A comparative survey study on current prescribing trends in proton pump inhibitors and H2 receptor antagonists among practitioners in private set up and tertiary care teaching rural hospital

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ABSTRACT

Acid-peptic disorders affect 60% population during the course of a year. Approximately 40% of adults in the USA have complaints of heartburn every year. The prevalence rate of GERD in developed nations is tightly linked with age, with adults aged 60 to 70 being the most commonly affected. As proton pump inhibitors and H2 receptor antagonists are by far the most commonly used form of acid suppression, this survey study was planned to gather detailed information about these agents from practitioners who frequently prescribe these medications.

MATERIAL AND METHOD: A total of 50 practitioners were included in the study; 25 from private set up and 25 from a tertiary care teaching rural hospital. The feedback questionnaire that contained various questions, related to the drugs used in acid peptic disorders, were distributed to find out the various indications for which consultants prescribed them, the frequency of use, choice of preparation, feedback on their use and any adverse effects that were noticed. Descriptive analysis was performed on all the variables to obtain the frequency and percentage followed by application chi-square test in order to find the significance and p< 0.05 were considered as significant.

RESULTS: Most common indications for use antiulcer agents are gastroesophageal reflux diseases (76%) and peptic ulcer (22%). Proton pump inhibitors are preferred over H2 receptor antagonists. Parenteral preparations are used in an emergency. Ranitidine is administered intravenously more commonly than pantoprazole.

Keywords: Proton pump inhibitors, H2 Receptor antagonists, Acid peptic disorders.

1. INTRODUCTION

Studies conducted to analyze the various pattern of drug use have shown that clinician overprescribe drug(s), practice polypharmacy and use of branded expensive drugs are the most common problems of drug use pattern. Improving pattern of drug use and methodology of prescription would improve financial and public health standards.

The variation in the pattern of drug use is largely a contribution by the P (Personal) – drug concept. The P drug varies between different countries, amongst physician of the same country or region. This is due to the difference in personal choices, essential medicine list, availability of the drug, cost of the drug, different national formulary standards and medical practices. The concept of P drug has universal acceptability.

Acid-peptic disorders affect 60% population during the course of a year. Approximately 40% of adults in the USA have complaints of heartburn every year. The incidence of GERD in the US is 3-7% and prevalence is 3%; thus making GERD one the most common gastrointestinal (GI) disorders with resultant costs of more than US$10 billion per year. Peptic ulcer disease (PUD) also affects several million people in the USA every year. The information pertaining to the burden of acid peptic disorders in Asia is limited as compared to other western countries. In India incidence of GERD in pregnancy is 30%-50% and prevalence is 80%.
Based on symptom surveys, recurrent vomiting is reported in two-thirds of 4-month-old infants but is present in only 5% to 10% of infants by 1 year of age. Beyond infancy, up to one-fourth of children and adolescents have recurrent abdominal pain, whereas only 5% report heartburn or epigastric pain [7].

The prevalence rate of GERD in developed nations is tightly linked with age, with adults aged 60 to 70 being the most commonly affected. There are no data that support sex predominance with regard to GERD [8].

The established indications of use anti ulcer agents are acid-peptic disorders mainly comprising of peptic ulcer disease, Gastro esophageal reflux disease (GERD), as a pre-anesthetic medication, pre-chemotherapy medication and also in other various causes leading gastric mucosal injury such as stress, post-burns, and trauma. Although most acid-peptic cases follow a relatively benign course, they can be associated with severe erosive esophagitis; stricture formation and Barrett's metaplasia, in turn, is associated with a small but significant risk of adenocarcinoma. So, appropriate treatment at an early stage is of primary concern [9].

According to guidelines of The American College of Gastroenterology (ACG), management of acid-peptic disorders comprises of various treatment options, including lifestyle modification, patient-directed therapy, acid suppression, use of promotility agents, maintenance therapy and surgery [10].

The cornerstone of management of acid-peptic disorders is the administration of agents that decrease gastric acid secretion, thereby decreasing esophageal acid exposure. Histamine - 2 receptor antagonists (H2:RAs) and proton pump inhibitors are in standard divided doses achieves complete symptom relief in approximately 60% of patients and heals esophagitis in about 50% of patients [11]. In 33 randomized trials that included more than 3,000 patients with erosive esophagitis, more patients experienced symptom relief and healing of esophagitis with PPI therapy (approximately 80 percent) than with H2:RA therapy (50 to 60 percent) [10].

As proton pump inhibitors and H2 receptor antagonists are by far the most commonly used form of acid suppression, this survey study was planned to gather detailed information about these agents from practitioners who frequently prescribe these medications. This study gives an insight into the education of practitioners in the future.

2. MATERIAL AND METHOD

A prospective survey study was conducted with an aim to compare the pattern of use of the proton pump inhibitors and H2 receptor blockers among private practitioners and tertiary care teaching rural hospital. The study was initiated after approval by the institutional ethics committee of Sumandeep Vidyapeeth.

A total of 50 practitioners were included in the study; 25 from private set up and 25 from the tertiary care teaching rural hospital. The feedback questionnaire that contained various questions, related to the drugs used in acid peptic disorders, were distributed to find out the various indications for which consultants prescribed them, the frequency of use, choice of preparation, feedback on their use and any adverse effects that were noticed.

The study was initiated after approval by the institutional ethics committee of Sumandeep Vidyapeeth.

3. STATISTICAL ANALYSIS

All data obtained were analyzed using the Microsoft Excel software. Descriptive analysis was performed on all the variables to obtain the frequency and percentage followed by application chi-square test in order to find the significance and p< 0.05 were considered as significant.

4. RESULTS

Indications: As shown in table-1 most common indications for use antiulcer agents are gastroesophageal reflux diseases (76%) and peptic ulcer(22%). As depicted in table -2, for the treatment of GERD and peptic ulcer, proton pump inhibitors are preferred over H2 receptor antagonists.

### Table-1: Most common reasons for using antiulcer agents

<table>
<thead>
<tr>
<th>Indications</th>
<th>Private set up(%)</th>
<th>TRH</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>GERD</td>
<td>18(72%)</td>
<td>20(80%)</td>
<td>38(76%)</td>
</tr>
<tr>
<td>Peptic Ulcer</td>
<td>6(24%)</td>
<td>5(20%)</td>
<td>11(22%)</td>
</tr>
<tr>
<td>Non-ulcer dyspepsia</td>
<td>1(4%)</td>
<td>0</td>
<td>1(2%)</td>
</tr>
</tbody>
</table>

### Table-2: A Preferred group of the drug for each indication

<table>
<thead>
<tr>
<th>Indication</th>
<th>Proton pump inhibitors</th>
<th>H2 receptor antagonists</th>
</tr>
</thead>
<tbody>
<tr>
<td>GERD</td>
<td>49(98%)</td>
<td>1(2%)</td>
</tr>
<tr>
<td>Peptic Ulcer</td>
<td>45(90%)</td>
<td>5(10%)</td>
</tr>
<tr>
<td>Non-ulcer dyspepsia</td>
<td>40(80%)</td>
<td>10(20%)</td>
</tr>
</tbody>
</table>
Preferred group: It was observed that out of 25 private practitioners 23 doctors prefer to use proton pump inhibitors; only 2 doctors prefer H2 receptor antagonists. But in tertiary care teaching, rural hospital 19 doctors prefer to use proton pump inhibitors and 6 doctors prefer H2 receptor antagonists. All practitioners prescribe single and combined preparations; antiemetics are most commonly prescribed among combined preparations. H2 receptor antagonists are preferred in pediatric age group because of availability of liquid formulation of these drugs. Both groups of drugs can be safely used in pregnancy. When we look into the drug preference in emergency conditions, in pediatric age group H2 receptor antagonists and in adults proton pump inhibitors are prescribed.

Dose and dosage form: In emergency, parenteral preparations are used. Ranitidine is administered intravenously either as an intermittent bolus dose of 50 mg every 6-8 hours or as a continuous infusion in a dose of 6.25-12.5 mg/hour. Pantoprazole is administered intravenously in a dose of 40 mg once daily till the patient is able to take oral medications. In pediatric patients, lansoprazole and omeprazole are used in a dose of 1-2 mg/kg/day and ranitidine is used as 2 teaspoonfuls of 10 ml of syrup twice daily or 4 teaspoonfuls of 20 ml of syrup at bedtime.

Cost-effectiveness: It has been observed that out of 50 practitioners, 45 practitioners consider cost and quality of drugs.

Adverse drug reaction: No major adverse drug reactions.

5. DISCUSSION

Acid-peptic disorders are the commonest indications for proton pump inhibitors and H2 receptor antagonists. Ample data from clinical trials and observational experience have confirmed the utility of these agents in the treatment of acid peptic diseases, with differential efficacy and safety characteristics.

Proton pump inhibitors are more potent inhibitors of acid secretion than H2 receptor antagonists in that they irreversibly bind to H+, K+-ATPase in the gastric parietal cell canaliculus and inhibit acid secretion. Acid secretion resumes only after new pump molecules are synthesized, providing a prolonged (up to 24- to 48-hour) suppression of acid secretion, despite the much shorter plasma half-lives (0.5-2 hours) of the parent compounds. Because they block the final step in acid production, the proton pump inhibitors are effective in acid suppression regardless of other stimulating factors like histamine, gastrin, and acetycholine. The H2 receptor antagonists inhibit acid production by reversibly competing with histamine for binding to H2 receptors on the basolateral membrane of parietal cells. Duration of action of H2 receptor antagonists is 10-12 hours, which facilitates twice a day administration. Whereas proton pump inhibitors have prolonged duration of action of 24 to 48hrs, once daily dose is preferred [9,12].

Proton pump inhibitors are more effective than H2 receptor antagonists in the treatment of acid-peptic disorders. Healing rates after 4 weeks and 8 weeks of therapy with proton pump inhibitors are ~ 80% and 90%, respectively; the corresponding healing rates with H2 receptor antagonists are 50% and 75%, respectively [9]. In a Double-blind multicentre trial comparing omeprazole and ranitidine, a significantly higher rate of healing of peptic ulcer was demonstrated with omeprazole at 2 weeks and 4 weeks [13]. The other randomized controlled trial also demonstrated that lansoprazole was more effective than H2-receptor antagonists in patients with Zollinger-Ellison syndrome [14]. The other randomized, double-blind, three-dosing regimens, three-period crossover study also proved that gastric acid suppression on omeprazole superior to famotidine [15].

H2 receptor antagonists are considered the drugs of choice for children because of well established pediatric doses and availability of medications in liquid forms. Although proton pump inhibitors are superior in the healing of esophagitis in children, their use is restricted in patients who require complete acid suppression e.g. infants with chronic respiratory disease or neurologic disabilities [16, 17].

H2 receptor antagonists and proton pump inhibitors have been labeled as category B drugs; animal studies are proved to be teratogenic but human clinical trials are not still conclusive [12]. The various crossover and case-controlled studies have been concluded a statistically significant association between use of acid-suppressive drugs in pregnancy and the risk of childhood asthma [18].

The Proton pump inhibitors have been demonstrated to be safe and well-tolerated drugs but short-term adverse effects like a headache, dizziness, diarrhea, fatigue, rashes and abdominal pain have been reported in 5% of the patients taking proton pump inhibitors. Chronic therapy of proton pump inhibitors carries an increased risk of bacterial enteritis due to decreased gastric acidity allowing colonization of ingested pathogens and also infection with clostridium difficile [19]. Long-term use of proton pump inhibitors has also been associated with increased risk of hip fractures, and community-acquired pneumonia [20].

The H2 receptor antagonists generally are well tolerated, with a low (<3%) incidence of adverse effects. Side effects include diarrhea, headache, drowsiness, fatigue, muscular pain, and constipation. Less common side effects include confusion, delirium, hallucinations, slurred speech, and headaches. Long-term use of cimetidine at high doses decreases testosterone binding to the androgen receptor and inhibits a CYP that hydroxylates estradiol. Clinically, these effects can cause galactorrhea in women and gynecomastia, reduced sperm count, and impotence in men [9,12].

In spite of the above-mentioned concerns with use of H2 receptor antagonists and proton pump inhibitors, these drugs have become one of the most commonly prescribed medications worldwide. Some reports suggest that up to 60% of patients suffering from dyspepsia are on these drugs without proper indication [21]. The concern regarding overprescribing of these agents are emerging. The incidence of improper use of PPIs varies from 40-70% in various studies [22].
Since these agents are highly effective in the treatment of acid-peptic disorders, they are available as Over the Counter (OTC) in India. Due to lack of drug dispensing rules, Over the Counter (OTC) drugs are often misused. It has been observed the use of OTC drug is highest amongst medical students and nursing staff. In a survey study on OTC drugs, highly significant use of H2 receptor antagonists and proton pump inhibitors was found among medical students compared to nursing and clerical staff [23].

6. CONCLUSION
We conclude that proton pump inhibitors are preferred over H2 receptor antagonists in adults but in the pediatric age group of patients, H2 receptor antagonists are preferred by practitioners.

7. LIMITATIONS
As it was the survey study conducted among 50 practitioners it may not represent the behavior of all practitioners in general. Future studies can be carried out in different parts of India, including urban and rural areas.

8. DECLARATION
It was a self-funded study conducted after obtaining Institutional Ethical Committee approval. Competing interest none.

9. ACKNOWLEDGEMENTS
We would like to express our gratitude to all the respondents for spending their valuable time to answer our questionnaire that helped us to successfully complete our study. Authors are also thankful to the institutional ethical committee of Sumanddeep Vidyapeeth that permitted to conduct such a survey study.

10. REFERENCES
[12] [www.drugs@fda.com accessed on 19/4/14.