

Use of Proton Pump Inhibitors – A drug utilization study

Shabbir Rafik Pendhari^{1,*}, Kedar Shashikant Joshi², Ramchandra Prabhakar Limaye³¹Tutor, ²Assistant Professor, ³Professor, Dept. of Pharmacology, Bharati Vidyapeeth Deemed University Medical College & Hospital, Sangli***Corresponding Author:**

Email: itsshabbir@gmail.com

Abstract

Background: In 2006 PPI was the third most frequently prescribed drug in Australia. In United States, UK and New Zealand similar trends were observed. Utilization of proton pump inhibitors is increasing continuously. Differential drug utilization of PPIs are observed along with NSAIDs with antibiotics, Utilization of PPI alone is less, and some newer adverse drugs reactions are being reported, so we planned a study to find out the actual burden of PPI in our area.

Methods: 50 registered pharmacies were selected. Then data collection was done after consent of patient or relative having PPI containing prescription and photos of prescription were taken, without any personally identifiable information of patient or physician.

Results: 1466 prescription containing PPI were obtained during study. (69.85%) prescriptions were containing NSAIDs along with the PPI. while 55% AMA were used by the physician during the study period. PPI is preferred and prescribed as gastroprotective agents alone or along with antimicrobials and NSAIDs, thus they will reduce the gastrointestinal adverse effects, of concomitant drugs.

Conclusion: 45.05% burden of PPI is there in study area observed. PPI are mostly used along with NSAIDs and/or AMA, for their ability to produce gastro protective effect. But their contribution towards adverse effect is to be evaluated.

Keywords: PPI, Drug utilization, NSAIDs, Antimicrobial agents

Access this article online	
Quick Response Code:	Website: www.innovativepublication.com
	DOI: 10.5958/2393-9087.2016.00020.0

Introduction

The drug utilization studies aim to evaluate factors related to the prescribing, dispensing, administration and use of medicine along with its related consequences like therapeutic or adverse effects¹. Drug utilization studies are continuous programs which help us to review, to analyze and to interpret the trends of drug used against pre-determined standards² at various levels of the healthcare system. From time to time various drug utilization studies are required to improve management strategies and quality of life of patients³. Prescription writing requires regular updation of knowledge and skill, as it reflects the clinical judgments and prescribing pattern. For rational prescription updated knowledge and adherence of prescribing policies is must, while irrational prescription leads to unproductive and risky treatment⁴. This will lead to either exacerbation or prolongation of illness or increase cost of treatment⁴ or increase duration of hospitalization or death also.

Aim and Objectives

Aim: To establish burden of PPI in Sangli Miraj Kupwad corporation area

Rational use of medicine is defined by the WHO as, 'Patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for adequate period of time and at the lowest cost to them and their community'. Prescribing and dispensing studies are one of the best studies to determine rational prescribing habits^{5,6}.

Utilization of proton pump inhibitors (PPI) increasing continuously, in Australia⁷ 18500 prescriptions were dispensed in 1990 after that it increased to around 1.7 million prescriptions in 1996⁸, while till 2006 it became the third most frequently prescribed drug in the same country⁴. In United States only United states of America, UK and New Zealand have also reported similar high utilization of PPI^{9,10,11,12}.

In India there are various drug utilization studies of non-steroidal anti-inflammatory drugs (NSAIDs), antimicrobial agents, in tertiary care hospital in emergency unit, on Out Patient Department (OPD) basis patients and of In- Patient Department (IPD) patients are done but very less studies of specifically of drug utilization of PPI. Various percentage of drug utilization of PPI are observed along with NSAIDs with antibiotics. Utilization of PPI alone is less, and some newer adverse drugs reactions are being reported¹³, so we planned a study to find out the actual burden of PPI in our area with following aims and objectives

Objectives: To find information about

- The burden of PPI in Sangli Miraj Kupwad corporation area.
- PPI being sold higher or least in this area.

- Age sex and diagnosis of the patient using PPI.
- Common drugs prescribed along with PPI.
- To calculate the most common Anti-Microbial Agents (AMA) used along with PPI
- To calculate the most common NSAIDs used along with PPI

Materials and Methods

The permission was taken from Institutional Ethical Committee of Bharati Vidyapeeth Deemed University Medical College and Hospital Sangli to do the pharmacy based drug utilization study. The list of registered pharmacies in Sangli-Miraj-Kupwad(SMK) Corporation was taken from Chemist and Druggist Association, Sangli. Then by using random table the random 50 pharmacies were selected for drug utilization study. Then on the day of data collection, by verbal consent of patient or relative having PPI containing prescription photos of prescription was taken. The age and sex of patient was asked to that person having the prescription. And the information was filled in tabulated form which having details of age, sex, diagnosis (if available), PPI with dose and frequency prescribed and co-prescribed

drug. **No personally identifiable information about patient or physician was collected.** Such nearly 50 prescriptions or bills were collected from each pharmacy. Total 1466 prescriptions were collected from the SMK corporation area.

Inclusion criteria

- Prescriptions from patients coming to the selected Pharmacy on that selected day during the prescription collection day
- Prescription containing PPI
- Patient giving permission to collect the details of prescription

Exclusion criteria

- Prescriptions without PPI prescribed
- Patient's denial for giving the information from the prescription.

Observations and Results

We reviewed 3254 prescriptions and out of which 1466 prescription containing PPI were selected for the study; this means nearly 45% prescriptions content the PPI.

Table1: Demographic data

Demographic data for pharmacy based study							
Sr. No.	Age Group	No. of Patients	Male	Female	% No. of Patients	% Male	% Female
1	1-10	07	05	02	0.48%	0.34%	0.14%
2	11-20	47	26	21	3.21%	1.77%	1.43%
3	21-30	112	61	51	7.64%	4.16%	3.48%
4	31-40	219	112	107	14.94%	7.64%	7.30%
5	41-50	217	113	104	14.80%	7.71%	7.09%
6	51-60	216	117	99	14.73%	7.98%	6.75%
7	61-70	147	99	48	10.03%	6.75%	3.27%
8	71-80	59	35	24	4.02%	2.39%	1.64%
9	81-90	12	05	07	0.82%	0.34%	0.48%
10	91-100	02	01	01	0.14%	0.07%	0.07%
11	Without age details	428	224	204	29.20%	15.28%	13.92%
	Total	1466	798	668	100.00%	54.43%	45.57%

Out of 1466 patients, there were 798 male while 668 were female. Most of the patients were from age group 31 to 60. 652 patients were from age group 31 to 60. There only 02 patients from 91-100 age group.

Average age of the patients was 47.55 ± 16.16 years (mean \pm sd), with lowest age is 06 years and oldest aged patient was of 97 years. Average brand prescribed per prescription was (mean \pm sd) 4.83 ± 2.10 . It ranges from 01 to 17 brands per prescription. Median and mode of prescription of study was 5 each. While nearly (mean \pm sd) 8.93 ± 5.67 drugs were prescribed per prescription. Generic drugs per prescription range from 01 to 43. Median was 8 while mode of the drug per prescription was 6.

Table 2: Commonly prescribed PPIs

Sr. No.	Commonly prescribed proton pump inhibitors		%
	PPI	No of Prescriptions	
1	Rabeprazole	586	39.97%
2	Pantoprazole	585	39.90%
3	Omeprazole	189	12.89%
4	Esomeprazole	90	6.14%
5	Ilaprazole	30	2.05%
	No of prescriptions containing PPI	1466	100%
	Total PPI prescribed	1480	45.48%
	Prescriptions observed	3254	

Total five PPI were used in our study area. Out of this rabeprazole (586) and pantoprazole (585) were most commonly prescribed proton pump inhibitors observed. Nearly 40% each pantoprazole and rabeprazole were prescribed.

Table 3: PPI used along with NSAIDs

Sr. No.	Commonly prescribed NSAIDs	No of prescriptions (Separate)	% Out of 1466	% Out of 1024
1	Paracetamol	396	27.01%	38.67%
2	Diclofenac	228	15.55%	22.27%
3	Aceclofenac	180	12.28%	17.58%
4	Nimesulide	70	4.77%	6.84%
5	Ibuprofen	40	2.73%	3.91%
6	Etodolac	27	1.84%	2.64%
7	Lornoxicam	26	1.77%	2.54%
8	Eterocoxib	22	1.50%	2.15%
9	Ketorolac	12	0.82%	1.17%
10	Mefenamic acid	09	0.61%	0.88%
11	Piroxicam	06	0.41%	0.58%
12	Naproxen	05	0.34%	0.49%
13	Meloxicam	02	0.14%	0.20%
14	Aspirin	01	0.07%	0.10%
	Total	1024	69.85%	100.00%

Each prescription counted for number of NSAIDs or AMAs prescribed for 1024 (69.85%) prescriptions contained NSAIDs along with the PPI. Totally fifteen types of NSAIDs were used by the physicians during the study.

Internal division

More than 38% of NSAIDs contains paracetamol while 22% prescriptions were of diclofenac. Aceclofenac was another more commonly prescribed NSAID with 22%. Aspirin as NSAIDs is a least commonly prescribed NSAIDs.

Table 4: PPI used along with the antimicrobial agents

Sr. No.	Commonly Prescribed Antimicrobial Agents	No. of Prescriptions (separated)	%out of 1466	%out of 790
1	Fluroquinolones	204	13.92%	25.82%
	Ofloxacin	126	8.59%	15.95%
	Levofloxacin	39	2.66%	4.94%
	Ciprofloxacin	29	1.98%	3.67%
	Moxifloxacin	09	0.61%	1.14%
	Norfloxacin	01	0.07%	0.13%
2	Cephalosporins	199	13.57%	25.19%
	Cefixime	77	5.25%	9.75%
	Cefuroxime	58	3.96%	7.34%
	Cefpodoxime	24	1.64%	3.04%
	Ceftriaxone	13	0.89%	1.65%

	Cefoperazone	10	0.68%	1.27%
	Cephalexin	07	0.48%	0.89%
	Ceftazidime	04	0.27%	0.51%
	Cefadroxil	03	0.20%	0.38%
	Ceftamerpivoxil	02	0.14%	0.25%
	Cefotaxime	01	0.07%	0.13%
3	Anthelmintics	147	10.03%	18.61%
	Albendazole	71	4.84%	8.99%
	Ivermectin	62	4.23%	7.85%
	Mebendazole	14	0.95%	1.77%
4	Antiamoebic	139	9.48%	17.59%
	Ornidazole	84	5.73%	10.63%
	Metronidazole	35	2.39%	4.43%
	Nimorazole	10	0.68%	1.27%
	Tinidazole	09	0.61%	1.14%
	Secnidazole	01	0.07%	0.13%
5	Rifaximin	53	3.62%	6.71%
6	Penicillins	97	6.62%	12.28%
	Amoxicillin	73	4.98%	9.24%
	Cloxacillin	11	0.75%	1.39%
	Ampicillin	05	0.34%	0.63%
	Dicloxacillin	04	0.27%	0.51%
	Piperacillin	03	0.20%	0.38%
	Penicillin	01	0.07%	0.13%
7	Beta Lactamase Inhibitors	87	5.93%	11.01%
	Clavulanic acid	73	4.98%	9.24%
	Sulbactam	12	0.82%	1.52%
	Tazobactam	02	0.14%	0.25%
8	Aminoglycosides	26	1.77%	3.29%
	Amikacin	14	0.95%	1.77%
	Gentamicin	05	0.34%	0.63%
	Neomycin	04	0.27%	0.51%
	Streptomycin	02	0.14%	0.25%
	Framycetin	01	0.07%	0.13%
9	Macrolides	26	1.77%	3.29%
	Azithromycin	21	1.43%	2.66%
	Clarithromycin	03	0.20%	0.38%
	Roxythromycin	02	0.14%	0.25%
10	Oxazolidine	13	0.89%	1.65%
	Linezolid	13	0.89%	1.65%
11	Anti-tubercular drugs	39	2.66%	4.94%
	Ethambutol	12	0.82%	1.52%
	Isoniazid	11	0.75%	1.39%
	Rifampicin	10	0.68%	1.27%
	Pyrazinamide	06	0.41%	0.76%
12	Antiviral drugs	14	0.95%	1.77%
	Emtricitabine	02	0.14%	0.25%
	Lamivudine	02	0.14%	0.25%
	Tenofovir	02	0.14%	0.25%
	Stamivudine	02	0.14%	0.25%
	Acyclovir	01	0.07%	0.13%
	Efavirenz	01	0.07%	0.13%
	Lopinavir	01	0.07%	0.13%
	Ritonavir	01	0.07%	0.13%
	Zidovudine	01	0.07%	0.13%

	Nevirapine	01	0.07%	0.13%
13	Antifungal drugs	11	0.75%	1.39%
	Fluconazole	11	0.75%	1.39%
14	Tetracyclines	08	0.55%	1.01%
	Doxycycline	08	0.55%	1.01%
15	Antimalarial	07	0.48%	0.89%
	Artemether	02	0.14%	0.25%
	Lumefantrine	02	0.14%	0.25%
	Primaquine	02	0.14%	0.25%
	Chloroquine	01	0.07%	0.13%
16	Sulfonamides	10	0.68%	1.27%
	Sulfamethoxazole	05	0.34%	0.63%
	Trimethoprim	05	0.34%	0.63%
17	Carbapenem	02	0.14%	0.25%
	Meropenem	02	0.14%	0.25%
	Total	790	53.89%	100.00%

17 different types of classes of anti-microbial agents, (55%) were used by the physicians. Totally 790 (53.88%) prescriptions contained antimicrobial agents.

Internal division

Out of these 790 prescriptions containing AMA fluoroquinolones and cephalosporins were more commonly used (25% each). But the number of prescription of ofloxacin were highest with 126 (15%).

Table 5: Prescriptions with NSAIDs and AMA

Sr. No.	Drug utilization based on pharmacy		
	Prescription	No. of prescriptions	% (Absolute)
1	PPI without NSAIDs and AMA	489	33.36%
2	PPI with NSAIDs	430	29.33%
3	PPI with AMA	326	22.24%
4	PPI along with NSAIDs and AMA	221	15.08%
5	Total Number prescriptions containing PPI	1466	100.00%

When we evaluate the different in fixed dose combinations of PPI used in study we observed that 51% cases PPI were used FDC with other drugs. 45% (660 out of 1466) prescriptions were FDC with domperidone which was significantly high as compared with other FDCs. We also observed that 1.43% prescriptions contain PPI FDC with NSAIDs.

Discussion

In our study totally 3254 prescriptions were reviewed out of which 1466 prescription contains PPI, so nearly 45.05% burden of PPI is there in study area. The rabeprazole and pantoprazole were most commonly prescribed drug while omeprazole, esomeprazole and ilaprazole were other commonly used PPI. Average age of the patients was 47.55 ± 16.16 years (mean \pm sd), with lowest age was 06 years and oldest aged patient was 97 years. Average no of brands prescribed per prescription was (mean \pm sd) 4.83 ± 2.10 . It ranged from 01 to 17 brands per prescription. While nearly (mean \pm sd) 8.93 ± 5.67 drugs were prescribed per prescription. Drugs per prescription ranged from 01 to 43. Median was 8 while Mode of the drugs per prescription was 6. Totally 1024 (69.85%) contained NSAIDs along with the PPI.

While out of 1466 PPI containing prescriptions, 790 (53.89%) prescriptions contained antimicrobial agents.

Only few drug utilization studies of PPI are available in India like, Rajani Patil et.al¹⁴ who observed PPI utilization in which they observed nearly 54% of burden of PPI on study population which is higher than our studies. 53% of burden was seen by Farooq Akram et.al¹⁵, while some studies of drug utilization of PPI shows similar results seen by Nousheen et.al¹⁶ with 46.72% of burden in in-patients. Jarchow-MacDonald¹⁷ also observed 41% of use of PPI in the UK among elderly patients.

Rajani Patil et.al¹⁴ (24%), Nousheen et.al¹⁶ (32%) observed that NSAIDs were prescribed along with PPI. Some study showed utilization NSAIDs, antimicrobial agents, in Emergency room, or in hypertensive patients etc. in which drug utilization of PPI along with other

drug were observed. Drug utilization studies of NSAIDs like; Raghavendra B et. al¹² observed that 32.58% gastro-protective drugs were prescribed along with NSAIDs out of which 81% were of PPI. Similarly Dhananjay Kulkarni et. al¹⁸ observed 61% gastro-protective drugs were prescribed along with NSAIDs out of which 41.80% were of PPI. Ingle et. al⁶ (45.22%) Jhanwar P et. al¹⁹ (38%) observed PPI were prescribed along with NSAIDs. This is less as compared with our studies. While some study with higher utilization of PPI was seen like; Christian et. al²⁰ (80%), Teeling et. al²¹ (75.18%).

Rajani Patil et. al¹⁴ (68%), Nousheen et. al¹⁶ (71%) reported use of antimicrobials along with PPI. Again some of the studies of drug utilization of AMA, the percentages of prescribing PPI along with AMA were

Khan et. al²² (32%) and Pyarelal et. al²³ (45.38%). In another study Jewargi et. al²⁴ observed that 98% patients of CHF from a tertiary care hospital were on AMA, out of which 73% patients were on PPI.

Similarly our observations did not report patients with CHF being prescribed with PPI. The results of our study are found to be comparable with some of the studies like Patil R et. al and Nousheen et. al. This indicates that PPI are preferred and prescribed as gastroprotective agents alone or along with antimicrobials and NSAIDs. Thus they will reduce the gastrointestinal adverse effects of NSAIDs and some antimicrobials, but in due course of time may give rise to some other adverse effects.

Table 6: Use of PPI in Fixed Drug Combination

PPI in Fixed Drug Combination (FDC)			
Sr. No.	Drug in combination with PPI	No of Patients	%
1	Domperidone	660	45.02%
2	Levosulpride	45	3.07%
3	Itopride	23	1.57%
4	NSAIDs	21	1.43%
5	No combination	717	48.91%
	Total	1466	100.00%

Conclusion

Our study indicates that PPI are still depended upon by many of the physicians for their ability to produce gastro protective effect. Especially when NSAIDs or some antimicrobials are simultaneously administered. However their contribution towards adverse effect is to be evaluated with continued pharmacovigilance studies.

References

- Gama H. drug utilization studies. *Arquivos de medicina*. 2008.22(2/3):69-74.
- Kumar A, Dalai CK, Ghosh A, Kray M. Drug utilization study of co-administration of non-steroidal anti-inflammatory drugs and gastroprotective agents in an orthopaedics outpatients department of a tertiary care hospital in West Bangal. *Int j basic and clinpharmacol*. 2013(March-April);2:199-202.
- Tamilselvan T, Veerapandiyani AK, Karthik N. Study on drug utilization pattern of chronic renal failure patients in a tertiary care hospital. *Int j pharm pharm sci*. 2014;6(9):482-484.
- Cheekavolu C, Pathapati RM, Kudagi BL, Saginela SK, makineedi VP, Siddalingappa et al. Evaluation of drug utilization patterns during initial treatment in the emergency room: a retrospective pharmacoepidemiological study. *Int scholarly research network ISRN pharmacology*.2011.Article ID 261585 pages 3.
- WHO policy perspectives on medicines. Promoting rational use of medicine: core components. Geneva: WHO;2002.
- Ingle P, Patil PH, Lathi V. study of rational prescribing and dispensing of prescriptions with non-steroidal anti-

inflammatory drugs in orthopedic outpatient department. *Asian j pharm clin res*.2015;8(4):278-281.

- Peter M, John M, Donald JB, Juile L. Compliance with restrictions on the subsidized use of proton pump inhibitors in Australia. *Br.j.clin.pharmacol*.1998;46:409-411.
- Geevasinga N, Patrik LC, Angela CW, Simon DR. Proton pump inhibitors and acute interstitial nephritis. *Clin. gastro. hep*. 2006;4:597-604.
- www.drug.com/stat/top100/2013/sales on date 13/01/2016.
- www.drug.com/stat/top100/2013/units on date 13/01/2016.
- Proton pump inhibitors: when is enough, enough? *Brit.j.pharmacol.issue*:8-15.
- Raghavendra B, Narendranath S, Ullal SD, Kamath R, Pain MRSM, Kamath S et al. trends in prescribing gastroprotective agents with non-steroidal anti-inflammatory drugs in an orthopedic outpatient unit of a tertiary care hospital. *J. clin. daog. Research* 2009;3:1553-56.
- Stephen O. Proton pump inhibitors uncommon adverse effect. *Austrfam physician*. 2011 sep;40(9):705-708.
- Patil R, Aithal S, Hooli TV, Varun HV. Drug utilization study of proton pump inhibitors inpatients of a tertiary care hospital: a cross-sectional study. *NJIRM*. 2015;6(5):62-65.
- Farooq A, Huang Y, Lim V, Huggan PJ, Merchant RA. Proton pump inhibitors: are we still prescribing them without valid indication? *AMJ*.2014;7(11):465-470.
- Nousheen, Tadv NA, Shareef SM. Use of proton pump inhibitors in general practice. Is it rationale? *Int.j.med.res.health.sci*.2014;3;1:37-42.
- Jarchow-MacDonald AA, Mangoni AA. Prescribing pattern of Proton pump inhibitors in older hospitalized patients in a Scottish health board. *Geriatrgerontol int*. 2013;13:1002-1009.

18. Kulkarni D, Guruprasad NB, Acharya A. a study of prescription pattern of non-steroidal anti-inflammatory drugs in medicine outpatient clinic of a rural teaching hospital. *J evolution medical dental sci.* 2013(Aug);2(32):6089-6095.
19. Jhanwar P, Sharma N, Maheswari P, Jhanwar A. drug utilization pattern in prescribing gastroprotective drugs with non-steroidal anti-inflammatory drugs in a an orthopaedic outpatient unit of a tertiary care hospital of Rajasthan. *Int j pharmaceutical sic review res.*2012;14(1);18.
20. Christian RP, Rana DA, Malhotra SD, Patel VJ. Evaluation of rationality in prescribing, adherence to treatment guideline and direct cost of treatment in intensive cardiac care unit: a prospective observational study. Downloaded from. Reviewed on 23 march 2016.
21. Teeling M, Kathline B, Feely J. have COX-2 inhibitors influenced the co-prescription of anti-ulcer drugs with NSAIDs? *Br j clinpharmacol.* 2003;57(3);337-343.
22. Khan FA, Singh VK, Sharma S, Singh P. A prospective study on the antimicrobial usage in the medicine department of a tertiary care teaching hospital. *J clin diages.* 2013(Jul);7(7):1343-1346.
23. Pyarelal, Gupta A. A prospective study on drug utilization of antimicrobial agents in patients suffering from pelvic inflammatory disease in tertiary care teaching hospital. *Ind j basic applied med res.* 2015(Jun);4(3):589-595.
24. Jewargi PKB, Mala RD. Drug utilization study in congestive heart failure at a tertiary care hospital. *Sch J App Med Sci* 2015;3(2):857-862.