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Analysis of Outcomes of Proton Pump Inhibitors and H2 Receptors Antagonist

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Abstract: ***In now days proton pump inhibitors are prescribing more and more by Indian physicians not only in pepticulcer, 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 Proton pump inhibitors (PPI) are prescribing more and more by Indian physician and surgeons. 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 associate with decreased adherence to prescription medication. Hence this study was done to assess the outcomes of proton pump inhibitors [PPI] drugs and H2 receptor antagonist. Our other objectives were to assess therapeutic appropriateness with standard guideline, ADR &Drug Interactions related to PPI &H2 receptor antagonist.***

Keywords: PPI, Appropriateness Use, H2 Receptor Antagonist

1. Introductions

H2–receptor antagonists like Ranitidine, which is the first-choice H2–receptor antagonist in most patients, has fewer side effects than cimetidine and is less likely to cause interactions with renal or hepatic impairment, concurrent multiple therapy and those on high doses for hypersecratory states. Ranitidine is the recommended injectable H2-receptor antagonist. Cimetidine is effective in treating gastric and duodenal ulcers and will also relieve peptic esophagitis. It inhibits drug metabolism and so should be avoided in patients stabilized on Warfarin, Phenytoin, Theophylline and Aminophylline. Proton pump inhibitors (PPIs) like Omeprazole, Lansoprazole and Pantoprazole, produce profound gastric acid suppression, and are the most effective treatment for gastro –esophageal reflux disease. They are effective short term treatments for gastric and duodenal ulcers. They may achieve a faster healing rate than H2-receptor antagonists, but the relapse rate is similar. PPIs are also used in combination with antibacterial for Helicobacter pylori eradication. Following an initial short healing course of full dose PPI, the majority of patients can stop treatment or should be maintained on the lowest possible dose to control symptoms or taken on demand in response to symptoms. Maintenance therapy with PPIs may be indicated for patients with complications of reflux disease such as erosive ulceration, structuring esophagitis, Barrett's esophagus, Zollinger-Ellison syndrome and largyngopharyngeal reflux or in the prophylaxis of NSAIDs induced peptic ulceration and may require longer treatment with full or high dose PPI. PPIs are generally well tolerated. The most common adverse reactions seen in adults are flatulence, headache, diarrhea, nausea, abdominal pain, and vomiting. The use of PPIs has also been associated with drug interactions, fractures, hypomagnesemia, and Clostridium difficile-associated diarrhea (CDAD). Clinically significant drug interactions with PPIs are rare. Chronic acid suppression can minimize the effectiveness of any medication requiring an acidic environment for absorption. Commonly prescribed medications affected by acid suppression are ampicillin esters, digoxin, atazanavir, ketoconazole, and iron salts. There is also risk of drug interactions between PPIs and other medications that are metabolized via the cytochrome P450 system. While specific interactions are not well documented, there is substantial evidence regarding an interaction between clopidogrel and omeprazole.

2. Study Design

This study is a hospital based prospective and observational study conducted IGIMS Patna, India, (April 2018 to March 2019) Study population The study was conducted in the Department of Surgery ward, Medicine ward, Obs and Gynae ward ICU Sampling method. The study method involves selection of patients based on the inclusion and exclusion criteria.

Inclusion Criteria
All patients admitted to the Surgery ward, Medicine ward, Obs and Gynae ward, ICU, only adults of either sex including Pregnant/lactating mothers were taken.

Exclusion Criteria
All pediatric patients

3. Methods

1) Price in Indian rupees (INR) of proton pump inhibitors manufactured by different pharmaceutical companies in India, in the same strength India, obtained from Current index of medical specialists (CIMS) January to April 2019 edition and from DrugToday Oct to Dec 2018, 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 table 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: Percentage cost variation = (Maximum cost-Minimum cost/minimum cost) x 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 Injectables, 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.

4. Results

Appropriateness of PPI Based on 5 parameters and criteria, a medicine or medicine combination could have a score of minimum 0 to a maximum of 10 in the appropriateness scale. After assigning score to each medicine of a prescription with either 0 (inappropriate) or 2 (most appropriate), an average score of appropriateness for medicines in a prescription was obtained by dividing the total score of all medicines by number of medicines in that particular prescription. Then, the prescriptions were allotted to following 3 categories Appropriateness of H2 Blockers Based on 5 parameters and criteria, a medicine or medicine combination could have a score of minimum 0 to a maximum of 10 in the appropriateness scale. After assigning score to each medicine of a prescription with either 0 (inappropriate) or 2 (most appropriate), an average score of appropriateness for medicines in a prescription was obtained by dividing the total score of all medicines by number of medicines in that particular prescription. Then, the prescriptions were allotted to following 3 categories.

5. Discussion

Although the use of PPIs has increased significantly over a period of time in Europe and North America, this study shows that the overall use of PPIs (e.g., pantoprazole), is higher than that of H2RAs (such as ranitidine) at least among our patients. The proportion of elderly patients was higher in this study because they harbor serious co-morbid illnesses that bring them to the hospital and require admission for longer periods. A study conducted for over one year in a single hospital in showed that only 22.5% of all outpatient prescriptions of pantoprazole had a proper indication. A recent study revealed that 22% of hospitalized patients had received SUP in a non ICU setting, out of which 54% were discharged and given ASDs without proper indication, . Similarly, studies published in Europe and Ireland showed that 51% and 57% of their patients respectively, were given PPIs improperly. Maclaren et al. had illustrated in their study that even after implementation of intravenous PPI guidelines, prescribing practices for SUP did not show any improvement. Most of the patients were on PPI (omeprazole). This is comparable to what had been reported by Daley et al. in their study where 63.9% of ICU clinicians chose an H2RA as their firstline drug while 23% chose PPIs, when asked for their preferred choice between H2RAs and PPIs. From the clinicians who chose PPIs, about 64.7% used them when H2RAs failed initially. The frequency of prescribing pantoprazole was found to be higher in patients with an existing risk factor and was mostly recommended by physicians. The reason was that they had the highest number of patients, most of them elderly who were on aspirin or anticoagulants for either stroke prevention or cardiac ischemia. In the surgery department, most prescriptions were issued by orthopedic surgeons, followed by general surgeons. Their patients had major surgeries and were either on NSAIDs for pain management, anticoagulants for deep vein thrombosis prophylaxis or on both drugs. Our study reveals that there is significant evidence that ASDs are not being misused. 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.14-16 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.17 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.17 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).18 Hence, it was need to draw attention to the prices of various drug formulation brands available to reduce the cost of therapy.19 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.20 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.

6. Conclusion

PPI prescribing without documented valid indications is highly prevalent in our practice. Approaches to tackle this medication safety issue could include documented physician review of PPI indications at each patient contact. We further recommend interventions such as pharmacist advice being documented in electronic medication records, and flagging medications that lack appropriate indications. Continuous medical education with focus on rational drug use and evidence based medicine should form part of the program of the hospital. They should be involved in collection and presentation of prescribing data as part of clinical audit ad also education of patients/caretakers.. Also hospitals should consider developing controlled policies like formulary restriction, stop-orders for specific indications, and automatic switch-order to oral PPI if patient is receiving oral feeding. Educating physicians and surgeons through newsletter and electronic email alert detailing appropriate indications (evidenced-base) of IV PPI can also reduce the misuses of IV PPI. PPI can constitute a type of policy in its own right, with its own frameworks and innovation-related goals and even its own specialized agencies. However, PPI can also be understood as a policy instrument that seeks to uplift the capabilities within procuring bodies, and improve the framework conditions to enable the general public procurement practice to ask for and buy more innovations. High-dose, chronic PPI use is prevalent, despite a high degree of comorbidity in the target population and significant treatment failures. There are opportunities for substantial cost savings in relation to PPI prescribing if implementation of clinical guidelines in terms of generic substitution and step down therapy is implemented on a national basis. 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.

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