ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 15, Issue 1, 2022

Online - 2455-3891
Print - 0974-2441

Research Article

THE PHARMACOECONOMIC IMPACT OF GASTRO-PROTECTIVE AGENTS AT A TERTIARY CARE HOSPITAL

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Received: 21 October 2021, Revised and Accepted: 30 November 2021

ABSTRACT

Objectives: The study aimed to evaluate the pharmacoeconomic impact of gastro-protective agents (GPA) by carrying out cost-benefit analysis (CBA) and cost-effective analysis (CEA).

Methods: This prospective observational study was carried out by simple randomization technique at Karnataka Institute of Medical Science, Hubballi. Data used were socio-economic details based on modified B. G Prasad scale. Current Index of Medical Specialists updated version March 2021 was used for CBA and CEA. Regression analysis was the statistical tool used in the study.

Results: A total of 120 participants were included in the study. 57.5% were male and 42.5% were female. 3.33% were pediatrics, 32.5% were young adults, 37.5% were elder adults and 26.67% were geriatrics. Out of 120 samples, 94 participants were prescribed with pantoprazole, other drugs prescribed include domperidone and pantoprazole, rabeprazole, and ranitidine. The CBA revealed ratio of benefits over costs for pantoprazole was 3.86, ranitidine was 9.31, pantoprazole and domperidone was 0.84 and rabeprazole was 0.84. Additional cost of 138.30 Indian Rupee must be spent on pantoprazole over ranitidine to get cost-effective treatment without disease for one whole year.

Conclusion: The CBA revealed that maximum patients received benefits for pantoprazole. CEA gives an idea on best effective treatment over two drugs of different class. Our study concludes that pantoprazole is deemed to be superior over other drugs of GPA prescribed among study participants.

Keywords: Proton pump inhibitors, Histamine-2 receptor antagonist, Cost-effectiveness, costs and benefits, B G Prasad Income scale.

 DOI: http://dx.doi.org/10.22159/ajpcr.2022v15i1.43412. Journal homepage: https://innovareacademics.in/journals/index.php/ajpcr

INTRODUCTION

The ability of a pharmacological treatment to minimize or prevent gastric mucosal injury/necrosis caused by a range of ulcerogenic and necrotizing agents is known as gastro-protection [1]. Gastroprotective agents include H2RA: Ranitidine, Cimetidine, Gastro-prokinetics: Levosulpiride, Itropride, Domperidone, Proton pump inhibitor (PPI): Pantoprazole, Omeprazole, Esmoprazole. PPIs non-competitively antagonize H^+/K^+ adenosine triphosphatase (ATPase), the enzyme in gastric parietal cells responsible for transporting H^+ ions into the gastric lumen. Different doses of these drugs are recommended, but at equivalent doses, these agents are remarkably similar when used in the treatment of acid-related disorders. They help in the prevention of NSAID associated ulcers. The H2RAs have different pharmacological properties in terms of drug metabolisms and acid inhibitory capacities [2]. Pharmacoeconomics is a collection of illustrative and analytic tools for evaluating pharmaceutical interventions that connect individual patients to the larger health-care system [3]. Techniques used in Pharmacoeconomics are cost-minimization analysis (CMA), cost-effectiveness analysis (CEA), cost-utility analysis, cost-benefit analysis (CBA), cost of illness analysis. Pharmacoeconomics is research on health outcome as it is a patient-centered outcome increasing the quality of life (QOL) in years especially when comparing a non-pharmacological therapy or preventive methods such as surgical and screening interventions. The quality-adjusted life-year (QALY) has a major outcome in making clinical decisions [3].

CBA

The CBA is a method for determining which solutions give the best approach for adoption and practice in terms of labor, time, and cost savings. It compares the overall cost of each alternative to the intervention measures' outcomes or benefits in monetary units [4]. It includes direct medical savings, direct non-medical savings, indirect costs, and intangible costs.

CEA

CEA is a pharmacoeconomic model which summarized the health benefits and resources used by competing health care programs. It is a technique used to aid in decision-making between alternatives when the costs are measured in natural unit changes in health. Treatment with dissimilar outcomes can also be analyzed by this method. The result of CEA is expressed as ratio i.e., average cost-effectiveness ratio and Incremental Cost-Effectiveness Ratio [4].

METHODS

Study site

This study will include the inpatients who are admitted in the Karnataka Institute of Medical Science Hubballi.

Study design

Prospective observational study.

Sampling technique

Simple Randomization Method was applied in the study where the random number of participants (120) were chosen in the most effective way derived from inclusion and exclusion criteria mentioned in the study.

Study period

The study was carried out for a period of 5 months from December 2020 to April 2021.

Inclusion criteria

The study included inpatients of general medicine, female general ward, male general ward, surgery ward. Participants of all age groups, male and female participants, pregnant and lactating participants were involved in the study.

Exclusion criteria
Outpatients were evicted from the study.

Source of data
Medical case sheets, treatment chart, laboratory investigations, past medical history, past medication history, clinical progress chart, nurse charts, interactions with patients, interactions with patient's caregiver, Current Index of Medical Specialists [4], MODIFIED B G PRASAD Scale 2020 published on March 31, 2020 [5].

Study procedure
By inclusion criteria, the participants were selected and verbal explanation regarding the study and its outcome was discussed with the participants and interviewed after their will to participate [6]. The following data were obtained: Socio-demographic details (includes age, sex, occupation, and income status as per MODIFIED B.G PRASAD scale) [5], Medical history, medication history, laboratory data, progress chart, and drugs. Pharmacoeconomic impact of gastro-protective agents (GPA) was recorded and documented by CBA, cost-effectiveness analysis. Suitable recommendations were provided to the participants and the clinical theme to prevent or resolve Pharmacoeconomic burden of prescribed GPAs.

Statistical analysis
The test performed in the study was linear regression using Microsoft Excel free version 2010. The test measures the relationship between the variables, i.e., income (dependent variable), costs (independent variable). The outcome measures of this test are to find the variance as to how much the sestatus income is affecting the costs and benefits of GPAs among the study participants.

Table: 1 Demographics of study participants

Age	Category	Number	Percentage
1 month–18 years	Pediatrics	4	3.33
18–39	Young Adults	39	32.5
40–59	Elder adults	45	37.5
60 and above	Geriatric	32	26.67
Gender		**Number**	**Percentage**
Male		69	57.5
Female		51	42.5
Type of Family		**Number**	**Percentage**
Nuclear		76	63.3
Joint		44	36.6
Income scale			
BGP scale	**Class**	**Number**	**Percentage**
	I	29	48.09
	II	26	21.66
	III	20	16.67
	IV	12	10
	V	33	27.5
	Sum	120	

Ethical approval
Ethical clearance for this study was obtained from Institutional Ethical Committee KLE College of Pharmacy, Hubballi. Reference number: KLECOPH/IEC/2020-21/06.

RESULTS AND DISCUSSION

Distribution of demographic characteristics
The study included 120 participants with the age group of 1 month–60 years and above. In total population, 57.5% were male and 42.5% were female. 3.33% were pediatrics, 32.5% were young adults, 37.5% were elder adults and 26.67% were geriatrics. Income was dispersed according to modified B G Prasad scale 2020. In total population, Class I were 48.09%, Class II -21.66%, Class III-16.67%, Class IV-10%, Class V-27.5%, and families were distributed by two types nuclear and joint (Table 1).

Often used gastro-protective drugs is pantoprazole. In our study most commonly, prescribed categories of drugs were PPI, H2RA, Domperidone. Most frequently prescribed drugs were pantoprazole and ranitidine.

CBA
A cost-benefit ratio is a CBA that measures and aims to outline the value for money of a scientific research. A BCR is the ratio of a research study that benefits to its cost expenses stated in monetary terms [7].

In this study, the benefit-cost ratio was found out for PPIs and H2RAs. Pantoprazole, rabeprazole and combination therapy pantoprazole and domperidone were commonly prescribed under PPIs and ranitidine was commonly prescribed under H2RAs (Table 2). Comparison of benefit-cost ratio of these drugs gives sound knowledge on the economic burden that the patient experiences with different treatments. Benefit/cost ratio of more than 1 signifies higher benefits than costs similarly, ratio less than 1 signifies costs greater than benefits and ratio equal to 1 indicates benefits equal to costs. By conducting the study, we found that pantoprazole and domperidone (ratio of 0.87, combination therapy) and rabeprazole (ratio of 0.84, monotherapy) had greater costs compared to benefits whereas pantoprazole (ratio of 3.86) and ranitidine (ratio of 9.31) had greater benefits compared to costs (Fig. 1).

CEA
According to a study conducted in 2008 by Vonkeman *et al*., the additional cost-effectiveness ratio was € 37,899 per severe gastrointestinal event prevented [8]. In our study, we included Cost-effectiveness analysis by comparison of two treatments by ICER formula. ICER signifies the outcome or a result of an economic evaluation. ICER gives a summary measure of economic value of an intervention compared with an alternative. It provides a ratio of extra cost per unit health effect for the most expensive therapy versus alternative [9].

According to a 2016 study by Permsuwan *et al*., the cost of saxagliptin was $17,316 per 7.552 QALYs, whereas the cost of sulfonylurea was $15,474 for 7.528 QALYs [10]. In our study the result is based on the cost-effectiveness threshold which means, to establish a willingness

Table 2: Pharmacoeconomic analysis of various gastro-protective agents

Module	Drug class	Drug name	No. of drugs prescribed	Costs	Benefits	B/C ratio
CBA	PPI	Pantoprazole	94	448.71	1128.38	2.51
		Rabeprazole	3	328.8	276.6	0.84
		Pantoprazole+Domperidone	8	285.31	124.66	0.43
	H2RA	Ranitidine	15	81	754.3	9.31
CEA		**Cost of PPI (INR)**	**Cost of H2RA (INR)**	**Effect of PPI**	**Effect of H2RA**	**ICER**
	Total	42179.21	1068	388	24	138.30/QALY
	Average	448.71	76.2	4.04	1.5	

CBA: Cost-benefit analysis, PPI: Proton-pump inhibitors, H2RA: Histamine-2 receptor antagonist, INR: Indian Rupee, CEA: Cost-effective analysis, ICER: Incremental cost-effective ratio, QALY: Quality adjusted life years

to pay value for the outcome of interest [11]. For a given treatment if the ICER is above the threshold cost it will be too expensive whereas if the ICER lies below the threshold the treatment can be judged cost-effective. The effect of samples having PPI prescription was compared with prescribed with H2RAs. The ratio was expressed in unit/QALY. The QALY was calculated by quantitative non-monetary health units. (Units of scores 1–5) [12].

Table 3 represents willingness to pay based on the sestatus of modified BGP income scale 2020 [5,11] among 120 participants, the average threshold for BGP I was 255.7INR similarly, 255.7INR for BGP Class II, BGP III. 217.5INR for BGP IV 180INR, 103.9INR for BGP V. The average cost of PPI was found to be 431.8INR and the average cost of H2RA was found to be 76.2INR. Average score of effects calculated in non-monetary health units of PPI was 4.04 out of 5 and H2RA was 1.5 out of 5. The ICER of costs of treatments (PPI and H2RA) divided by effects of treatments was 138.30INR/QALY. The above result signifies that sestatus BGP income scale 2020 of class I to IV have cost-effective treatments whereas Class V has expensive treatment based on their respective threshold cost. Therefore, by comparing the willingness to pay threshold of different sestatus income scale of BGP class 2020 we conclude that class V (threshold of 103.9INR) of BGP scale will be deemed too expensive for the given treatment cost/QALY (138.30INR) (Fig. 2).

Findings of comparison between NSAIDs v/s NSAIDs and PPI

Studies conducted by Pendhari *et al*., Lee *et al*. (2016) and many others stated that NSAID administration caused many side effects which include stomachache and heartburn, stomach ulcers, and proneness to bleed [13]. Hence, NSAID's were co-administered with PPI to reduce NSAID's – induced gastrointestinal events as it is safe and included in many of the guidelines. Collateral usage of PPIs was markedly higher in the controls than in the cases, as per a 2008 publication by Vonkeman *et al*. (cases 14 (13.5%) and controls 77 (27.1%); p=0.005). The total costs associated with serious NSAID ulcer complications was (13.8 × € 8,375) = € 115,676.

Our study objective was to evaluate the pharmacoeconomic impact of GPAs prescribed with NSAIDs. In Table 4, the average cost of NSAID's used in total population was 400.62 INR i.e. (4.006%). A total of 56 samples were found out to be combination therapy {NSAID +PPI} and average cost of NSAID+PPI was 653.89 INR i.e. (6.538%) (Table 4). Hence, we found out that the impact of PPI cost on NSAID users had load of 2.53%. Hence, the use of PPIs must be restricted in patients having the potential to gastric bleeding or GERD (Fig. 3).

Studies evaluating the cost comparison between the systems involved v/s PPI

Table 5 in the study depicts comparison of diseases related to various organ systems involved along with the prescription of GPAs. Various systems involved in this study are the integumentary system, central nervous system (CNS), cardiovascular system, cancer, infectious diseases, renal system, hematology, immune system, pulmonary system, skeleton-muscle system, and endocrine system. The treatment cost of each system corresponding to the GPA cost was calculated to find out the pharmacoeconomic burden of GPA on various systems and is expressed in percentage. Thus, the following are the results of the study (Table 5).

In the study of 120 participants, an average of 0.68% PPI burden was observed in integumentary system whose average treatment cost was 22.01%. Similarly, 1.62% PPI burden on CNS (44.012%), 1.65% PPI burden on anti-cancer therapy (71.46%), 3.96% PPI burden on infectious diseases (17.312%), 1.86% PPI burden on the renal system, 8.15% PPI burden on hematological system (95.73%) and 7.86% PPI burden on the immune system, 3.18% PPI burden on pulmonary system (22.9%), 4.37% of PPI burden on skeleton-muscle system (23.175), and 4.28% PPI burden on the endocrine system (29.73%) related diseases. From the above data collected it can be concluded that the highest percentage of pharmacoeconomic burden of PPI was observed in the hematological system, immune system, CVS, infectious diseases and GI system, pulmonary system, skeleto-muscle system, endocrine system, and least pharmacoeconomic burden of PPI was observed in the dermatological system and CNS related diseases (Fig. 4).

In this study, the most common disease of the hematological system was iron deficiency anemia, drugs given were Inj. Vitcofol, Inj. Iron

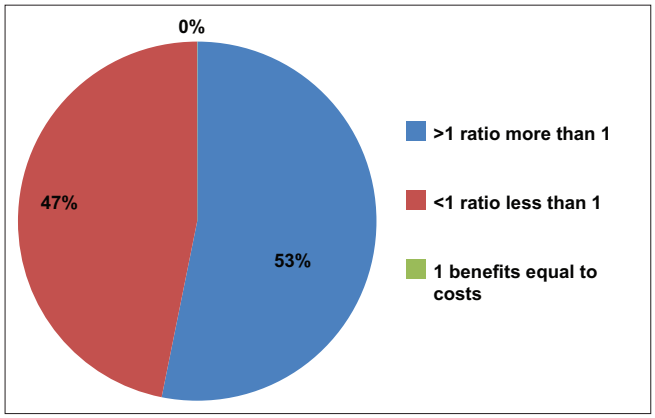


Fig. 1: Pie chart representing cost-benefit analysis of pantoprazole prescribed among study participants

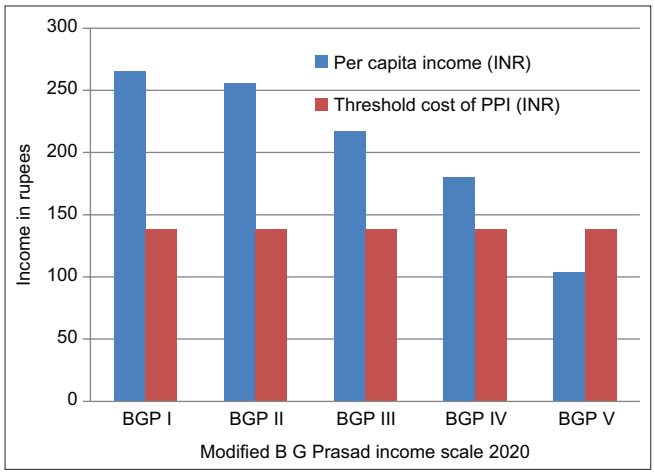


Fig. 2: Comparison of willingness to pay with threshold cost of proton-pump inhibitors

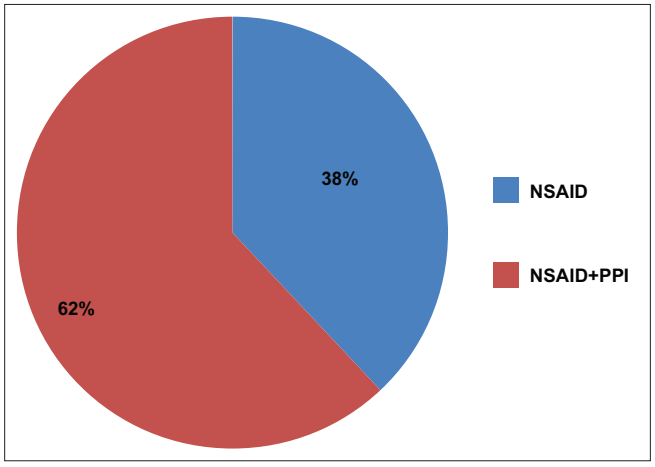


Fig. 3: Pie chart representing the percentage of costs between non-steroidal anti-inflammatory drugs and non-steroidal anti-inflammatory drugs v/s proton-pump inhibitors

sucrose. Administration of PPI with iron sucrose injection or any other iron supplements results in reduced iron bioavailability. Administration of pantoprazole leads to long-lasting inhibition of gastric acid which in turn inhibits iron absorption. Hence, the use of PPIs should be avoided in patients with Anemia and histamine 2 antagonists or other GPAs can be preferred for less severe conditions as they do not affect iron absorption and in turn is cost-effective compared to PPI.

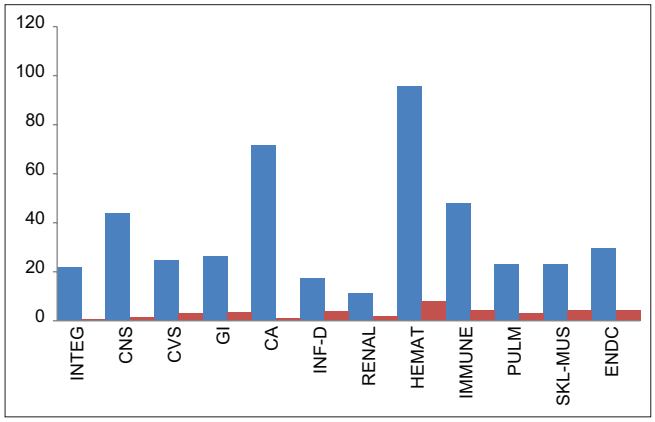


Fig. 4: Bar graph representation of cost comparison between system involved v/s Proton-pump inhibitors among the study participants

Table 3: Findings of willingness to pay among the study participants

Modified BGP Income scale 2020	Average in INR
BGP I	265.7
BGP II	255.7
BGP III	217.5
BGP IV	180
BGP V	103.9

INR: Indian rupee

Table 4: Findings of comparison of costs between NSAIDs v/s NSAIDs and PPIs

Category	No. of drugs prescribed	Cost	Percentage
NSAID	56	400.62	4.006
NSAIDs+PPI	56	653.89	6.538

PPI: Proton-pump inhibitors, NSAIDs: Non-steroidal anti-inflammatory drugs

Table 5: Studies evaluating cost comparison between system involved versus PPI

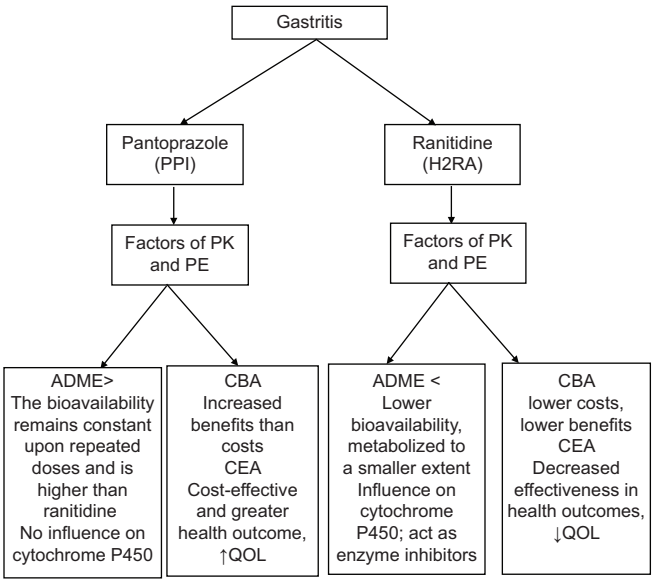
Systems involved	Average	
	Treatment cost (%)	PPI cost (%)
Integ	22.01	0.68
CNS	44.01	1.62
CVS	24.59	3.05
GI	26.25	3.52
CA	71.46	1.65
INF-D	17.31	3.96
Renal system	11.13	1.86
Vascular system (Hemat)	95.73	8.15
Immune system	47.86	4.37
Pulm	22.90	3.18
Skl-Mus	23.17	4.37
Endc	29.73	4.22

PPI: Proton-pump inhibitors, Integ: Integumentary system, CNS: Central nervous system, CVS Cardio-vascular system, GI: Gastro-intestinal system, CA: Cancer, INF-D: Infectious diseases, Pulm: Pulmonary system, Skl-Mus: Skeleto-muscle system, Endc: Endocrine system

Statistical analysis

Regression analysis was the statistical tool used which explained the variability of income by the set of independent variables, i.e., cost and benefit. Linear regression was done using Microsoft Excel free version. A linear regression analysis helps to find the variances of two variables. Here income is dependent variable, costs and benefits are independent variables. Lower R2 signifies high variance in the study. R^2 was found to be 0.9%. 0.9 represents strong positive association between two variables, i.e., income of the study participants is strongly associated with costs of GPAs mainly PPIs. p value was found to be 0.0031.

Algorithm representing the pharmacoeconomic decision analysis of PPI and H2RA from the study



CONCLUSION

Pantoprazole is the commonest drug prescribed in hospitalized patients to prevent gastritis or as prophylaxis in NSAIDs drug adverse reaction. Pantoprazole has lesser pharmacoeconomic burden when compared to other PPI monotherapy and combination therapy. The CBA revealed that the patients receiving pantoprazole had greater benefits compared to other drugs. The word cost-effective can be termed to the patients who receive greater health outcomes with respect to life years gained or QOL with least expenses towards treatment. PPIs are commonly prescribed in patients receiving NSAIDs in order to prevent adverse effects caused by NSAIDs such as heartburn, stomach ulcers, gastric bleeding. Hence thorough evaluation on patients prone to such adverse effects must be done in order to avoid unnecessary PPI prescriptions as long-term use of pantoprazole or other PPIs may lead to thrombocytopenia. These methodologies can be used by clinicians and other decision-makers to analyze and compare the total cost of treatment options as well as the results associated with these alternatives to compare the costs and outcomes of pharmaceutical interventions. The study should be conducted in large population to provide precise results. Costs and Benefits are converted to monetary values which can be inaccurate. This study has limited evidence, hence designing the model through specific software to provide evidence-based data is recommended.

ACKNOWLEDGMENT

We take it as a privilege to acknowledge Dr. AHMV Swamy Principal KLE College of Pharmacy and medical staff of KIMS Hubballi for the infrastructure support in completion of the research, we extend our heartfelt thanks to Dr. Yogesh U Hiremath Pharm. D and Dr. Sachin V

Desai MBBS, M.D. Community Medicine for their valuable guidance and thorough review of the research.

AUTHORS CONTRIBUTION

All the authors have contributed equally in the completion of thesis.

CONFILCT OF INTEREST

None.

AUTHORS FUNDING

None.

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