IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

Review On Drug Interaction

[1]Amol wadhve, [2]Usha Akhare, [3]Savita Hollkar, [4]Komal kute, [5]Shradha bhalerao
[1]principal, [2]lecturer, [3]student, [4]student, [5]student
[1]MSBTE,
[2]MSBTE,
[3]MSBTE,
[4]MSBTE,
[5]MSBTE

Abstract

Drug interactions occur when two drugs are co-administered and both are metabolized by the same P450.

One drug can then inhibit the metabolism of another drug leading to high serum levels and extended biological activity and Sometime toxicity.

Drug interactions are a major problem in human therapy especially with CYP3A4, a P450 involved in metabolism of over 60% of all therapeutically used drugs [6].

In addition, CYP3A4 activity is affected by foods and natural products such as grapefruit juice and is a target for induction by ligands of the nuclear receptor PXR.

Drug-drug interactions (DDIs) result from changes in the pharmacokinetics (PK) of the drug or its metabolites due to changes in absorption, distribution, metabolism, or degradation, due to improved. or poor

pharmacodynamics (PD). Effect

Drug interactions can occur for many reasons, including direct chemical reactions, interactions by increasing or decreasing P450, competition for binding to albumin, and others. Sometimes it can be identified, but not in many cases.

Most clinical programs require evaluation of potential drug interactions with other medications that may be frequently used.

Food-drug interaction may also occur, and should be assessed as well.

Introduction

A drug interaction occurs when a patient‟s response to a drug is modified by food, nutritional supplements, formulation excipients, environmental factors, other drugs or disease. Interactions between drugs (drug–drug

Interactions) may be beneficial or harmful. Harmful drug interactions are important because they account for 10- 20% of adverse events requiring hospitalization and can be avoided.

1 Elderly patients are especially true vulnerable – with a strong relationship between increasing age, the number of drugs prescribed and the frequency of potential drug–drug interactions.

2 Knowing how drug–drug interactions occur and how to manage them is an important part of clinical practice.

Definition of Drug interaction

“An interaction is It is said to occur when the effect of one drug is altered by another drug. presence of another drug, herbal medicine, food, drink or by some environmental chemical agent” - Stockley's

Incidence of drug interactions

Approximately 3–26% of adverse reactions related to hospital admissions are due to drug-drug interactions
* Global prevalence of potentially inappropriate prescribing ranges from 13–35%
Up to 11.1% of patients actually experiencing symptoms due to drug interactions.

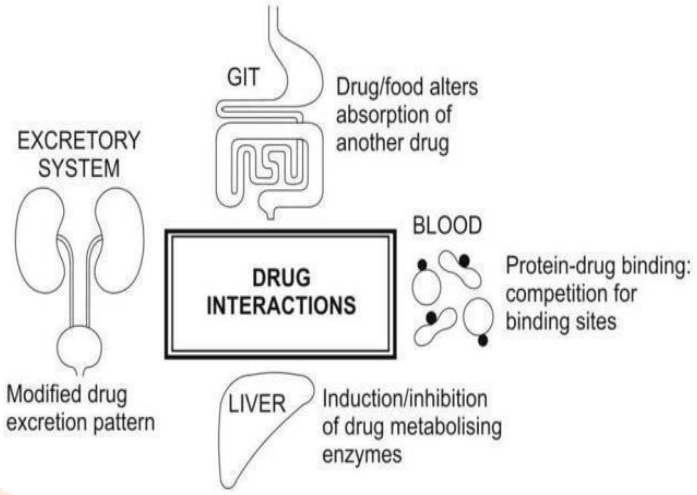

Fig. drug interaction

CAUSES OF DRUG INTERACTION

There are many reasons for interacting drugs. For example, a drug can change the pharmacokinetics of another. Alternatively, drug interactions may result from competition for a single receptor or signalling pathway.
Main factors contributing for drug interaction

1) Multiple drug therapy
2) Multiple prescribers
3) Multiple pharmacological effects of drug
4) Multiple diseases / illness
5) Poor patient compliance
6) Advancing age of patient
7) Drug related factors

Relevance and classification of drug interactions

A drug an interaction occurs when the ranges of action of two drugs overlap, and the action of one affects the action of the other.
All physicians involved in drug prescribing should be aware of the
Potential for drug interaction, but particularly those involved in anaesthesia and Take special care where there is an increased potential for drug interactions. due to polypharmacy.
A patient may receive 9 or 10 drugs as part of It's your medicine.

❖ Types of Drug Interactions

Important types of drug interactions are:

1. Drug-drug interactions
2. Drug -Food interaction
3. Drug-chemical interaction
4. Drug-laboratory test interactions
5. Drug-disease interactions

❖ **The net effect of a drug- interaction is;** Generally Measure - increase or decrease the effect.
The quality is low - the effect is faster and slower
Recently, there has been an increase in heavy rainfall.

Mechanisms of Drug Interactions

Behavioural drug-drug interaction: altered compliance when one drug alters the patient‟s behaviour to modify compliance with Another drug for example - the more willing the patient is to take the drug the better the symptoms.
Pharmaceutics drug-drug interactions: outside the Body is a physical-chemical interaction that occurs over time. drugs are mixed with i.v. infusions causing precipitation or inactivation of active principles before it is
administered.
For ex.- precipitation of sodium thiopentone within an intravenous dose.

Fig. mechanism of drug interaction

❖ Pharmacokinetic drug-drug interactions :

The concentration or effect of these interactions occurs when one drug alters the systemic concentration of another drug and changes its magnitude or duration.
present at the site. The effect of pharmacodynamics drug interactions occurs. when interacting drugs have either additive effect.

❖ A taxonomy of interactions

The proposed taxonomy of chemical interactions consists of a hierarchical set of categories.
The definition a chemical interaction in this text is different from that in mixture toxicity, where an interaction is defined as different from an incremental dose-response. In this article, the term „chemical interaction‟ is more broadly defined (see Text Box). An interaction between two chemicals does not the need for a common source is a common way. of exposure, or concurrent exposure nor does it imply that both chemicals will independently cause a common AO. Rather, an interaction is considered to If two substances or toxic effects disrupt a common node in the combined AEP-AOP framework and cause a change in the probability of occurrence, an event has occurred. of an AO.

❖ Surface of the skin

The most widely the area studied is chemical-chemical interactions with the skin surface. Factors such as altered solubility, precipitation, supersaturation, solvation, volatility and physicochemical effects such as altered surface tension from the presence of surfactants, changed the absorption capacity and micelle formation are all increased the potential of interaction.

Chemicals in a mixture may act independent of one another or the presence of other components may modulate an observed effect.

In addition, when a chemical is applied topically on the skin as a component of a chemical mixture, the amount freely available for subsequent It can be really hard to get involved.

This applies to the concentration gradient required to concentrate on chemical processes and adnexal structures and their products such as hair, sebum or sweat.

TABLE 1

Examples of typical additive and antagonistic pharmacodynamic interactions

Substance I	Substance II	Possible effect
Additive interactions		
NSAIDs	SSRI, phenprocoumon	Increased risk of bleeding
NSAIDs	Glucocorticoids	Increased risk of gastric bleeding
ACE inhibitors	Spironolactone, amiloride	Hyperkalemia
SSRIs	Triptans	Serotonin syndrome
Tricyclic antidepressants	Low-potency neuroleptics	Increased anticholinergic effects
Quinolones	Macrolides, citalopram	QT-interval prolongation, torsade de pointes
Antagonistic interactions		
Acetylsalicylic acid	Ibuprofen	Reduced effects
ACE inhibitors	NSAIDs	Reduced effects
Levodopa	Classical neuroleptics	Reduced effects
Phenprocoumon	Vitamin K	Reduced effects

❖ Chemical Drug–Excipient-Interaction

Physical interactions, it has been argued, are non-existent. Chemical interactions, and ultimately can be both beneficial and detrimental to the final product. Instead, chemical reactions occur.

detrimental effect on the product where a separate product is formed following a chemical reaction between the reactants.

Boiling reactions between organic acids (e.g. citric acid) and sodium bicarbonate in the presence of aqueous media produce carbon dioxide (CO2), this CO2 helps break down the solid dosage form for the oral

administration of the drug mixture.

However, precautions Must be in storage (not exposed to moisture) and during preparation (RH. medium of the product.

❖ Drug-laboratory test interactions

Results of numerous routinely performed and highly specialized BLTs in serum and other biological material can be influenced by one or more drugs that are prescribed to Therefore, DLTIs are a major source of diagnostic and treatment errors (19).

This emphasizes the importance of knowledge and continual education regarding the possible DLTIs, for medical doctors, pharmacists and laboratory Specialist (20). Polypharmacy is defined as the simultaneous use of five or more drugs (21).

The prevalence of polypharmacy in adults aged 65 years or It is more than 26.3-39.9% in 17 European countries and Israel, with the lowest Polypharmacy in Switzerland, Croatia and Slovenia (26.3%) 27.3% and 28.1% respectively), and highest prevalence in Portugal.

❖ Drug-disease interactions

The number of times that a drug recommended for each of the three index conditions would be contraindicated or should be avoided in the presence of any of the other 11 conditions. Drug-disease interactions were not
common, with the exception of those related to Chronic kidney disease, usually caused by type 2 diabetes..
Chronic kidney disease was involved in 27 of the identified 32 drug-disease interactions for drugs recommended in the clinical guideline for type 2 diabetes and all of the six and 10 drug-disease interactions for the guidelines for depression and heart failure, respectively. But the guidelines for type 2 diabetes and heart failure each
specifically discussed just one of these identified interaction. For type 2 diabetes this recommendation was for the need to avoid treatment with thiazolidinedione's. in people with comorbid heart failure.

❖ Excretion Interactions

Renal excretion

Only the free fraction of a drug that is dissolved in the blood plasma can be removed through the kidney.
Therefore, drugs that are tightly bound Proteins are not available for renal excretion until they are metabolized and may be lost as metabolites.
Creatinine clearance is used as a measure of kidney functioning but it is only useful in cases where the drug is excreted in an It appears unchanged in the urine
Renal excretion of drugs follows the same mechanisms as all other organic solutes: passive filtration, reabsorption and active secretion.
Finally, drug delivery is a dynamic process that depends on mechanisms related to molecular diffusion and competition between substrates.
Therefore, these are key sites where interactions It may occur between medications.

❖ Interactions at the metabolic level

Inhibition of drug metabolism is a frequent cause of drug interactions. Most Metabolic interactions are caused by the. competition for the Cytochrome P450 (CYP) enzymes, which are expressed in the liver, catalyze half of the phase I more than half of the drugs (16).
Interactions with CYP3A4 are particularly marked, since this isoenzyme has a particularly broad substrate spectrum (e15). Some of the CYP3A4 substrates, inhibitors, and inducers are identical with those of P-gp, indicating a synergistic defence mechanism against foreign It is a substance that is created in development.

❖ Anticoagulants

The most relevant interactions are those relating to drugs with a narrow therapeutic spectrum, such as ciclosporin or preprohormone. As already It has been mentioned, the vitamin K antagonists. can trigger life- threatening haemorrhage and contribute to the incidence of medical drug-related hospitalizations.
The cause could be interactions with older macrolide antibiotics such as erythromycin and clarithromycin, which inhibit cytochrome P450 3A4 is important in prohormone metabolism. Azithromycin shows almost no interaction with the cytochrome P450 system.
The calcium channel blockers verapamil and azole antimycotics can be highly potent CYP3A4 inhibitors.
Ketoconazole inhibits the cytochrome P450 system so strongly that it is now used as a standard inhibitor in the clinical development of medical drugs, in order to test interactions with CYP3A4 among others.

DRUG INTERACTION RISK FACTOR

Drug -drug interaction occur when two or more drug prescription or OTC drug react with each other, some drug interactions can make the drug you take less effective and some combination of drug can be dangerous.

Following the drug interaction risk factor;

- Poly pharmacy

There are many other advisors. There are many solutions.

- Genetic make up
- Special population e. It is old, fat and critical patient.
- Specific illness E.g. Hepatic disease,
- Renal dysfunction,

Narrow Prescription drugs

- Digoxin, insulin, lithium, antidepressiva Warfarin .

❖ CONCLUSION

It is possible to take advantage of positive drug interactions. However, the negative interactions are usually of more interest because of their pathological significance, and there are many unexpected, and may even go undiagnosed.

By studying the conditions that Favor the appearance of interactions, it should be possible to prevent them, or at least diagnose them in time.

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