Cost variation analysis of proton pump inhibitors available in Indian market

Akash Chandra, Manish Kumar, Lalit Kumar*, Harihar Dikshit

ABSTRACT

Background: In now days proton pump inhibitors are prescribing more and more by Indian physicians not only in peptic ulcer, gastroesophageal reflux disease, gastritis but also along with non steroidal anti-inflammatory drugs to overcome the side effects as gastric irritation and discomfort by non steroidal anti inflammatory drugs. There are many brands of PPI drugs available in Indian market. Costly drugs can lead to economic burden which results in decreased compliance or even non-compliance. Non-compliance leads to incomplete treatment which tends to increase morbidity. Increase in the patient medication cost was found to associated with decreased adherence to prescription medication. Hence this study was done to assess the cost variation of proton pump inhibitors [PPI] drugs.

Methods: The maximum and minimum price of each brand of the drug in INR was noted by using CIMS January to April 2018 edition Drug Today April to June 2018 Vol-1. The cost ratio and the percentage cost variation for individual drug brands was calculated. The cost of 10 tablets/capsules was calculated in case of oral drug and the cost of one 1 vial or ampoule was noted in case of injectable drug. At last the cost ratio and percentage cost variation of various brands was compared.

Results: Percentage variation in cost for proton pump inhibitors marketed in India was found to be tablet/capsule Esomeprazole [20mg]: 141.17, tablet/capsule Esomeprazole [40mg]: 196.29, capsule/tablet Omeprazole [20mg]: 569.53, Tablet/capsule Pantoprazole [40mg]: 248.8, tablet/capsule Rabeprazole [20mg]: 815.78, capsule/tablet Lansoprazole [30mg]: 173.33, Inj. Esomeprazole [40mg] 1 vial: 81.81, Inj. Omeprazole [40mg] 1vial: 47.95, Inj. Pantoprazole [40mg] 1vial: 66.66, Inj. Rabeprazole [20mg] 1vial: 176.625.

Conclusions: Tablet Rabeprazole [20mg] shows highest cost ratio and percentage cost variation as 9.15 and 815.78. While Inj. Omeprazole [40mg] 1 vial shows lowest cost ratio and percentage cost variation as 1.47 and 47.95.

Keywords: PPI, Compliance, Percentage cost variation, Cost ratio

INTRODUCTION

Proton pump inhibitors are very important drugs for GIT disorders as peptic ulcer, gastroesophageal reflux disease, gastritis, oesophagitis, zollinger ellison’s syndrome etc. In now days proton pump inhibitors are prescribing in more and more amount by the Indian physicians not only in GIT disorder but also along with NSAIDS (Non steroidal anti-inflammatory drugs) to overcome the side effects by NSAIDS. Evidence emerged by the end of the 1970s that the newly discovered proton pump (H+/K+ ATPase) in the secretory membrane of the parietal cell was the final step in acid secretion. Literature from anaesthetic screenings led attention to the potential antiviral compound pyridylthio acetamide which after further examination pointed the focus on an anti-secretory compound with unknown mechanisms of action called timoprazole. Timoprazole is a pyridylmethylsulfanyl benzimidazole and appealed due to its simple chemical structure and its
surprisingly high level of anti-secretory activity.\textsuperscript{5} Optimization of substituted benzimidazoles and their antisecretory effects were studied on the newly discovered proton pump to obtain higher $p$ $K_a$ values of the pyridine, thereby facilitating accumulation within the parietal cell and increasing the rate of acid-mediated conversion to the active mediate. As a result of such optimization the first proton pump inhibiting drug was released on the market, omeprazole.\textsuperscript{6} Other PPIs like lansoprazole and pantoprazole would follow in its footsteps, claiming their share of a flourishing market, after their own course of development. Proton pump inhibitors are prodrugs and their actual inhibitory form is somewhat controversial. In acidic solution, the sulfenic acid is isolated before reaction with one or more cysteines accessible from the luminar surface of the enzyme, a tetracyclic sulfenamide. This is a planar molecule thus any enantiomer of a PPI loses stereo specificity upon activation.\textsuperscript{7} The effectiveness of these drugs derives from two factors: their target, the H^+/K^+ ATPase which is responsible for the last step in acid secretion; therefore, their action on acid secretion is independent of the stimulus to acid secretion, of histamine, acetylcholine, or other yet to be discovered stimulants. Also, their mechanism of action involves covalent binding of the activated drug to the enzyme, resulting in a duration of action that exceeds their plasma half-life.\textsuperscript{8} Patients from poor socioeconomic background must have access to the correct drug at the nominal price. Costly drugs can lead to economic burden which results in decreased compliance or even non-compliance. Non compliance leads to incomplete treatment which tends to increased morbidity. There is a gross variation in the cost of different brands of same generic drugs available in Indian market. Increase in the patient medication cost was found to be associated with decrease adherence to prescription medication.\textsuperscript{9} Cost analysis is the study in which comparison of costs of two or more alternative medication is made without regard to outcome.\textsuperscript{10,11} Studies conducted in past show a wide variation in cost of branded and generic versions of same drugs.\textsuperscript{12,13}

Hence the present study was conducted to evaluate the cost variation amongst the different brands of proton pump inhibitors available in India.

**METHODS**

1. Price in Indian rupees (INR) of proton pump inhibitors manufactured by different pharmaceutical companies in India, in the same strength were obtained from Current index of medical specialists (CIMS) January to April 2018 edition and from Drug Today April to June 2018, vol-1 as they are readily available source of drug information and are updated regularly.
2. The cost of 10 tablets/capsules and that of one ampoule /vial was calculated.
3. The cost of drugs was also crosschecked at pharmacy or retail drug store.

4. Difference in the maximum and minimum price of the same drug formulation manufactured by different pharmaceutical companies and percentage variations in prices are calculated.
5. The cost of injectable drugs and oral drugs in forms of tablet and capsule should be calculated separately.
6. The cost ratio, calculated as the ratio of the costlier brand to that of the cheapest brand of the same drug, calculated as follows:

Cost ratio = Price of the costliest brand/Price of the least costly brand.

7. The percentage cost variation of each drug should be calculated as follows:

   \[
   \text{Percentage cost variation} = \left( \text{Maximum cost}\times\frac{\text{Minimum cost}}{\text{minimum cost}} \right) \times 100.
   \]

8. Maximum percentage cost variation and cost ratio of a particular drug should be noted down.
9. Minimum percentage cost variation and cost ratio of a particular drug should be noted down.

**Inclusion criteria**

- Drugs belong to group of proton pump inhibitors only should be included.
- Doses form of PPI Drugs will be only capsule or tablets.
- Drugs belong to branded manufacturing companies should be included.
- Drugs belong to same strength should be included.

**Exclusion criteria**

- PPI drugs in combinations with other drugs as prokinetic drugs are excluded.
- PPI Drugs available in doses form of syrup are excluded.
- The drug formulation being manufactured by only one company or being manufactured by different strengths are excluded.
- Drugs belong to bogus manufacturing companies should be excluded.

**RESULTS**

The analysis of data showed a large variation in costs of different brands of proton pump inhibitors available in Indian market. Percentage variation in cost for proton pump inhibitors marketed in India was found to be:

| Drug Formulation | Price (INR) |
|------------------|-------------|
| Esomeprazole [20mg] | 141.17 |
| Esomeprazole [40mg] | 196.29 |
| Omeprazole [20mg] | 569.53 |
| Pantoprazole [40mg] | 248.8 |
| Rabeprazole [20mg] | 815.78 |
| Lansoprazole [30mg] | 173.33 |
| Pantoprazole [40mg] | 81.81 |
| Omeprazole [40mg] | 47.95 |
| Rabeprazole [20mg] | 66.66 |

International Journal of Basic & Clinical Pharmacology | August 2018 | Vol 7 | Issue 8 | Page 1627
176.625. Tablet Rabeprazole [20mg] shows highest cost ratio and percentage cost variation as 9.15 and 815.78. While Inj. Omeprazole [40mg] 1 vial shows lowest cost ratio and percentage cost variation as 1.47 and 47.9.

Capsule Rabeprazole [20mg] shows maximum cost ratio as: 9.15 and maximum percentage cost variation as: 815.78

Injection Omeprazole [40mg, 1 vial] shows minimum cost ratio as: 1.47 and minimum percentage cost variation as: 47.95.

It can prefer those drug who possess cost ratio less than 2 and percentage cost variation less than 100, so we can prefer injection Omeprazole [40mg, 1 vial].

Table 1: Drug costs, cost ratio and percentage cost variation of proton pump inhibitors available in Indian market.

| Drug                | Dose     | No. of brands | Maximum price (Rs) | Minimum price (Rs) | Cost ratio | Percentage cost variation |
|---------------------|----------|---------------|--------------------|--------------------|------------|--------------------------|
| Tab/Cap. Esomeprazole | 20mg     | 14            | 41                 | 17                 | 2.41       | 141.17                   |
| Tab/Cap. Esomeprazole | 40mg     | 25            | 80                 | 27                 | 2.96       | 196.29                   |
| Tab/Cap. Omeprazole | 20mg     | 147           | 87.04              | 13                 | 6.69       | 569.53                   |
| Tab/Cap. Pantoprazole | 40mg    | 267           | 87.20              | 25                 | 3.48       | 248.8                    |
| Tab/Cap. Rabeprazole | 20mg     | 205           | 87                 | 9.50               | 9.15       | 815.78                   |
| Tab/Cap. Lansoprazole | 30mg    | 40            | 82                 | 30                 | 2.73       | 173.33                   |
| Inj. Esomeprazole   | 40mg, 1vial | 15           | 140                | 77                 | 1.81       | 81.81                    |
| Inj. Omeprazole     | 40mg, 1vial | 3            | 34.40              | 23.25              | 1.47       | 47.95                    |
| Inj. Pantoprazole   | 40mg, 1vial | 152          | 70                 | 42                 | 1.66       | 66.66                    |
| Inj. Rabeprazole    | 20mg, 1vial  | 32           | 120                | 43.38              | 2.76       | 176.625                  |

DISCUSSION

India is known to export medicines to various countries at low cost but faces the challenge of access to affordable and quality medicines for its own population. The Indian market has over 100,000 formulations and there is no system of registration of Medicines. More than one company sells a particular drug under different brand names apart from the innovator company. This situation has led to greater price variation among drugs marketed. These wide variations in the prices of different formulations of the same drug have severe economic implications in India. Unlike developed countries, people in developing countries pay the cost of medicines out-of-pocket. In India, more than 80% health financing are borne by patients. Patients have to pay more unnecessarily if costly brands are prescribed. Many poor people frequently face a choice between buying medicines or buying food or other necessities due to limited resources and high pricing of drug. So, medicine prices do matter. Ideally the drugs of cheaper brands should be prescribed to save the patient’s money and to enhance the compliance. In India, doctors have less awareness in the cost difference of different brands of the same drug. It is felt that physicians could provide better services and reduce costs of drugs if information about drug prices was readily available. In India more than 80% health financing is borne by patients. Studies have shown that providing a manual of comparative drug prices annotated with prescribing advice to physicians reduced their patients drug expense especially in a disease like hypertension which needs long term treatment. Rational prescribing involves selecting the cost-effective treatment. The costly brand of same generic drug is scientifically proved to be in no way superior to its economically cheaper counterpart. People living in developing countries pay heavy cost of medicines. The situation becomes more complex due to the presence of number of brands with variety of names and prices. There is a need for concerted action from regulatory authorities, doctors, pharmacists and general public at large to address this issue of proton pump inhibitors price variation. The excess profit margins presently being shared by pharmaceutical traders must be passed on to consumers which is a feasible and economically viable. The price variation assumes significance when the cost ratio exceeds 2 and percentage cost variation exceeds 100. By this fact the above analysis showed that there is not much significant price variation among injectable proton pump inhibitors as comparison to oral proton pump inhibitors. Tablet Rabeprazole [20mg] shows significant cost ratio and percentage cost variation as 9.15 and 815.78 while injection Omeprazole does not show significant cost ratio and percentage cost variation as 1.47 and 47.95 which are <2 and 100. Significant price variation creates economic burden on poor patients. Costs of drugs are controlled by the drug cost control order 2013 (DPCO). Hence, it was need to draw attention to the prices of various drug formulation brands available to reduce the cost of therapy. The treating physician should be made aware of the cheapest drug available among the various brands so that the patient bears lesser burden of treatment cost. Government of India has opened few generic drug stores in some states that sell generic medicines manufactured by public sector companies. The
quality of generic medicines available on these stores at cheaper rates should be tested and compared with popular branded drugs and results should be widely published. Studies involving comparative evaluation on quality of branded and their generic counterpart may be made mandatory for the generic manufacturer and their reports should be made public to promote generic use and prescription.

CONCLUSION

In now days prices of few drugs are under government control through DPCO. Hence the physician should always remember that he should not avoid treating the patients with a particular drug because it is expensive and should rather balance his therapeutic decisions in prescribing a particular drug by considering the patients socioeconomic status.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Forte JG, Lee HC. Gastric adenosine triphosphatases: a review of their possible role in HCl secretion. Gastroenterology. 1977 Oct;73(4 Pt 2):921-6.
2. Snaeder W. Drug prototypes and their exploitation. Wiley;1996:414-415.
3. Hemenway JN. Case Study: Omeprazole (Prilosec). Prodrugs. Biotechnology: Pharmaceutical Aspects. Springer, New York, NY; 2007:1313-1321. ISBN 978-0-387-49782-2.
4. Olbe L, Carlsson E, Lindberg P. A proton-pump inhibitor expedition: the case histories of omeprazole and esomeprazole. Nature reviews drug discovery. 2003 Feb;2(2):132-9 (PMID 12563304).
5. Senn-Bilfinger J, Sturm E. The Development of a New Proton-Pump Inhibitor: The Case History of Pantoprazole. Analogue-based Drug Discovery; 2006:115-136. ISBN 978-3-527-60800-3.
6. Lindberg P, Carlsson E. Esomeprazole in the Framework of Proton-Pump Inhibitor Development. Analogue-based Drug Discovery; 2006:81-113. ISBN 978-3-527-60800-3.
7. Shin, Moo J, Keith M, Olga V, Sachs G. The gastric HK-ATPase: Structure, function, and inhibition. Pfuiigers Archiv - European Journal of Physiology. 2008;457(3):609-22.
8. Sachs G, Shin, Moo J, Olga V, Lambrecht N, Iskandar Y, Munson K. The Gastric H, K ATPase as a Drug Target. J Cli Gastroenterol. 2007;41(2):226-42.
9. Eaddy MT, Cook CL, O’Day K, Burch SP, Cantrell CR. How patients cost-sharing trends affects adherence and out comes: a literature review: PT. 2012;37:45-55.
10. Ahuja J, Gupta M, Gupta AK, Kohli K. Pharmacoeconomics. Natl Med J India. 2004;17:80-3.
11. Sanchez LS. Pharmacoeconomics: Principles, methods and applications. In: Dipiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey ML, Eds. Pharmacotherapy: A pathophysiological approach. 7th Ed. McGraw Hill; New York; 2008:1-2.
12. Das SC, Mandal M, Mandal SC. A critical study on availability and price variation between different brands: impact on access to medicines. Indian J Pharm Sci. 2007;69(1):160-3.
13. Chawan VS, Gawand KV, Badwane SV. Cost analysis of oral hypolipidemic agents available in India. Int J Basic Pharmacol. 2014;3:954-7.
14. Thomas M. Rational drug use and essential drug concept. In: Parthasarathi G, Nyfort Hasen K, Editors. A Textbook of Clinical Pharmacy Practice. 1st Ed. Himayatnagar, Hyderabad: Orient Longman; 2004:72 3.
15. Creese A, Kotwani A, Kutzin J, Pillay A. Evauating pharmaceuticals for health policy in low and middle-income country settings. In: Freemantle N, Hill S, eds. Evaluating pharmaceuticals for health policy and reimbursement. Massachusetts, USA: Blackwell Publication; (in collaboration with WHO Geneva); 2004:227-243.
16. Mahal A, Karan A, Engelgau M. The Economic Implications of Non-Communicable Disease for India. Washington, DC: World Bank; 2010. Available at: http://siteresources.worldbank.org/HEALTHNUTRITIONANDPOPULATION/Resources/281627-1095698140167/Economic_Implications_of_NCD_for_India.pdf.
17. Rataboli PV, Garg A. Confusing brand names: nightmare of medical profession. J Postgrad Med. 2005;51:13-6.
18. Drug Cost Control, Government of India; Order, 2013. Available at: http://www.appaindia.nic.in/DPCO2013. pdf.
19. Vieira JL, Portal VL, Moriguchi EH. How much do we pay for a benefit? A descriptive cost analysis of the use of statins. The need for a national cost-effectiveness analysis. Arq Bras Cardiol. 2001;76(5):409-18.
20. Kumar L, Dinkar JK, Mohan L, Dikshit H. Cost variation analysis of antimalarial drugs available in India. Int J Rese in Med Sci. 2017 Aug 26;5(9):4051-4.

Cite this article as: Chandra A, Kumar M, Kumar L, Dikshit H. Cost variation analysis of proton pump inhibitors available in Indian market. Int J Basic Clin Pharmacol 2018;7:1626-9.