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Research Article

Cost-minimization analysis of proton pump inhibitors in India

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ABSTRACT

Background: Peptic ulcer disease significantly lowers quality of life. The proton pump inhibitors (PPIs) are the most potent suppressors of gastric acid secretion. Although similar in terms of efficacy and safety, PPIs have important differences in their costs. Prescription of costly brands adversely affects expenditure on health care system by patients. Therefore, we conducted this cost-minimization study of all available PPIs to help doctors in selecting the cheapest available option.

Methods: Cost-minimization analysis (CMA) compares the cost of equally effective therapeutic options for the given condition. The cost of all PPIs brands available was collected from CIMS (July 2015) and Drug Today (July 2015). Cost range, cost ratio and mean cost of the generic drug was calculated.

Results: 1122 PPI brands are available in India. Pantoprazole is most commonly available with 494 brands and dexrabeprazole has only 6 brands. All the PPIs are available in oral and injectable formulations except ilaprazole and dexrabeprazole which are available in oral formulations only. Omeprazole 20 mg and 40 mg is the cheapest in both oral and injectable form respectively while ilaprazole 10 mg is the costliest amongst all oral formulations and rabeprazole 40 mg is the costliest in injectable preparations. Highest cost ratio for oral PPIs is for omeprazole 20 mg and lowest is for omeprazole 10 mg. This variation is mostly due to large numbers of brands available for omeprazole.

Conclusions: Prescription of costly brands adversely affects patient's economy and thereby health seeking behaviour. Therefore knowledge of the doctor about drug cost and its application in practice would be an added benefit to the patient and society.

Keywords: PPIs, CMA, Acid peptic diseases, Cross-sectional study

INTRODUCTION

Inevitable changes in lifestyle and food habits of Indian population due to rapid urbanization along with excessive use of various medications are the reasons for excessive gastric acid secretion.^{1,2} The increased gastric acid secretion destructs mucosal lining of gastrointestinal tract leading to ulceration, erosive esophagitis, erosive gastritis and gastro esophageal reflux disease (GERD) etc.³

The prevalence of GERD in western countries ranges from 10% - 44%. Prevalence of GERD in northern Indian population is 16.2% similar to developed countries.⁴ In Asian countries its prevalence is increasing.^{5,6} Also 30%

surgical ward patients suffer from acid peptic disorder.³ According to a systematic review, patients with peptic ulcer disease had significantly lower quality of life. The direct medical costs of these GERD patients based on several countries national estimate were US\$ 163-886 per patient.⁷ Though various options available to treat acid peptic diseases, proton pump inhibitors (PPIs) are the most potent suppressors of gastric acid secretion.⁸

There are seven PPIs available for clinical use in Indian market i.e. omeprazole, esmoprazole, lansoprazole, rabeprazole, dexrabeprazole, ilaprazole and pantoprazole. These are the mainstay of treatment in gastric and duodenal ulcers, GERD, erosive esophagitis,

self-treatment of heartburn, pathological hypersecretory conditions like Zollinger-Ellison syndrome, prevention and treatment of non-steroidal anti-inflammatory drugs (NSAIDS) associated gastric ulcers. Also, the risk of duodenal ulcers recurrence associated with *H. pylori* infection is reduced. All PPIs have found to have equivalent efficacy at comparable doses. Although similar to each other in terms of efficacy and safety, PPIs have important differences in their costs. Prescription of costly brands by the doctors adversely affects expenditure on health care system by patients, thereby imparts burden on patient's economy also. Therefore, we conducted this cost-minimization study by cross sectional analysis of all available PPIs brands to help doctors in selecting the cheapest available option amongst these medicines.

METHODS

The simplest type of pharmaco-economic analysis is cost-minimization analysis (CMA) which compares the cost of equally effective therapeutic options for the given condition. All PPIs are equivalent in efficacy at comparable doses. Equivalent doses for various PPIs have been mentioned in comparison to the standard dose of omeprazole 20 mg. For 20 mg of omeprazole, equivalent doses for esomeprazole is 20 mg, for lansoprazole is 30 mg, for pantoprazole is 40 mg and for rabeprazole is 20 mg. ¹²

The cost of all PPIs brands available was collected from CIMS India (July 2015) and Drug Today India (July 2015). 9,10 Cost range, cost ratio and mean cost of the generic drug was calculated. Cost range is range of drug from minimum to maximum cost. Cost ratio is calculated as the quotient of maximum cost over minimum cost.

The mean cost of generic drug has been calculated as sum of the costs of all brands divided by total number of brands available for the same generic drug. While calculating mean cost, brands with price information available are considered only for adding the prices and dividing by number of brands, as considering other brands would significantly show falls decrease in mean cost value of the drug. The cost taken into consideration is per ten tablets/ capsule or per single vial. Cost is calculated in Indian National Rupees (INR).

RESULTS

Among the 1122 brands of various PPIs available in India, Pantoprazole has highest numbers of brands i.e. 494 (44%) brands, rabeprazole has 297 (26.47%) brands, omeprazole has total 231 (20.59%) brands, lansoprazole has 52 (4.63%) brands, esmoprazole has 26 (2.32%) brands in the market, ilaprazole has 16 (1.43%) brands and dexrabeprazole has only 6 (0.53%) brands (Figure 1).

Esmoprazole is available as 20 mg, 40 mg oral formulation and 40 mg injectable formulation with 15, 19 and 6 brands of each respectively. Rabeprazole is

available as 10 mg, 20 mg oral formulation and 20 mg, 40 mg injectable formulation with 20, 285, 30 and 1 brands of each respectively. Lansoprazole is available as 15 mg, 30 mg oral formulation with 14 and 49 brands of each respectively. Pantoprazole is available as 20 mg, 40 mg oral formulation and 20 mg, 40 mg injectable formulation with 29, 418 and 2, 209 brands of each respectively.

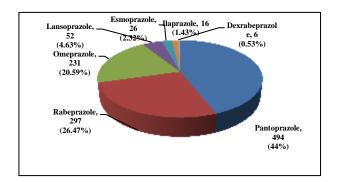


Figure 1: Total brands available in the market for each proton pump inhibitor.

Ilaprazole is available as 5 mg and 10 mg oral formulation with 6 and 15 brands of each respectively. Omeprazole is available as 10 mg, 20 mg, 40 mg oral formulation and 40 mg injectable formulation with 13, 229, 6 and 4 brands of each respectively. Dexrabeprazole is available as 5 mg and 10 mg oral formulation with 3 and 6 brands of each respectively (Figure 2).

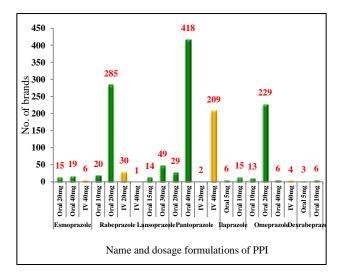


Figure 2: Total number of brands available for each dosage formulations.

Cost of oral esmoprazole for 20 mg ranges from 17-45 INR with cost ratio 2.65, for 40 mg ranges from 23-65 INR with cost ratio 2.83. Cost of oral rabeprazole for 10 mg ranges from 5-45 INR with cost ratio 9, for 20 mg ranges from 9.50- 86.5 INR with cost ratio 9.11. Cost of oral lansoprazole for 15 mg ranges from 21.80-52.50 INR with cost ratio 2.41, for 30 mg ranges from 41-82 INR with cost ratio 2. Cost of oral pantoprazole for 20 mg ranges from 18.55-58 INR with cost ratio 3.13, for 40 mg

ranges from 13.33-99 INR with cost ratio 7.43. Cost of oral ilaprazole for 5 mg ranges from 31.65-54.50 INR with cost ratio 1.72 and for 10 mg ranges from 66.40-96 INR with cost ratio 1.45. Cost of oral omeprazole for 10 mg ranges from 19.80-25.50 INR with cost ratio 1.29, for 20 mg ranges from 4-105 INR with cost ratio 26.25, for

40 mg ranges from 39-85.28 INR with cost ratio 2. Cost of oral dexrabeprazole for 5 mg ranges from 18-71 INR with cost ratio 3.94 and for 10 mg ranges from 35-86 INR with cost ratio 2.46 (Table 1).

Table 1: Proton pump inhibitors with their number of brands, minimum and maximum price, cost range, cost ratio and mean cost of each formulation.

Drug and formulations	Formulations	Total brands	Minimum price	Maximum price	Cost range	Cost ratio	Mean cost
Oral Preparati	ons						
Esmoprazole	Oral 20 mg	15	17	45	28	2.65	28.98
	Oral 40 mg	19	23	65	42	2.83	48.94
Rabeprazole	Oral 10 mg	20	5	45	40	9.00	23.13
	Oral 20 mg	285	9.5	86.5	77	9.11	44.57
Lansoprazole	Oral 15 mg	14	21.8	52.5	30.7	2.41	28.98
	Oral 30 mg	49	41	82	41	2.00	45.39
Pantoprazole	Oral 20 mg	29	18.55	58	39.45	3.13	36.25
	Oral 40 mg	418	13.33	99	85.67	7.43	76.47
Ilaprazole	Oral 5 mg	6	31.65	54.5	22.85	1.72	47.5
	Oral 10 mg	15	66.4	96	29.6	1.45	72.3
Omeprazole	Oral 10 mg	13	19.8	25.5	5.7	1.29	23.84
	Oral 20 mg	229	4	105	101	26.25	37.70
	Oral 40 mg	6	39	85.28	46.28	2.19	61.09
Dexrabeprazole	Oral 5 mg	3	18	71	53	3.94	48.6
	Oral 10 mg	6	35	86	51	2.46	53.9
Injectable prep	arations						
Esmoprazole	IV 40 mg	6	63	95.70	32.7	1.52	80.83
Rabeprazole	IV 20 mg	30	46	89	43	1.93	64.87
	IV 40 mg#	1	68.8	-	-	-	68.8
Pantaprazole	IV 20 mg	2	54.39	79.5	25.11	1.46	66.94
	IV 40 mg	209	41	168	127	4.10	56.89
Omeprazole	IV 40 mg	4	23.25	43	19.75	1.85	30

 $^{\# \}rightarrow$ only one price is available; hence cost-range and cost-ratio cannot be calculated

Whereas for injectable esmoprazole, cost range of 40 mg is 63-95.70 INR and cost ratio is 1.52. Cost range of injectable rabeprazole for 20 mg ranges from 46-89 INR with cost ratio 1.93 and for 40 mg is 68.80 INR. Injectable pantoprazole has cost range 54.39-79.50 INR for 20 mg with cost ratio 1.461, cost range is 41-168 INR for 40 mg with cost ratio 4.10. While 40 mg injectable omeprazole has cost range 23.25-43 INR and cost ratio of 1.85 (Table 1).

We have calculated mean cost for all the available dosage form of PPIs in Indian market, which are listed in Table 1. Mean cost of esmoprazole 20 mg oral, 40 mg oral and 40 mg IV are INR 28.98, INR 48.94 and INR 77.86 respectively. Mean cost of rabeprazole 10 mg oral, 20 mg oral, 20 mg IV and 40 mg IV are INR 23.13, INR 44.57, INR 61.20 and INR 68.80 respectively.

Mean cost of lansoprazole 15 mg and 30 mg oral are INR 28.98 and INR 45.39 respectively. Mean cost for pantoprazole 20 mg oral, 40 mg oral, 20 mg IV and 40 mg IV are INR 36.25, INR 76.47, INR 66.94 and INR 56.89 respectively. Mean cost for ilaprazole 5 mg and 10 mg oral are INR 47.50 and INR 72.30 respectively. Mean cost for omeprazole 10 mg, 20 mg oral, 40 mg oral and 40 mg IV are INR 23.84, INR 37.70, INR 61.09 and INR 30 respectively. Mean cost of dexrabeprazole 5 mg oral and 10 mg oral are INR 48.60 and INR 53.90 respectively (Table 1).

DISCUSSION

PPIs are the prodrugs which are activated in an acid environment of stomach. Activated drug binds to sulfhydril groups of cysteines in gastric H⁺ K⁺ ATPase to

inactivate these pumps irreversibly. Hence acid secretion requires synthesis of new pump molecule. PPIs inhibit daily gastric acid production by 80%-95% in typical therapeutic doses for 24-48 hours. They are effective in suppressing gastric acid secretion irrespective of the other stimulating factors. Around 51.4% of outpatient department patients are prescribed PPIs in their prescription. In hospitalized patients prescription of these drugs is also around 80%. Since, PPIs consume a large portion of the budget of the patient expenditure. This adversely affects the compliance of the patients. This study can help the doctors to choose the best PPIs depending on the economic status of the patient.

Pantoprazole is the most commonly available PPIs with 494 brands, followed by 297 brands of rabeprazole. Recently marketed PPIs dexrabeprazole has least numbers of marketed brands i.e., 6 brands only. All the PPIs are available in oral and injectable formulations except lansoprazole, ilaprazole and dexrabeprazole which are available in oral formulations only.

Omeprazole 20 mg and 40 mg is the cheapest in both oral and injectable form respectively while ilaprazole 10 mg is the costliest amongst all oral formulations and rabeprazole 40 mg is the costliest in injectable preparations available in the market. Amongst oral preparations, omeprazole 20 mg is also having the most expensive brand while pantoprazole 40 mg has the costliest brand amongst injectable PPIs. This may be because omeprazole is the oldest approved PPI. It is available in various generic formulations making it the cheapest PPI brand. Ilaprazole is newly approved PPI. Therefore non availability in generic formulation makes it the costliest drug in oral formulations.

By considering mean cost of all the brands, rabeprazole 10 mg is the cheapest oral PPI and pantoprazole 40 mg is the costliest PPI with mean cost of INR 76.47 while esmoprazole 40 mg and omeprazole 40 mg are having the highest and lowest mean cost for the injectable PPIs.

Highest and the smallest cost range in oral preparations of PPIs is for omeprazole 20 mg and omeprazole 10 mg respectively. In injectable preparations pantoprazole 40 mg and omeprazole 40 mg respectively have the highest and lowest cost range.

Highest cost ratio for oral PPIs is for omeprazole 20 mg and lowest is for omeprazole 10 mg. This variation is mostly due to large numbers of brands (229) available for omeprazole 20 mg. For injectable formulations, highest and lowest cost ratios are for pantoprazole 40 mg and 20 mg respectively. This might be because of availability of large number of brands for injectable pantoprazole 40 mg (209). The no. of brands for injectable pantoprazole 20 mg are only 2 which might be responsible for its lowest cost ratio. Least pharmacokinetic interactions amongst first generation PPIs along with availability in generic forms favour the highest number of pantaprazole

prescription amongst PPIs in India and might be the reason for highest availability of oral and injectable brands of pantaprazole, ultimately the mean cost is highest for oral pantaprazole and injectable pantoprazole is also having costliest brand, highest cost range and cost ratio. ^{15,16}

A decrease in drug expenditure can be achieved by changing PPIs prescribing practices. As all PPIs are equally effective, cost of treatment can be easily lowered without compromising clinical efficacy. This will be helpful in increasing the compliance of the patient to any drug therapy.

CONCLUSION

PPIs are prescribed in large numbers in day to day practice. Prescription of costly brands adversely affects expenditure on health care system, patient's economy and thereby their health seeking behavior. Therefore knowledge of the doctor about drug cost and its application in practice would be an added benefit to the patient and society.

We have included only those brands of PPIs which are mentioned in the CIMS India and Drug today India only. Therefore, few brands might have been missed which are not mentioned in these two index. Also, various fixed dose combinations (FDC) of these PPIs with many other drugs are not taken into consideration while doing this study. Prices of all the available brands are not included in the analysis, as few brands are mentioned in the CIMS and Drug Today without mentioning there price.

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Ethical approval: The study was approved by the

Institutional Ethics Committee

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