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A CLINICAL COMPARATIVE OBSERVATIONAL STUDY ON IRRATIONAL USE OF PROTON PUMP INHIBITORS AND H2 RECEPTOR BLOCKERS

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Abstract

Aim : The main aim of the study is to analyse the irrational use of PPIs and H2 Receptors antagonist that is prescribed without detecting any FDA Approved indications and to reduce the pill burden.

Background: The incidence of improper use of PPIs varies from 40-70% in various studies. The prescriptions of proton pump inhibitors (ppis) have raised concern due to possible long-term adverse events caused by them .

Conclusion: Irrational use of H2 receptor antagonists and PPIs increased with advanced age, increase in number of medications, multiple diagnoses and increased length of hospitalization. Effects and interactions were commonly encountered in many cases. Proper Guidelines for physicians and counseling for the patients is required in order to reduce overuse and to prevent long term adverse effects of the drugs.

Keywords: Irrational use, H2 receptor antagonists, Proton pump inhibitors

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INTRODUCTION

In the primary care, proton pump inhibitors (PPIs) are one of the most often given classes of drugs and are regarded as a significant advancement in the treatment of acid-peptic illnesses. Various acid-peptic illnesses, such as gastroesophageal reflux disease, peptic ulcer disease can now be treated more effectively to proton pump inhibitors.[1] Omeprazole, lansoprazole, and rabeprazole, three proton pump inhibitors, seem to be equally effective Histamine type 2 receptor antagonists (H2RAs), which inhibit the histamine receptor on parietal cells in order to cure acid-related illnesses, are one of the two primary types of medications used to treat these conditions and using PPIs, which block the hydrogen pump in the parietal cell directly and without activating any membrane receptors.[2] Guidelines on the use of acid suppressants presumably result from a lack of awareness of the potentially harmful side effects of these medications given their well-documented effectiveness in symptom relief and recovery. Concerns about the usage of PPIs and potential side effects such bone fractures, dementia, cardiac events, renal illness, or infections continue to appear in addition to the economic burden associated with their widespread use.[3] This review's goal is to provide an overview of the potential dangers of using PPI as a tool for decision-making and patient counselling.[4] In actuality, H2RAs provide an inadequate suppression of post-prandial stomach acid output and have a very short (4–8 h) duration of action.

As an outcome, these medications must be taken at least twice daily to effectively reduce acid.

They also discuss the pharmacodynamic phenomena of tolerance, which appears after two weeks of repeated dosing and causes a gradual reduction in acid suppression.[5] Contrarily, PPIs regulate both basal and food-stimulated acid secretions, resulting in a more thorough and prolonged (10–18 h) acid suppression than H2RAs. Tolerance to PPIs has also never been noted.[6] Omeprazole has a short half-life of 30 minutes to an hour in healthy persons and a half-life of roughly 3 hours in hepatic impairment patients.[5][6] Omeprazole preferentially accumulates in parietal cells, where it forms a covalent connection with H+/K+ ATPase, which it irreversibly blocks. As a result, the drug's pharmacological impact lasts significantly longer.[7]

The H2 receptor blockers act by binding to histamine type 2 receptors on the basolateral (antiluminal) surface of gastric parietal cells, interfering with pathways of gastric acid production and secretion. The selective H2 blockers are less potent in inhibiting acid production than the proton pump inhibitors (which block the common, final step in acid secretion) but, nevertheless, suppress 24 hour gastric acid secretion by about 70%.[8] The effect of H2 blockers is largely on basal and nocturnal acid secretion, which is important in peptic ulcer healing.

NONCOMPLIANT PPI PRESCRIPTIONS

PPIs may be violated in hospital and ambulatory care settings, according to several reports.In some hospitals, just 19% of PPI prescriptions are appropriate. Before recommending a proton pump inhibitor, a number of factors should be considered, such as the following: (i) dosages, length of therapy, and clinical justifications for using a PPI, along with an evaluation of the appropriateness of the course of action; (ii) whether the use of H2-receptor antagonists is appropriate prior to recommending a proton pump inhibitor; and (iii) how frequently patients receiving a proton pump inhibitor for gastroesophageal reflux disease.[9]

PPIS AND ITS MECHANISM OF ACTIONS :

Omeprazole

Omeprazole is a selective and irreversible proton pump inhibitor that reduces stomach acid secretion by specifically inhibiting the hydrogen-potassium adenosinetriphosphatase (H+,K+,-ATPase) enzyme system that occupies the secretory surface of parietal cells. Through an exchange with potassium ions, it prevents the ultimate passage of hydrogen ions into the stomach lumen. [10] Omeprazole is referred to as a gastric acid pump inhibitor because the H +, K +-ATPase enzyme system is thought to function as the acid (proton) pump of the stomach mucosa. No of the stimuli, omeprazole suppresses both baseline and induced acid production. Omeprazole has the capacity to inhibit the hepatic cytochrome P450 mixed function oxidase system but lacks anticholinergic or histamine H 2-receptor antagonist characteristics.[11]

Lansoprazole:

It is a substituted benzimidazole derivative that becomes active in the canaliculi of the stomach parietal cell's acidic environment.[12]

Pantoprazole :

Pantoprazole belongs to the class of PPIs known as benzimidazoles. While benzimidazoles have a slower rate of metabolism than the other two families, their blood stream presence is shorter. There H+ The H+/K+ ATP pumps are permanently inhibited by pantoprazole, according to its mode of action. With a drop in the pH of the environment, pantoprazole breaks down more quickly.

It follows that the stomach, which contains the H+/K+ ATP pumps (particularly, within the parietal cells of the stomach lining), would be the ideal location for this drug to act.

This is the conclusive stage in the generation of stomach acid.[13]

As a result, pantoprazole binding to these pumps stops acid results for up to 24 hours. The maximum effect happens between two and six hours following drug administration, with a quick commencement of action.

Additionally, the liver breaks down pantoprazole, primarily by CYP2C19 demethylation and sulfation. It is unknown what significance these metabolites may have.[14]

H2 RECEPTOR BLOCKERS AND ITS MECHANISM OF ACTION :

Ranitidine:

H2-receptors for histamine are competitively inhibited by ranitidine. Gastric parietal cells' ability to temporarily block H2-receptors lowers the volume and concentration of the digestive fluid. Compared to food-stimulated acid secretion, baseline and nocturnal acid secretion are more sensitive to ranitidine's acid-lowering effects. [15]

POTENTIAL ADVERSE EFFECTS OF PPI USE :

Loss of Bone Density and Fracture Risk

Two theories include interfering with the absorption of calcium salts and inhibiting bone remodelling, albeit the precise mechanism through which PPIs could cause bone fracture is unknown. According to the first theory, hypochlorhydria may prevent the absorption of calcium salts, which could result in secondary hyperparathyroidism and subsequent bone resorption to maintain calcium levels. According to the second theory, osteoclasts and a bone-specific proton pump are directly inhibited, disrupting bone remodelling and increasing bone fragility without changing bone mineral density.[16]

Iron Deficiency

Because dietary iron shifts from its ferric to ferrous form by stomach acid, malabsorption may result from acid suppression caused by PPIs or H2RA. If neglected, iron deficiency can result in problems including anaemia and asthenia.[17]

Vitamin B12 Deficiency

By preventing the cleavage of vitamin B12 from food proteins, PPIs and H2RAs that decrease stomach acid can cause vitamin B12 malabsorption. Lack of vitamin B12 can result in anaemia or neurological damage if left untreated.[18]

Blood system disorders:

Disorders of the blood system have been documented, including reversible occurrences of anaemia, leukopenia, granulocytopenia, and thrombocytopenia as well as more serious causes of agranulocytosis, pancytopenia, or neutropenia. The long-term effects of marrow hypoplasia or marrow aplasia, aplastic anaemia, and acquired immune hemolytic anaemia are possible.[16][17][18]

Cardiac disorders:

Arrhythmias, such as tachycardia, sinus bradycardia, asystole, and extrasystole, can cause cardiac problems. There is a chance for premature ventricular beats and atrioventricular block with sinus pauses. Additionally, some people may develop heart palpitations and an increase in blood pressure; these side effects usually go away after the medicine is stopped.[16][17][18]

Vision and eye disorders:

Blurred vision and changes in intraocular pressure are possible, but these effects usually go away once the person stops taking the medicine.[19]

POTENTIAL ADVERSE EFFECTS OF H2 RECEPTOR BLOCKERS :

The most common side effects linked to Ranitidine is heartburn and reflux medications are temporary in nature and generally stop when you discontinue use.[20] They may include:

Headache ,

Nausea,

Vomiting,

Diarrhea

PICTORIAL REPRESENTATION OF ADVERSE EFFECTS OF PPI :

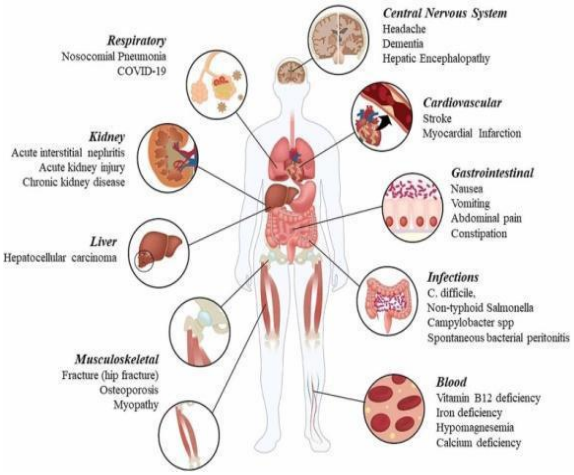

Figure [1][30]

IMPACT OF IRRATIONAL USE OF PPIS :

The effect of pharmaceutical interventions on the prudent use of PPIs was examined in a study. The findings show that medication therapy interventions enhanced the proportion of patients with logical justification, increased the accuracy rate of administration method, and decreased mean PPI prices, mean total drug costs, mean hospitalisation expenses, and mean therapy duration over a six-month period.[21] Pharmaceutical interventions were able to better promote the prudent

use of PPIs by participating in pharmacy rounds with doctors and implementing educational group activities throughout the process of pharmaceutical care. Irrational prescribing was pushed by doctors who wanted to profit from drug purchases.

According to various therapeutic situations, research have shown that patients utilise PPIs at a high rate of irrational usage, ranging from 25% to 67%.[22] In their investigation, low-risk patients' prevention of stress ulcers and unnecessary gastro-protection, including patients undergoing various routine surgical operations, were the leading unreasonable reasons of PPIs in the control group. We therefore conducted a pre-to-post intervention research to assess the influence of pharmaceutical interventions on the sensible use of PPIs. Our findings demonstrated a notable rise in the number of patients with valid justifications recruited in the pharmacological intervention group.[23]

IMPACT OF IRRATIONAL USE OF H2 RECEPTOR BLOCKERS :

One of the top brands of antacids, Rantac, has the active component ranitidine, which has been the subject of debate for the past few years.[24]Due to worries about an impurity known as NDMA, which can cause cancer, certain Ranitidine formulations have been taken off the market in the US and Europe. However, the Indian regulator has not adopted any unfavourable positions or formulations. The drug ranitidine is still sold in the nation. Ranitidine has a multitude of side effects, particularly when taken at higher amounts than recommended by a doctor.

These reported side effects were observed during clinical trials, post-marketing surveillance, and patient monitoring despite the fact that a causative connection has not always been established.[25] Without medical intervention, headaches, aches and pains, nausea, vertigo, and other side symptoms swiftly go away. However, allergic responses are also conceivable. Ranitidine can cause anaphylactic shock if taken in a single dose.[26]

DISCUSSION :

Proton pump inhibitors (PPIs) may not be the best choice in situations that do not match the criteria for their use, according to mounting concerns. Both in hospitals and general practise, PPIs are still being prescribed irrationally.

It is crucial to assess the benefits and cost effectiveness of these medications against their negative effects, particularly for the older population where polypharmacy is still a major concern.[27]Studies by Christopher Tze Wei Chia in 2014 on the inappropriate use of proton pump inhibitors in a local setting and a study on the imprudent gastro-protective approach in the majority of specialist clinics of a tertiary hospital by Dr. Priti Dhande in the year 2013 all come to the conclusion that the elderly are more likely to use medication inappropriately as they get older, as there are more medications, diagnoses, and hospital stays, and this is true regardless of age. This point-prevalence study sought to examine the frequency, indications, and appropriateness of PPI use in hospitalised patients on a randomly selected day. Effects and interactions are frequently seen in numerous situations.[28] Without a thorough assessment of the need for therapy, acid suppression medications are started and sustained for extended periods of time.In order to minimise overuse and prevent long-term negative consequences of these drugs, doctors must follow the proper guidelines and provide patient counselling.

CONCLUSION :

In our execution, PPI prescriptions without verified, valid indications are extremely common. It should be made feasible to

address this pharmaceutical safety risk by having a physician analyse PPI indications in writing at each patient interaction. Additionally, we advise taking actions like reporting medications that don't have the right indications and documenting chemist recommendations in electronic medication records. With advancing age, a rise in the number of prescriptions, diagnoses, and length of hospitalisation, older patients are more likely to use medications irrationally. Effects and interactions are frequently seen in a variety of situations. Without a thorough assessment of the need for therapy, patients are started on acid-suppressing medications and kept on them for extended periods of time. In order to minimise irrational use+ and prevent long-term negative consequences of these drugs, doctors must follow the proper guidelines and provide patients with counselling. A better patient outcome will be achieved at a lesser cost if clinicians are more aware of the proper PPI prescription.

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CONFLICT OF INTEREST

There is no conflict of interest between the authors.

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