ejpmr, 2021,8(9), 744-746

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 2394-3211

EJPMR

OVERUSE OF PROTON PUMP INHIBITORS IN HOSPITAL SETTING: A CRITICAL REVIEW

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Article Received on 23/07/2021 **Article Revised on 12/08/2021** **Article Accepted on 02/09/2021**

ABSTRACT

PPIs are widely prescribed to treat acid-related diseases such as gastritis, peptic ulcer diseases (PUD), gastroesophageal reflux disease (GERD), gastrointestinal (GI) bleeding and Helicobacter pylori (H. pylori) infection and are used as gastro-protective drugs with other medications including non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids and anticoagulants, especially in elderly patients. Although, PPIs demonstrate an excellent safety profile, long-term and high dose use of PPI have alarming adverse effects. Inappropriate PPI use and the associated risks have dramatically increased over the last few decades. Also, several research studies have demonstrated that the overutilization of these agents has led to significant increases in hospital-related expenditures and adverse effects. Thus, it is essential to determine the overuse of PPI, so that an effective and rational follow-up plan can be implemented.

KEYWORDS: PPI, overutilization, adverse effects, expenditure.

INTRODUCTION

The resolution for management of various acid-related diseases set about with the discovery of proton pump inhibitors (PPIs) more than 25 years ago and has bring down the need for surgery.[1] The alleviation of acid-related diseases is intensified with suppression of gastric acid.[2] High prevalence of acid‑related diseases, as well as the potency, good tolerance, and acceptable costs escalate the use of PPI in hospitals and outpatient clinics.[3]

UNDERSTANDING PPI

PPIs are the most popular agents used worldwide for gastric acid inhibition.[4] They act by irreversibly blocking the hydrogen/potassium adenosine triphosphatase enzyme system (the H^+/K^+-ATPase, the gastric proton pump) of gastric parietal cells, inhibiting gastric acid secretion.

Pantoprazole, omeprazole, rabeprazole, lansoprazole, ilaprazole, esomeprazole, dexrabeprazole, dexlansoprazole are the PPIs available in the Indian market for clinical use. Although these agents have similar pharmacological actions as they share same molecular structure, there are slight differences among PPIs relating to their pharmacokinetic properties, metabolism, and Food and Drug Administration (FDA)-approved clinical indications.[5]

PPIs are majorly used for the treatment of gastro-esophageal reflux disease (GERD), in combination with antibiotics for eradication of *Helicobacter pylori* infection, healing and prophylaxis of non-steroidal anti-inflammatory drug-associated gastric ulcers, treatment of *H.pylori*-negative peptic ulcers and control of several acid hypersecretory conditions like Zollinger-Ellison syndrome.[1]

Short-term PPI therapy have been demonstrated to be safe, effective and well tolerated, while their long-term use is a global issue. The short term adverse effects reported in the patients taking proton pump inhibitors includes: headache, dizziness, diarrhoea, fatigue, rashes and abdominal pain. Chronic therapy of PPIs carries an increased risk of bacterial enteritis, hip fractures, and community acquired pneumonia, also infection with clostridium difficile.[6]

CLINICAL RESEARCH SUPPORTING OVERUSE

In hospital settings, the excessive and inappropriate use of PPIs has pointed in various research studies that may lead to significant increases in hospital-related expenditures, patient-related adverse effects, and drug-drug interactions.[7]

In a study conducted to determine trends in PPI use for 7 years in U.S. ambulatory settings, the majority of visits had no documented indication in all years, 62.92% of

patients had no indications for their use at the end of their study period.[8]

A questionnaire based observational study conducted by Muhammed Haroon et al revealed that 45% of prescriptions with PPI has no documentation of valid indications. In 20% of the studied prescriptions, NSAIDs/aspirin induced ulcer was the sole reason for PPI use. Also, it was noted that only 39% of these patients were aware of the reason for being prescribed a PPI. 65% of PPI users were on long-term high doses of PPI beyond the recommended durations, and puts patients at higher risk of complications. They suggested that a clear documented reasons for being on PPI can avoid inappropriate prescriptions.[9]

A survey of 45 hospitals in China conducted by Jie Ying et al showed that about 32.6%-56.8% of PPI prescriptions were considered as off-label medications. Their data showed that some PPI users had underlying risky comorbidities such as renal diseases (2.9%) and osteoporosis (2%). The DUI data showed that injectable rabeprazole, lansoprazole and both forms of pantoprazole, esomeprazole, and omeprazole were used in excessive doses.[10]

Chia C et al evaluated the appropriateness of PPI and has noted that on a randomly selected day 54.1% of PPI prescriptions were without indications recommended by the FDA.[11]

A recent study provides evidence that PPI is commonly prescribed inappropriately in the general population and that this trend is increasing. Multimorbidity and drugs with bleeding risks were found to be the strong determinants of potentially inappropriate PPI prescriptions (PIPPI). They recommended that addressing inappropriate PPI prescriptions could reduce polypharmacy and improve patient safety.[12]

THE RISKS OF OVERUSE

Adverse Events

There are emerging potential adverse effects or risks induced by PPI abuse or in conjunction with other drugs.[10] PPI‐induced inhibition of hydrochloric acid secretion causes iatrogenic hypochlorhydria and hypergastrinemia, resulting in parietal cell hypertrophy and enterochromaffin‐like cell hyperplasia, exposing patients to rebound hydrochloric acid hypersecretion.[3] The use of PPI is confederated to precarious for intestinal dysbiosis, specific infections including pneumonia and *C. difficile* infection (CDI), osteoporosis, nutritional deficiencies.[13]

In short-term treatment, PPIs have exceptional clinically relevant immediate adverse effects. The most frequent complaint found in clinical trial is headache in about 5.5% of subjects.[14] Community-acquired pneumonia is associated with the current and short-term use (<30 days) of PPIs, particularly at high doses. Furthermore, few literatures support the evidence for PPI associated hospital-acquired pneumonia.[15] and [16]

The analysis of a database of over 4000 patients by Cesare Tosetti et al highlight the fact that long-term prescription of PPI drugs is found in 15% of the population.[17] FDA has issued several warnings related to long-term use of PPIs in recent years.[7] PPIs are also responsible for some serious adverse reactions like hepatitis (lansoprazole, omeprazole), interstitial nephritis (omeprazole), visual disturbances quickly following intravenous infusion (omeprazole, pantoprazole) are rarely reported.[6]

Economic Impact

There are innumerable economic and financial out-turns associated with the overuse of PPIs, with costs shared between patients and insurance providers. Onuma Sattayalertyanyong et al conducted a prospective cross-sectional study in which the authors concluded that the cost of inappropriate and excessive PPI prescription needs to be controlled as the estimated cost of such use among inpatients was found to be $118,659 per year.[18] A clinical investigation in a tertiary care hospital found that PPI is used for low-risk gastrointestinal hemorrhage and such inappropriate use on inpatient costs $12,272.[19] In a prospective observational study on pattern of intravenous PPI use estimated direct cost of inappropriate use during a 4 month period was found to be $11,000. Another clinical study determined that an annual project cost savings maybe achievable if efforts were made to limit inappropriate use and selection of appropriate route of administration of PPIs within their hospital by an amount between $26,366 and $35,456.[20]

CONCLUSION

This study provide evidence that one of the most commonly prescribed medication in hospitals is inappropriately prescribed. Addressing inappropriate PPI recommendations could reduce polypharmacy and improve patient safety. A reduction in the rates of overutilization of PPIs in hospital settings should minimize both the risk of potential adverse effects and the health care costs.

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