine[GM] in ESI hospital Ayanavaram, Chennai. During the study, all eligible participants were accepted based on inclusion criteria. Inclusion and exclusion criteria for the study were established. Prescriptions of 152 patients of either sex who have been prescribed with PPIs and H2RAs for conditions other than gastroesophageal reflux disease, PUD, etc

and patients between the age group of 18-60years were included. Patients in emergency, life threatening medical or surgical conditions, pregnant and lactating women and patients with incomplete data were excluded. Patients who were seriously sick were excluded, as were those who were uninterested and did not give informed consent to participate in the study. After receiving clearance from the Institutional Ethics Committee (IEC), subjects were recruited for the study. The patient's demographic profile, receiving or current prescribing patterns of PPIs and H2RAs medications were recorded in a predesigned data collection record form. The primary goal of the research was to evaluate the irrational use of PPIs and H2RAs in terms of undesired indications, and to reduce pill burden. Patient demographics, medication chart with frequency and duration and diagnostic details were noted. Frequency of population taking PPIs and H2RAs based on gender, Frequency of drug prescription among different age groups, Frequency of population among gender, Frequency of population prescribed with PPIs and H2RAs, number of prescription with desired indication for PPI use, number of prescription with desired indication for H2RAs use, number of drugs prescribed per total number of prescriptions were calculated.

STATISTICAL ANALYSIS

Data was documented in Microsoft Excel and analysed using statistical analysis software (SPSS© Version 26.0) and expressed in terms of frequencies and in percentages. The patient's information was and will be kept confidential and anonymous during and after the research.

RESULTS:

Age distribution of patient

A tabulated and pie chart representation of age distribution of patients who were included in the research are shown below.

Table-1: Distribution of age group

The distribution of age group table shows that patients between the ages of 18 - 30 years made up 15% of the patient population, while patients between the ages of 51 - 60 years accounted for 43% of the total.

Age of Population in Years	Number of Patients(n=)	Percentage
18- 30	23	15%
31- 40	25	17%
41- 50	38	25%
51- 60	66	43%

Figure-1 Here's a pie chart representation of the same data mentioned above.

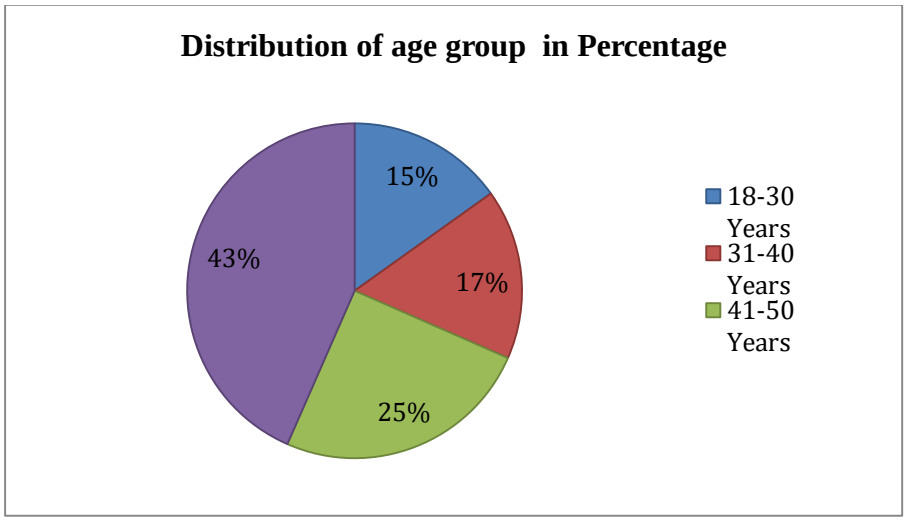


Table-2 : Distribution of gender

Among 152 patients, 93 patients (61.1%) are Male population whereas 59 patients (38.8%) are Female population. A test of proportions revealed that there were a few more male patients than female ones.

Gender	Number of Patients	Percentage
Male	93	61.1%
Female	59	38.8%

Figure-2 : Here's a bar chart representation of the same data as mentioned above.

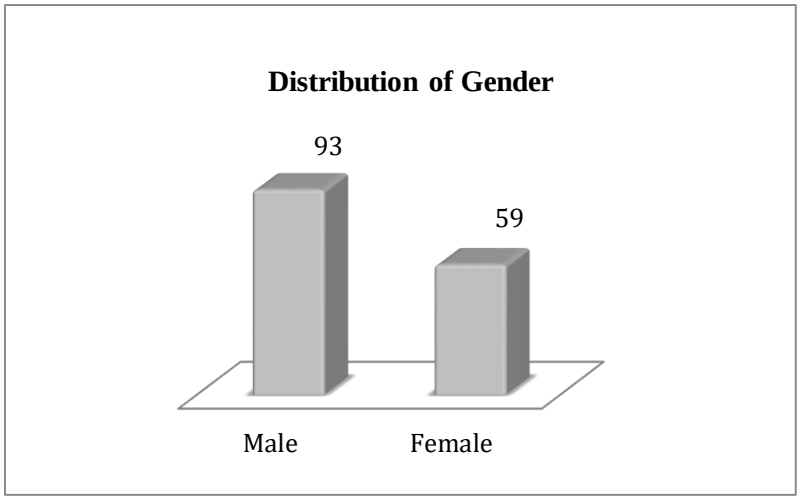


Table-3 : Distribution of population in years prescribed with PPIs and H2RAs

Out of 152 patients who are representing from different age groups, PPIs were most prescribed to the age group of 51-60 years old of (46%,n=55) and the least prescribed age group were 18-30 years old of (12%,n=15).

H2RAs were most prescribed to the age group of 51-60 years old of (35%,n=11) and the least prescribed age group were 31-40 years old of (10%,n=3).

Age group of Population in years	PPIs Prescribed	Percentage	H2RAs Prescribed	Percentage
18- 30	15	12%	8	26%
31- 40	22	18%	3	10%
41- 50	29	24%	9	29%
51- 60	55	46%	11	35%

Figure-3(A): Percentage of PPIs prescribed

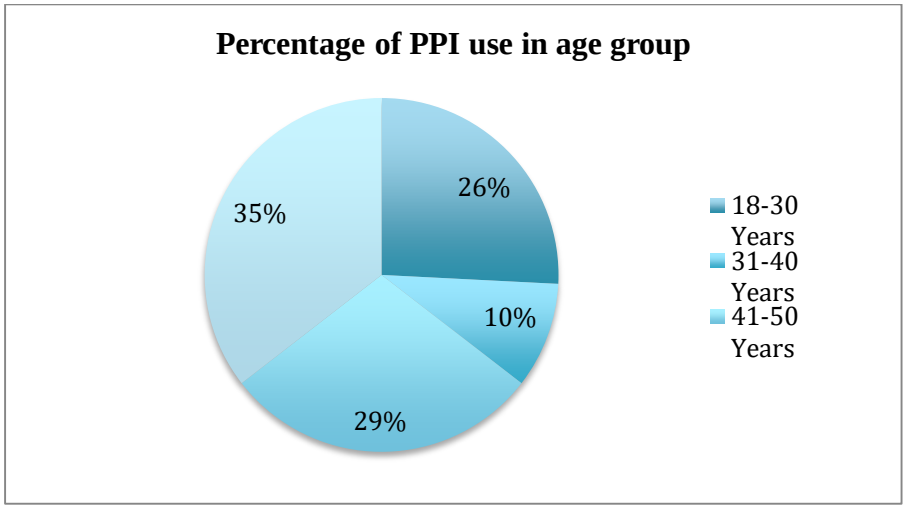


Figure-3(B): Percentage of H2RAs prescribed

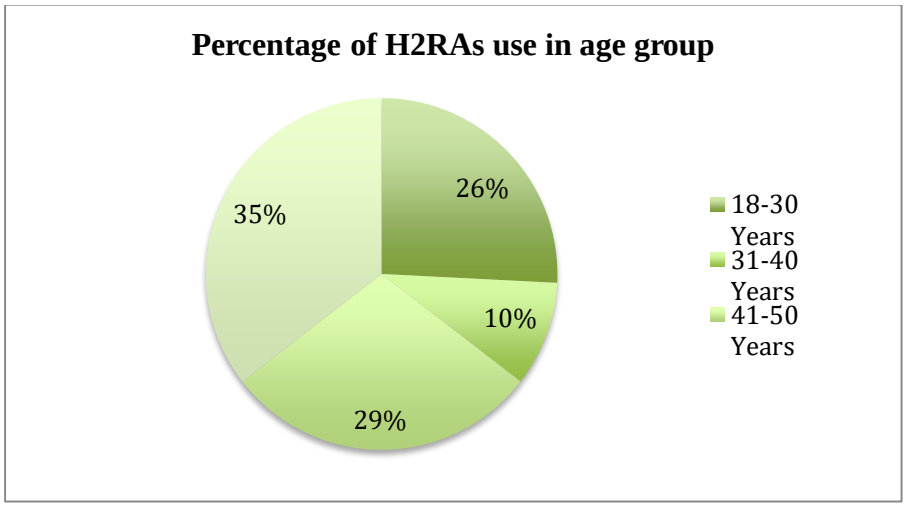


Table-4 : Distribution Of Drug Therapy

The majority of patients, 120 (79%), were receiving monotherapy and the remaining received dual therapy of 32(21%) respectively.

Drug Therapy	Frequency	Percentage
Mono Therapy	120	79%
Dual Therapy	32	21%

Figure-4

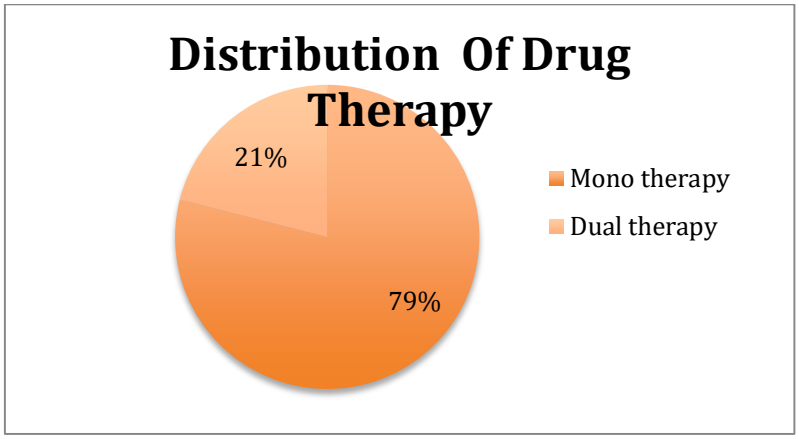


Table-5: PPIs Used

Among 152 patients in the study, Omeprazole was administered in 63 patients with holds (47%) followed by least administered was Lansoprazole in 1 patient (0%).

Name of PPIs	Frequency	Percentage
Omeprazole	63	47%
Pantoprazole	57	37%
Rabeprazole	34	33%
Lansoprazole	1	0%

Figure-5 : Here's a bar chart representation of the same data mentioned above.

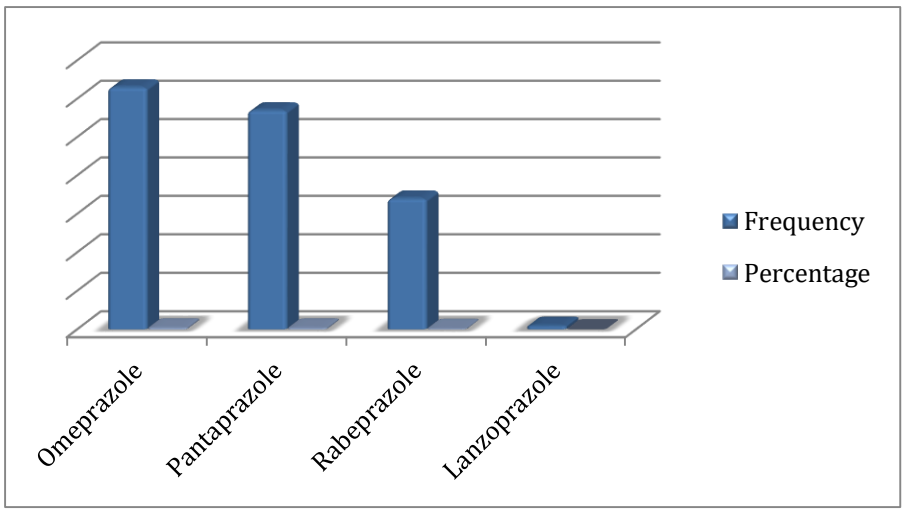


Table-6 : H2RAs Used

Among 152 patients Ranitidine was the only H2RAs that was prescribed in 32 patients that holds (21%)

Name of H2RAs	Frequency	Percentage
Ranitidine	32	21%

Figure-6: Here's a bar chart representation of the same data mentioned above.

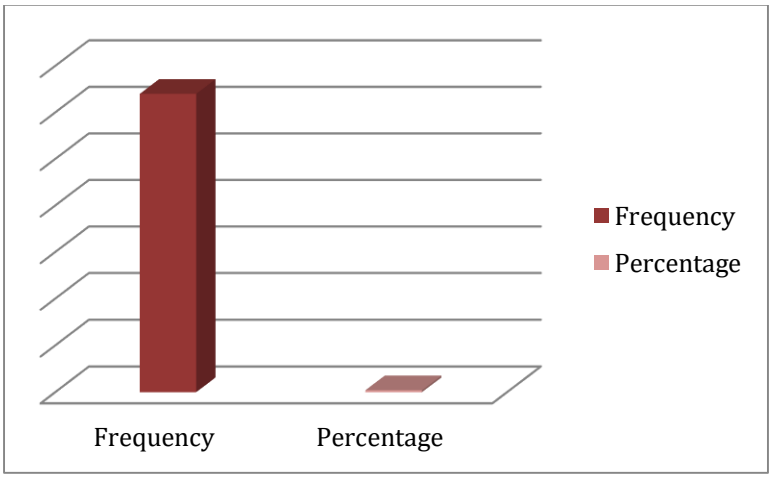


Table-7: Indications of PPIs

PPIs were co-prescribed with NSAIDS for 29 patients (24.1%), followed by for co-morbidities in 5 patients (4.1%), for CNS in 7 patients (5.8%), for other conditions in 35 patients (29.1%) and PPIs prescribed without detecting any justified indications were in 44 patients (36.6%)

Indications	Frequency	Percentage
NSAIDS	29	24.1%
Co morbidities	5	4.1%
CNS	7	5.8%
Others	35	29.1%
Without Indication	44	36.6%

Figure-7:

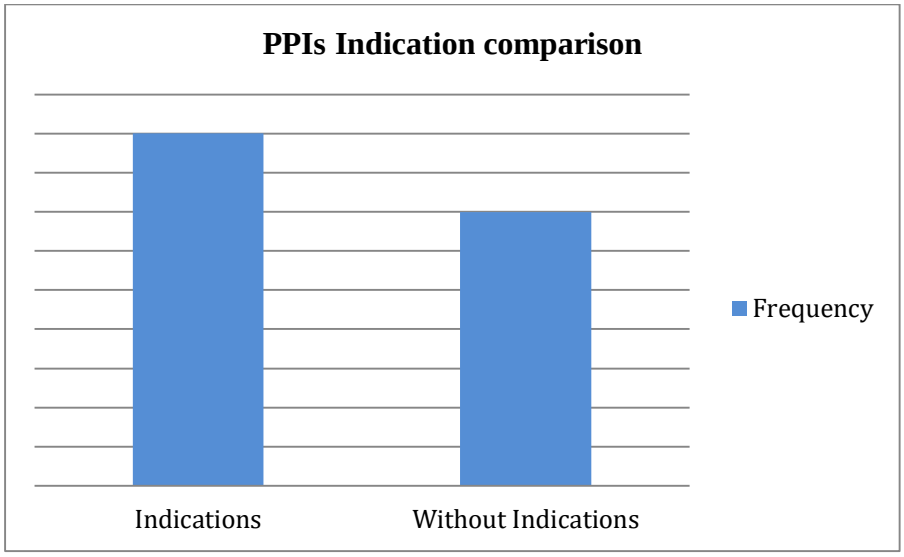


Table-8: Indications of H2RAs

H2RAs were co-prescribed with NSAIDS for 4 patients (12.5%), followed by for co-morbidities in 6 patients (18.7%), for other conditions in 8 patients (25%) and prescribed without detecting any justified indications were in 14 patients (43.7%).

Indications	Frequency	Percentage
Co-morbidities	6	18.7%
NSAIDS	4	12.5%
CNS	0	0%
Others	8	25%
Without Indication	14	43.7%

Figure-8:

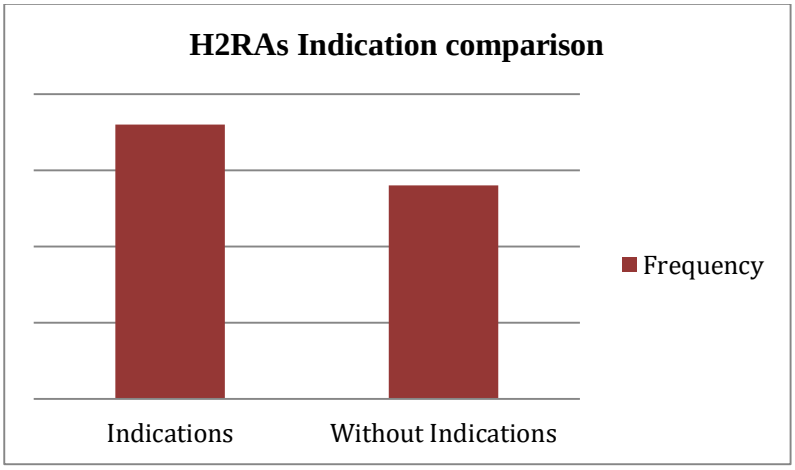


Table-9 : Route of Administration of PPIs and H2RAs

Among 155 PPIs that was prescribed both as mono therapy and dual therapy, 104 PPIs were given Orally and 14 PPIs as IV. And in total of 32 H2RAs prescriptions , 16 was given Orally and 16 was given as IV.

Route of Administration	PPIs	H2RAs
Oral	104	16
IV	51	16

Figure-9: Based on the bar chart it is clear that Oral PPIs were the most prescribed amongst all.

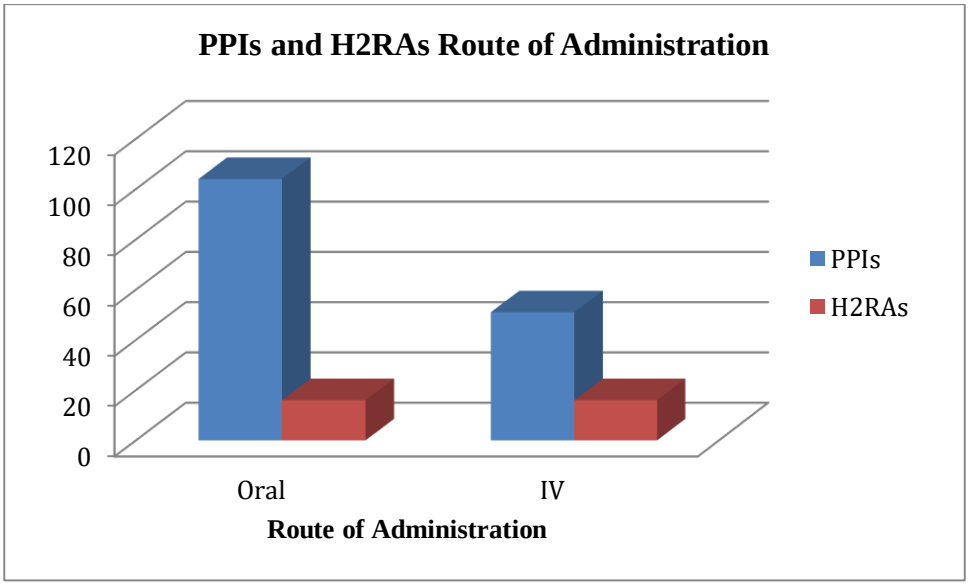


Table-10 : Duration of PPIs and H2RAs used

Among 152 patients in this study, most of the patients received PPI for a duration of 6 days in 32 patients (20.6%) followed by duration of 4 days in 30 patients (19.3%), duration of 5 days in 23 patients (14.8%), duration of 3 days in 22 patients (14.1%), duration of 2 days in 17 patients (10.9%), duration of 7 days in 12 patients (7.7%), duration of 8 days in 8 patients (5.1%), duration of 9 days in 6 patients (3.8%) and duration of 1 day in 2 patients (1.2%). Remaining 3 patients received PPI for 10+ days (1.9%) which was up to 15 days.

Similarly, duration of H2RAs used for maximum duration of 5 days in 6 patients (18.7%),followed by duration of 4 days in 6 patients (18.7%), duration of 2 days in 6 patients (18.7%), duration of 3 days in 5 patients (15.6%), duration of 6 days in 3 patients (9.3%), duration of 1 days in 3 patients (9.3%), duration of 8 days in 8 patients (25%), duration of 9 days in 6 patients (18.7%) and remaining patients received H2RAs for 10+ days (3.1%) which was up to 16 days.

Duration (Days)	PPIs	H2RAs
1	2	3
2	17	6
3	22	5
4	30	6
5	23	6
6	32	3
7	12	2
8	8	0
9	6	0
10+	3	1

Figure-10:

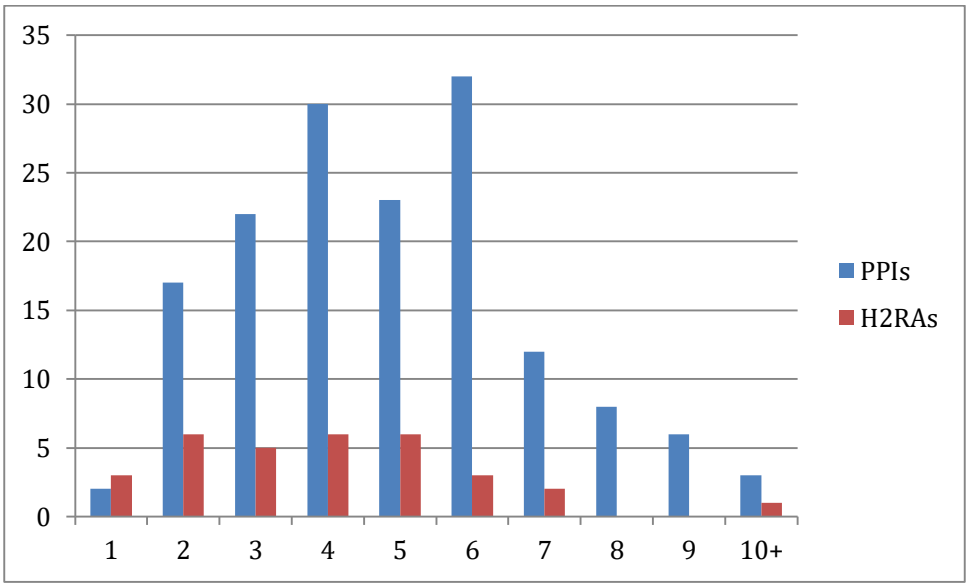
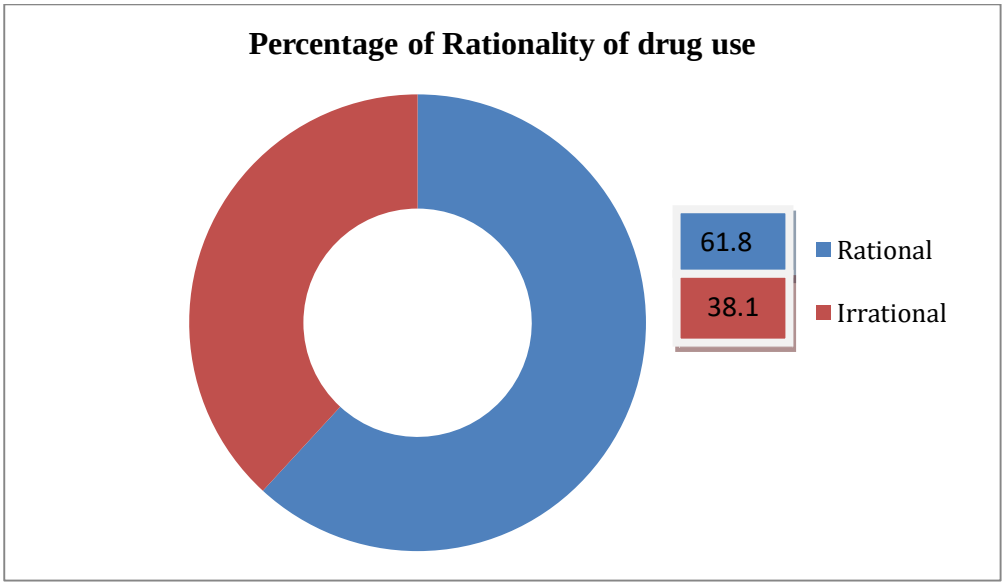


Table-11: Rationality of PPIs and H2RAs used

Among 152 patients, 94 patients received Rational therapy that holds 61.8% where as 58 patients received irrational therapy that holds 38.1%.

Rationality	Frequency	Percentage
Rational	94	61.8%
Irrational	58	38.1%

Figure-11



DISCUSSION:

According to the WHO's definition of rational drug use, the first objective is to consider patient's need for that particular drug.[9]The major indication for gastro-protective drugs in the current clinical scenario is prophylaxis or treatment with co-prescribed ulcerogenic drugs.[10] We have evaluated different drugs co-prescribed with PPIs and H2RAs in our study prescriptions. In this study, it was found that gastro-protectives were predominantly co-prescribed with NSAIDs, CNS drugs, for co-morbid conditions and drugs given without indications.

Our study holds the majority of patient population as male (61.1%, n=93) with remaining being female (38.8%, n=59) (Table-2)(Figure-2). Most of the patients under

The study were of age group from 51-60 years old (43%, n=66) (Table-1) (Figure-1),

Followed by the least category of patients was in the age group of 18-30 years old (15%,n=23).

In this study it was found that patients in the age group of 51-60 years old received large amount of PPIs of (46%,n=55), followed by patients in the age group of 41-50 years old received (24%,n=29), patients in the age group of 31-40 years received (18%,n=22) and the remaining patients of age group 18-30 years old received (12%,n=15) are the minority. Likewise H2RAs were prescribed to patients in the age group of 51-60 years old in majority (35%,n=11), followed by patients in the age group of 41-50 years old received (29%,n=9), patients in the age group of 18-30 years old received (26%,n=8) and the remaining patients in the age group of 31-40 years old received (10%,n=3) and are the minority (Table-3)(Figure-3).

The distribution of drug therapy for the entire 152 population included Mono therapy for 120 patients (79%) and Dual therapy for 32 patients (21%) (Table-4)(Figure-4).

Among the entire PPI prescriptions, Omeprazole was prescribed in majority of (47%,n=63) and Lansoprazole was the least prescribed drug to (n=1) patient.(Table-5)(Figure-5). And out of 152 patients, Ranitidine was the only drug under H2RAs that was prescribed to patients of (21%,n=32)(Table-6)(Figure-6) which concluded that PPIs were the most used most when compared to H2RAs. A similar observational study was conducted by Patel Dhande et al in 2013 and reported that

among all PPIs, Dexrabeprazole were more prominently used (73.7%) followed by Pantoprazole (24.6%).[11]

While tabulating the indication for drug use, PPIs were co-prescribed with NSAIDS for 29 patients (24.1%), followed by for co-morbidities in 5 patients (4.1%), for CNS in 7 patients (5.8%), for other conditions in 35 patients (29.1%) and PPIs prescribed without detecting any justified indications were in 44 patients (36.6%)(Table-7)(Figure-7).

H2RAs were co-prescribed with NSAIDS for 4 patients (12.5%), followed by for co-morbidities in 6 patients (18.7%), for other conditions in 8 patients (25%) and prescribed without detecting any justified indications were in 14 patients (43.7%)(Table-8)(Figure-8).

This significantly concluded that prescriptions of PPIs and H2RAs prescribed for desired indication were in majority when compare to prescriptions without indications.

Out of 152 patients the majority of 104 patients received PPI through oral route and 51 patients received through IV route. Whereas 16 patients received H2RAs through Oral route and 16 received through IV route.(Table-9)(Figure-9).In general the oral route was the majority in route of administration for patients compared to IV route during the study duration for our analysis.

In line to the current observational study with the population of 152 patients, the duration of PPI prescribed peaked in patient count by 32 patients for the duration of 6 days, followed by the least patient count of 2 patients were prescribed with PPIs for the duration of 1 day. The duration of H2RAs prescribed peaked in patient count by 6 patients for the duration of 5 days.(Table-10)(Figure-10).

As the research has demonstrated on various aspects, the rationality of drug use according to WHO's definition of rational drug use and on basis of majority of patients received medications with indication for desired duration exceeds the irrationality.[12] That is, among 152 patients, 94 patients received Rational therapy of 61.8% where as 58 patients received irrational therapy of 38.1%.(Table-11)(Figure-11) PPI are recommended to be taken as a single daily dose. Our findings also suggest that dose and dosing schedule of gastroprotectants are common medication errors in the prescriptions. Even though our results showed Rationality in drug use for 94 patients out of 152 selected patients, the irrational use of drugs in 58 patients holds 38.1% of total which should be taken into account for good clinical practice and to promote greater health care.

CONCLUSION:

The quality of health care, particularly as regards the rational use of drugs, depends on a wide range of factors, including a correct diagnosis, prescription of correct drugs, and adequate administration for required time. Clinicians prescribe PPIs and H2RAs without evaluating the need for them and hence patients may face the dire consequences of irrational use of these drugs. Rational drug prescribing policy must be implemented in all clinical settings to curb the misuse of gastro-protectants.

Even though, there are only considerable differences between Rational and Irrational use of PPIs and H2RAs from our research, utmost care should be taken while administering PPIs and H2RAs in patients receiving multiple drugs and other elder patients who are prone to take combination of drugs to attain a rational therapy.

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CONFLICT OF INTEREST

There is no conflict of interest between the authors.

REFERENCE:

1. The rational use of drugs. Report of the Conference of Experts, Nairobi,25-29 November 1985. Geneva,World Health Organization, 1987. [2] Scagliarini R, Magnani E, Pratico` A,
2. Bocchini R, Sambo P, Pazzi P. Inadequate Use of Acid-Suppressive Therapy in Hospitalized Patients and Its Implications for General Practice. Dig Dis Sci. 2005;50(12):2307–11.
3. Venkataraman R, Rashid M, Shrestha H. Inappropriate medication use and cost comparison analysis of proton pump inhibitors: evidence from an Indian tertiary care facility. Current Drug Safety. 2020 Jul 1;15(2):147-55.
4. Patel HR, Dhande P. Imprudent gastro-protective approach in majority of specialists' clinics of a tertiary hospital. Journal of Clinical and Diagnostic Research: JCDR. 2016 Mar;10(3):FC12.
5. Nasrin Shahsavani, D. R Raju Koneri, Balakeshawa Ramaiah, Shibi Mary Thomas, Assessment of prescribing Pattern of proton Pump inhibitor and histamine 2 receptor antagonist, Journal of Innovations in Pharmaceuticals and Biological Sciences, e-ISSN: 2349-2759 p-ISSN: 2395- 1095
6. Ali O, Poole R, Okon M, Maunick S, Troy E. Irrational use of proton pump inhibitors in general practise. Irish Journal of Medical Science (1971-).2019 May;188(2):541-4.
7. Helgadottir H, Bjornsson ES. Problems associated with deprescribing of proton pump inhibitors. International journal of molecular sciences. 2019 Nov 2;20(21):5469.
8. Tadvi NA, Shareef SM. Use of proton pump inhibitors in general practice: is it rationale?. International Journal of Medical Research & Health Sciences. 2014;3(1):37-42.
9. Agréus L, Storskrubb T, Aro P, Ronkainen J, Talley NJ, Sipponen P. Clinical use of proton-pump inhibitors but not H2-blockers or antacid/alginates raises the serum levels of amidated gastrin-17, pepsinogen I and pepsinogen II in a random adult population. Scandinavian journal of gastroenterology. 2009 Jan 1;44(5):564-70.
10. Teramura-Grönblad M, Bell JS, Pöysti MM, Strandberg TE, Laurila JV, Tilvis RS, Soini H, Pitkälä KH. Risk of death associated with use of PPIs in three cohorts of institutionalized older people in Finland. Journal of the American Medical Directors Association. 2012 Jun 1;13(5):488-e9.
11. Al-Aly Z, Maddukuri G, Xie Y. Proton pump inhibitors and the kidney: implications of current evidence for clinical practice and when and how to deprescribe. American Journal of Kidney Diseases. 2020 Apr 1;75(4):497-507.
12. K. K. F. Tsoi*,†,‡, H. W. Hirai* & J. J. Y. Sung*, Meta-analysis: comparison of oral vs. intravenous proton pump inhibitors in patients with peptic ulcer bleeding, Alimentary Pharmacology and Therapeutics, 2013; 38: 721-728 [a] 2013 John Wiley & Sons Ltd
13. Joel J. Heidelbaugh, Proton pump inhibitors and risk of vitamin and mineral deficiency: evidence and clinical implications, Therapeutic Advances in Drug Safety, (2013) 4(3) 125–133
14. Jarchow-Macdonald AA1, Mangoni AA, Prescribing patterns of proton

pump inhibitors in older hospitalized patients in a Scottish health board, , 2013 Oct;13(4):1002-9Geriatr Gerontol Int.

15. P. F. Haastrup, Rasmussen , J. M. Hansen ,R. D. Christensen , J. Søndergaard and D. E. Jarbøl General practice variation when initiating long-term prescribing of proton pump inhibitors: a nationwide cohort study, *BMC Family Practice*BMC series, 201617:57

16. Mark Reid, MD1,2*, Angela Keniston, MSPH1, Inappropriate Prescribing of Proton Pump Inhibitors in Hospitalized Patients, Journal of Hospital Medicine Vol 7 | No 5 | May/June 2012

17. N.M. Walker, J. McDonald, An evaluation of the use of proton pump inhibitors, *Pharmacy World and Science*, June 2001, Volume 23,

18. Soumana C Nasser, Jeanette G Nassif, and Hani I Dimassi, Clinical and cost impact of intravenous proton pump inhibitor use in non-ICU patients, World J Gastroenterol. 2010 Feb 28; 16(8): 982–986

19. Mohammed S. Alsultan, Ahmed Y. Mayet, Areej A. Malhani, and Mashael K. Alshaikh, Pattern of Intravenous Proton Pump Inhibitors Use in ICU and Non-ICU Setting: A Prospective Observational Study

20. Joanna K. Law, Chris N. Andrews, Robert Enns, Intravenous proton pump inhibition utilization and prescribing patterns escalation: a comparison between early and current trends in use,GIE, Volume 69, Issue 1

21.Jacob G. Hoove, Annabel L. Schumaker, Kevin J. Franklin, Use of Intravenous Proton-Pump Inhibitors in a Teaching Hospital Practice, *Digestive Diseases and Sciences*, September 2009, Volume 54, Issue 9

22 Pezeshkian S, Conway SE. Proton pump inhibitor use in older adults: long-term risks and steps for deprescribing. The Consultant Pharmacist®. 2018 Sep 1;33(9):497-503

23. Al-Aly Z, Maddukuri G, Xie Y. Proton pump inhibitors and the kidney: implications of current evidence for clinical practice and when and how to deprescribe. American Journal of Kidney Diseases. 2020 Apr 1;75(4):497-507.