Review Article

Drug Interaction, its Types, and Management: Proton Pump Inhibitors and their Interactions with Other Drugs

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ABSTRACT

Drug-drug interactions have these days attracted a lot of interest from the regulatory, scientific, and fitness care sectors everywhere in the world. Serious remedy interactions are more likely to include capsules with a restricted healing window or low healing index. It's miles the pharmacist's responsibility, in conjunction with that of the prescriber, to ensure that patients are knowledgeable of the possibility of adverse outcomes and what to do if they do. Due to their in-depth scientific knowledge, pharmacists can link sufferers' surprising signs to the ability to face the consequences of their remedy. Worldwide, people depend on drugs to prevent, treat, or mitigate a growing number of ailments. Drugs can have both positive and negative effects. Therapy's objective is to increase positive impacts while attempting to reduce the negative consequences. Each prescription medicine has a ratio of risk to reward. If using the medication has beneficial when the potential for side effects is greater than the danger, then the therapy is appropriate. This risk-benefit ratio might alter if you take one or more medicines that interact with one another. Due to an elevated risk from a medication interaction, a pharmacological therapy that was formerly safe and suitable may now be improper. Studies have revealed that the danger of such usage for the patient significantly rises when more than four medications are being delivered together.

Keywords: Drug-drug interactions, pharmacists, drugs.

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INTRODUCTION

In recent years, the regulatory, scientific, and healthcare communities have paid a lot of attention to the issue of drug-drug interactions (DDIs)[1]. Every year, a sizable number of new pharmaceuticals are released, and reports of novel drug interactions are rising. Therefore, doctors can no longer rely solely on recollection to steer clear of probable medication interactions.

The drugs most likely to cause issues with interactions are those with a narrow therapeutic index, steep dose-response curve, rapid first-pass metabolism (drug loss when it first goes through the liver), a tiny gap between therapeutic dosage, and hazardous doses a single, impermeable elimination pathway.[2]

The absorption, distribution, metabolism, excretion, or actual clinical action of the object medicine is altered by precipitant drugs. Common precipitant medications administered in primary care settings include NSAIDs and antibiotics. Serious drug interactions are more likely to include medications with a limited therapeutic window or low therapeutic index. Serotonin syndrome is a potentially fatal condition characterized by increased serotoninergic activity, which is frequently brought on by medication interactions.[3] Many additional substances operate as precipitants, some as objects, and others as both.

Types of drug interactions:

A drug interaction is described as concomitantly administered medications that interfere with each other's efficacy or safety profile. Usually, the object drug is the drug that is tormented by the interaction, while the Precipitant drug is the medication that reasons the interaction. Similarly, Drug interactions can be damaged down into two separate organizations: the ones that affect the pharmacokinetic profile of the item drug and those that affect the pharmacodynamic profile of the item drug.

1. **Pharmacokinetic interactions**:

Pharmacokinetic drug interactions are associated with adjustments within the attention of a remedy in body fluids and tissues. Those interactions can occur at any point within the absorption, distribution, metabolism, or elimination of a medicine. Absorption interactions generally occur inside the intestine. The absorption of medicinal drugs with pH-dependent dissolution can be affected by antacids, proton pump inhibitors, and histamine H2-antagonists. This type of interaction can arise with some of the oral cephalosporins. Similarly,

antacids (i.e., calcium carbonate or magnesium oxide) can chelate antibacterials inclusive of tetracyclines or fluoroquinolones in the gastrointestinal (GI) tract, preventing their absorption [4,5]. Any other commonplace absorption Drug interplay takes place whilst antibiotics alter the everyday GI plants and for this reason, have an effect on the metabolism and absorption of medicinal drugs inclusive of warfarin and Oestrogens.

Pharmacokinetic drug interactions may be related to the distribution and Protein binding of medications. Several delivery proteins play a function in the tissue distribution as well as the absorption and excretion of medicines [6]. One of the most studied delivery proteins is P-glycoprotein (PGP). This efflux transporter prevents the absorption of medicinal drugs from that tract. Rifampin is an inducer of PGP that leads to reduced absorption of medications that can be substrates for PGP. Further, PGP and other Shipping proteins are located at some stage in the body and deliver medicines to their websites of movement or elimination. That is a growing field of research where many greater clinically sizable drug interactions are likely to be discovered. Drug interactions concerning protein binding and drug displacement Have to turn out to be less vital clinically because regular-kingdom unbound drug Concentrations frequently redistribute and remain unaltered [7].

Drug metabolism is a website where many pharmacokinetic interactions Evolve. The metabolism of medications is split into stages. Section I metabolism will increase the polarity of medications thru oxidative transformation. Segment I reactions usually go through the CYP40 enzymes in the liver and small gut. Section II reactions in addition boom the polarity of medicinal drugs by conjugating them with endogenous companies which include glucuronides or sulfates. Drug interactions can arise in each segment I and II reaction. The precipitant drug can result in, inhibit, or simply be a substrate for these reactions (desk 1). When the precipitant drug inhibits the enzyme. It can achieve this either competitively or noncompetitively. Competitive inhibition happens while the metabolism of the precipitant drug by the enzyme prevents the metabolism of the item drug. Non-competitive inhibition takes place while the precipitant drug binds to the enzyme without being metabolized and forestalls the metabolism of the object drug. The onset and dissipation of those interactions are speedy. Mainly, isoniazid both competitively and noncompetitively inhibits numerous distinct CYP450 isoenzymes. While Isoniazid inhibits the metabolism of item medicines, their concentrations are almost expanded.

2. **Pharmacodynamic interactions:**

"Pharmacodynamic interactions" are interactions in which substances directly affect one another's effects. Sedatives, for instance, typically potentiate one another. The same is true of alcohol, which may amp up many medications' sleepy effects.

However, when mutually potentiating actions in the same direction are needed, as in the usage of antibiotics or the treatment of pain, a pharmacodynamic interaction is frequently really desirable. When one drug's activity is inhibited by another, the effects of the two drugs are antagonistic. Even barely apparent unwanted effects might potentially increase one another. For instance, QT prolongation may occur if fluoroquinolones are taken with macrolides like erythromycin. Life-threatening hyperkalemia can develop when ACE inhibitors and potassium-sparing diuretics such as amiloride are combined. Below is an illustration of pharmacodynamic interactions involving nonsteroidal anti-inflammatory medications (NSAIDs) [8]

SEVERITY AND SERIOUSNESS OF DRUG INTERACTION

On an arbitrary scale measuring the intensity of the undesirable occurrence, severity is a point. When referring to bad occurrences, the phrases "severe" and "serious" have quite distinct technical meanings. Although they can't be used interchangeably and need to be utilized carefully, they are readily mistaken. If a headache hurts severely, it is considered severe. We can gauge the severity using measures like the "Visual Analog Scale." On the other hand, a headache is rarely considered significant unless it also meets the criteria outlined above.

A significant adverse event, according to the American Food and Drug Administration, is one in which the patient experiences one of the following [9]:

Hospitalization (initial or prolonged)

- Death
- Life-threatening

Disability is defined as a major, ongoing, or permanent alteration, impairment, harm, or disruption of the patient's physical capabilities, quality of life, or body function/structure.

- Congenital anomaly
- Intervention is necessary to avoid lasting impairment or injury

Proton Pump Inhibitors and Its Interactions with Other Drugs:

PPI drugs:

a. Pantoprazole
b. Lansoprazole
c. Omeprazole
d. Esomeprazole
e. Rabeprazole

Table 1: Drug interactions involving PPI:

Sl. No.	Drugs interacting with PPI	Effects
1	Pazopanib	Concurrent use of PAZOPANIB and PROTON PUMP INHIBITORS may result in a reduction in pazopanib bioavailability.
2	Aceclofenac	Aceclofenac may decrease Pantoprazole's excretion rate, which could result in a higher serum level.
3	Acetaminophen	Pantoprazole may decrease Acetaminophen's excretion rate, which could result in a higher serum level.
4	Acetylsalicylic acid	Acetylsalicylic acid may decrease the excretion rate of Pantoprazole which could result in a higher serum level
5	Acyclovir	The excretion of Acyclovir can be decreased when combined with Pantoprazole.
6	Albendazole	The metabolism of Albendazole can be decreased when combined with Pantoprazole
7	Alclofenac	Alclofenac may decrease Pantoprazole's excretion rate, which could result in a higher serum level.
8	Cefazolin	The excretion of Cefazolin can be decreased when combined with Pantoprazole
9	Cefepime	Cefepime may decrease Pantoprazole's excretion rate, which could result in a higher serum level.
10	Cefotaxime	Cefotaxime may decrease Pantoprazole's excretion rate, which could result in a higher serum level.
11	Cetirizine	Pantoprazole may decrease Cetirizine's excretion rate, which could result in a higher serum level.
12	Ciprofloxacin	The metabolism of Pantoprazole can be decreased when combined with Ciprofloxacin.

MANAGEMENT OF DRUG INTERACTION

Most medications provide a list of possible drug interactions in the prescribing material. Numerous interactions might be unimportant because they are uncommon, insignificant, or only happen in certain circumstances. The most concerning drug interactions are those that significantly alter a medication's mechanism of action.

The majority of drug interactions are complicated and unexpected. A recognized interaction might not happen in every person. This can be explained by the fact that several variables impact the probability that a known interaction will take place. These variables include individual variations in their; [10, 11]

Genes, physiology, age, lifestyle factors (diet, exercise), underlying diseases, drug doses, the length of combined therapy, and the relative time of administration of the two substances are all factors that can affect interactions. In some cases, interactions can be avoided by taking two medications at different times. [12]

Speak with your primary care physician or pharmacist before beginning any new prescription or over-the-counter medication. Be careful to let them know if you take any vitamins or other supplements. Read the patient information sheet that was provided to you at the drugstore. Ask your pharmacist for an information sheet if you aren't provided one. Look for the "Drug Interaction Precaution" and any cautions on the prescription labels. Please carefully read these cautions.

Make a list of all the meds, vitamins, and supplements you use, including prescription and over-the-counter. With your pharmacist and all of your healthcare professionals, go through this list. If at all feasible, purchase both prescription drugs and OTC items from the same drugstore. Your pharmacist will be able to provide you with advice on drug interactions and adverse effects since they will have a record of all your prescription medications.

The pharmacist's responsibility in the prevention of medication interactions: It is the pharmacist's responsibility, along with that of the prescriber, to make sure that patients are informed of the possibility of adverse effects and what to do. Because of their in-depth medical expertise, pharmacists can link patients' unexpected symptoms to potential side effects of their medication. Clinical pharmacy procedures also guarantee that adverse drug reactions (ADRs) are kept to a minimum by avoiding medications with possible side effects in sensitive patients. As a result, the pharmacist has a crucial part in ADR prevention, identification, and reporting. [13]

Management of drug also interaction includes completely avoiding the combination: For some medication interactions, the danger is always greater than the benefit, thus it is best to stay away from the combination. Drug classes are frequently varied in terms of drug interactions (as previously mentioned), hence it is frequently possible to choose a non-interacting alternative for either the object drug or the precipitant drug. [14]

Describe the patient risk factors that raise the possibility of a negative outcome: According to published research and the clinical experience of doctors and pharmacists, the majority of patients who take interacting medication combinations do not experience negative side effects. [15] Significant data from published research and both the clinical experience of doctors and pharmacists point to an

increase in the likelihood of statin-induced myopathy as blood statin concentrations rise. Simvastatin should thus not be used more than 20 mg per day in individuals getting verapamil at the same time. [16]

Changing dose intervals to prevent interaction: Giving the object drug at least 2 hours before or 4 hours after the precipitant medicine will help you avoid drug interactions involving binding in the gastrointestinal system. In this manner, the object medication can enter the bloodstream before the precipitant medication does.

Changing the dosage of the target medication: Sometimes, if the dose of the object medicine is changed, it is feasible to administer the two interacting medications safely.

Monitoring for detecting earlier: In certain situations, when it's important to administer medicine combinations that interact, the interaction can be controlled by closely watching for signs of the interaction in the lab or the clinic. This will enable essential dose adjustments or drug discontinuation to be done. [17]

CONCLUSION

Drug interactions can be difficult to manage. We should have a basic understanding of drug interactions because new drugs are frequently brought to the market. It is necessary to frequently check medication regimens for possible drug interactions. When evaluating possible medication interactions, it's important to take into account the consequence of any interference, if it can be corrected, and whether the therapeutic benefit outweighs the danger of the interaction. Drug interactions are frequently not observed clinically because the possible offending agent's course of therapy (such as antibiotics) is brief due to patient characteristics, or because they are not recognized. New knowledge is produced frequently, particularly in the field of drug metabolism. Our understanding of DDIs has greatly improved over the past few years, especially in the area of the molecular mechanisms by which drugs interact. Our capacity to effectively apply this knowledge to particular patients, however, has lagged far behind. Pharmacists are in charge of keeping an eye out for drug interactions and alerting doctors and patients to any potential issues.

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