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Drug Interactions and its Management

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ABSTRACT

Poisons and medicine are often the same substance given with different intents.*"* –peter mere Latham. Drugs are considered as life saving material on earth only when given incorrect quantity. Otherwise, same drug acts as life threatening substance. Drug-drug interaction is most common phenomenon which occur with most of the cases. To avoid this proper care must be taken which include defining problem, screening and evaluation of treatment and many more. Various approaches and guidelines are given to overcome problems arising from drug-drug interaction. To manage Drug interaction basic information about drug is important like it's pharmacokinetics and pharmacodynamics. Absorption, distribution, metabolism and excretion are the part of pharmacokinetics while receptor action, synergism, antagonism are the effects of pharmacodynamics. New terms which include in the area are pharmacogenomics and pharmacogenetics this terms some time used interchangeably but they are not synonyms, pharmacogenomics means effects of total genetic makeup. And pharmacogenetics is inherited traits and polymorphism between genes.

INTRODUCTION

Synergism, antagonism and many others, terms are used to indicate drug actions, not alone but in combination. Each drug has its own unique properties with ability to combat with many disease. Most of the time individual drug therapy is not sufficient to get good result so physician with proper knowledge, choose a combination of drug but selection of proper medicament is crucial thing for better results otherwise it can causes hazardous effects. Drug interaction is most of the time unintentional in nature. Improper handling of medicines, lack of knowledge, excess use are some of the other reasons of drug interaction. Drug interaction management is not only responsibility of physician or pharmacist but also patient. Proper knowledge and follow up of instructions are important to avoid drug interaction.

Drug interaction

Drug interaction is defined as the reduction or enhancement of the clinical effects of a drug due to abnormalities in other drugs, foods, herbs, drugs, containers, or environmental factors such as tobacco or other drugs like opiates, morphine etc. Different types of (DDI) are Pharmacokinetics, Pharmacodynamics (PD) and Pharmacy (Pharmacology).

Pharmacists often encounter drug interactions. Risk assessment of such a potential interaction with the patient is the first step that needs to be taken before taking any action. Each pharmacy should have a consistent approach to infrared signals if intervention is necessary to avoid injury to the patient. The response to potential information technology depends on several factors, including the person viewing the alert, prescribing access to doctors and patients, perceived risk, and possible management options. We believe that identification alerts are appropriate and may pose a risk to the patient, because we have discussed inappropriate options for dealing with inappropriate signals.

Basic information is required.

It is important that pharmacists responding to AI signals have a general knowledge of DD, including general mechanisms, timing, various ways to eliminate drugs (including the cytochrome P450 [CYP] system and drug carriers) and inhibitors in general. Induction drug injection and an understanding of IT risk management. If the computerized alarm system does not provide this information, it can be used in many publications. Since the magnitude of the response to drug interactions significantly (6 times) between patients, pharmacists need to

know which drugs and patient factors increase or decrease the risk of a particular patient. In the previous columns, we discussed several factors that changed the level of interaction (for example, primary metabolism, genetics, comorbidities, medication and route of administration).

Interaction Technical Guidelines

April 17, 2010 John R. Horn, PharmD, FCCP, and Philip D. Hansten, PharmD pharmacists, evaluate and introduce risk with medication warnings. Risk assessment of such a potential interaction with the patient is the first step that needs to be taken before taking any action. Each pharmacy should have a consistent approach to infrared signals if intervention is necessary to avoid injury to the patient. The response to potential information technology depends on several factors, including the person viewing the alert, prescribing access to doctors and patients, perceived risk, and possible management options. We discussed options for action with inappropriate signals, so we believe that IR signals are suitable and may pose a risk to the patient. Essential Background Information The pharmacist who responds to ADI will understand the general mechanisms, the determinants of the IT program and the different ways to eliminate drugs (including the cytochrome P450 [CYP] system and the conveyor belt), drug inhibitors. publications. Since the magnitude of the response to drug interactions significantly (6 times) between patients, pharmacists need to know which drugs and patient factors increase or decrease the risk of a particular patient. In the previous column, we discussed several factors that changed the magnitude of the interaction (for example, primary metabolism, genetics, concomitant disease, drug administration, and route of administration). It is recommended that all pharmacists on your site approve a list of "dangerous" drugs (for example, with a narrow first-line treatment or high metabolism), which are usually prescribed to the patient, and determine how to respond to them. The potential and the potential for serious poor results will be very short. For example, warfarin + CYP2C9 or an inhibitor of colchicine and CYP3A4 or the P-glycoprotein inhibitor receptor will always require prescription drugs before starting. There are many ways to avoid the risk that a patient will be offered to a prescribed doctor, but the prescription is associated with all cases involving high-risk interactions. Providing safe and effective treatment options is the basis of good clinical support. Two generally accepted approaches to treating influenza of suspected alternative drugs and monitoring patient response There is no rule that better defines the replacement of objects or precursors. Often the choice is based on the availability of a suitable substitute or prescribed medication as soon as possible.

Pharmacists have a unique opportunity to provide alternative prescription therapy to one of the interacting drugs. Especially if the other two doctors are involved. Your doctor rarely recommends medicines prescribed by other doctors. Alternatives have similar pharmacological properties, but are not at risk of dangerous interactions. If one of the interacting drugs cannot be changed, and the patient decides to inject two drugs, a monitoring plan should be developed to detect signs of an adverse reaction and to respond adequately. Monitoring can be as simple as measuring biological signals, plasma concentrations, or certain pharmacodynamics parameters, such as internationally standardized indicators or electrocardiograms. It is important to think about the direction of the interaction so that monitoring is consistent with the appearance of measurable results. The patient's reactions to drug interactions are very different, but the reactions of the pharmacist are different. Physicians in the field must approve and respond to high-risk IT in the same way. Pharmacists should discuss various options for managing potentially harmful interactions and indicate the types and timing of recommended alternative medications and supervisory approaches. Standardized IT responses determine the best clinical support and minimize patient risk.

Pharmacokinetic -Pharmacokinetics studies are those study that consist effects of drug on body. They modify absorption, distribution, metabolism and elimination properties. Drug interaction may take place with one other and modify with concentration and give undesirable effects. Pharmacokinetics are classified as Homergic and Hetergic.

Homergic- drugs which shows same effect on organism are called as Homergic.

Hetergic – drugs showing different effect on organism are called as Homergic.

Pharmacodynamics-receptor activity, pharmacology, physiology and chemical actions are come under pharmacodynamics.

Receptor activity consist 2 parts either drug chronically react with its own receptor and activate them or interact with own receptor and deactivate them.

Pharmacological actions consist agonist and antagonistic activity of drug. Competitive and non competitive are classification of pharmacological activities, if 2 drugs have affinity for same receptor then this type of problem arises.

Physiological actions consist 2 drugs action on different receptor either they increase the action of another receptor or decrease the action of another receptor via cellular mechanism.

Chemical dynamics deals with interaction of one drug with another they prevent interaction of drug with different receptor.[10]

Synergistic effect -The interaction is called synergism if the interaction enhances the effectiveness of one or both drugs.

Antagonistic effect - If the interaction reduces the effectiveness of one or both drugs, two drugs are called as antagonistic to each other.

Partial agonist -Partial agonists bind and activate receptors, but are agents that have only partial activity against the receptor for a full agonist. They can also be considered as ligands exhibiting agonistic and antagonistic effects. In fact, when full agonists and partial agonists are present, the partial agonists act as competitive antagonists that compete with the full receptor agonist and reduce the total activity of the receptor, as seen with one full agonist. Clinically, a partial agonist can be used to activate the receptor to achieve the desired maximum response when there is an insufficient amount of endogenous ligands, or it can reduce the excessive stimulation of the receptor when an excessive endogenous ligand is present.

Adverse drug reaction is main outcome of drug interaction which classified as type a and type b. Type a interactions are those which can be predictable like hypoglycaemia with the use of insulin or other antidiabetics this are not generally a side effect but known adverse effect with excess or unintentional use. While type b is considered as genetically derived effects which are unknown to everyone which considered as either idiosyncrasy or allergy. Idiosyncrasy means the effects which have genetic origin and allergy is the reaction to particular medicine which is not stated anywhere but it present individually.

To manage Drug interaction basic information about drug is important like it's pharmacokinetics and pharmacodynamics. Absorption, distribution, metabolism and excretion are part of pharmacokinetics while receptor action, synergism, antagonism are the effects of pharmacodynamics. New terms which include in the area are pharmacogenomics and pharmacogenetics this terms some time used interchangeably but they are not synonyms, pharmacogenomics means effects of total genetic makeup. And pharmacogenetics is inherited traits and polymorphism between genes. Before going to deciding any plan for drug interaction

their is need to find which type of interaction is takes place like whether it is drug-drug interaction or drug-food interaction. Crucial steps for drug interaction management are by taking general measures and by studying the effects after drug action. [19]

General measures consist identifying risk factors for patients like age of patient whether it is paediatric or geriatric, diet of that patient whether he is underweight or overweight, it's brief medical history is important because many people have allergy of certain medicines. Smoking and alcoholism have more impact as compared to other factors because they can precipitate and cause toxic effects of many drugs.

Risks factors

Hereditary qualities: -Pharmacogenetics is the name given to the investigation of how your qualities impact your response to drugs and hereditary elements represent 20-95% of patient fluctuation. This field of pharmacology is quickly advancing and testing for liver catalyst varieties winding up progressively across the board. For instance, codeine requires digestion through CYP2D6 for transformation to one of its dynamic metabolites, morphine. 5-10% of patients are poor metabolizers - which implies that next to no codeine is changed over to morphine which results in lacking help with discomfort. Be that as it may, 1-2% of individuals are ultra-fast metabolizers and more codeine is changed over into morphine than typical, bringing about a higher danger of harmful responses including respiratory sorrow.

Kidney work -If your kidneys are not working at full limit, at that point symptoms are more probable on the off chance that you are taking medications that are discharged through the kidneys. Some different medications likewise stop to be successful when kidney work is decreased.

Genetics - Females have a lower movement of certain hepatic catalysts, a higher muscle to fat ratio to water proportion, and a diminished leeway of medications through the kidneys than men. Studies have demonstrated the frequency of medication actuated liver poisonous quality, gastrointestinal symptoms, hypersensitive skin responses, and long QT disorder is higher in females.[18]

Effects are classified as Major, minor and moderate.

Major -the effect can be life-threatening or harmful.

Minor- it gives mild effects

Moderate -The effect may reduce the patients clinical condition and further treatment or additional hospitalization. [1]

First drug	Second drug	Effect
ACE inhibitors	Potassium-sparing diuretics	Increased risk of hyperkalaemia
Aminoglycosides	Diuretics	Increased risk of ototoxicity
Carbamazepine	Many antidepressants	Anticonvulsant effects reduced
Digoxin	St John's wort	Plasma concentration of digoxin reduced
Griseofulvin	Warfarin	Anticoagulant effect reduced
Lithium	Many analgesics	Lithium excretion reduced
Nitrates	Sildenafil	Hypotensive effect increased
Simvastatin	Itraconazole Ketoconazole	Increased risk of myopathy
Sulphonylureas	Antifungals	Increased risk of hypoglycaemia
Warfarin	Many antibiotics	Anticoagulation may be increased

From: Reid and Chrome (2005)

[13]

Hypersensitivity reaction –

TYPES OF HYPERSENSITIVITY REACTIONS

Type I „immediate"	Type II	Type III	Type IV „delayed"
Antibody mediated			**T cell mediated**
specific IgE	cell surface antigen specifically reacting with antibody	aspecifically deposited soluble immuncomplex	MHC restricted T cell activation
mediators produced by mast cells	FcR mediated inflammation, inhibition of cell functions	FcR mediated complement activation, inflammation	cytokines, cytotoxicity
„classical allergy"	newborn haemolytic anaemia, penicillin sensitivity, M. gravis	Serum sickness, SLE	Contact dermatitis

mostly appear together with autoimmune diseases

[14]

Type 1 -Anaphylactic reactions are mediated by IgE antibodies produced by the immune system in response to environmental proteins (allergens), such as pollen, animal dander, or dust. This antibody (IgE) binds to fat cells containing histamine granules and basophils and causes inflammation. Type 1 hypersensitivity reactions can be observed with bronchial asthma, allergic rhinitis, allergic dermatitis, food allergies, allergic conjunctivitis and anaphylactic shock.

Type 2-IgG and IgM mediate cytotoxic mediated responses to the cell surface and extracellular matrix proteins. Immunoglobulins involved in this type of reaction damage cells by activating the complement system or phagocytosis. Type II hypersensitivity reactions may occur with immune thrombocytopenia, autoimmune haemolytic, anaemia, and autoimmune neutropenia.

Type 3 - They are also mediated by IgM and IgG antibodies, which react with the dissolved antigen to form an antigen-antibody complex. The complement system activates and induces neutrophils and secretes chemoattractant that cause inflammation and tissue damage during vasculitis and glomerulonephritis. Type III hypersensitivity reactions can be classically observed in serum diseases and Arthus reactions.[2]

Type 4 -Type IV depends on the interaction of the antigen with T-lymphocytes and is called delayed hypersensitivity or DTH. DTH responses include T-helper cell activation (CD4) and / or cytotoxic perforation (CD8 CTL). The subsequent secretion of cytokines causes various pathologies. In many cases, prolonged release of antigen and prolonged activation of sensitive T cells lead to an enhanced response, leading to excessive activation of macrophages. This case is the basis for the development of a wide range of inflammatory diseases, from erythema and oedema to the formation of granuloma, prolonged fibrosis and even tissue necrosis.[3]

Therapeutic alternatives

Alternative medicines are those medicines which are described when new medicine system can’t useful against particular disease. This system are generally have unproven standards or activities by standard scientific evidence they are based on holistic nature of medicine. It generally based on various approaches like homeopathy, Ayurveda, aromatherapy, acupressure etc.

Principles of alternative therapies

Placebo effect-it is method in which patient is convinced to get therapy by a substance which is not actually medicine but strong faith about treatment is created within patient mind so it create healing effect.

Nocebo effect- it based on negative impact of therapy. Current therapy is not suitable or IT is given with wrong direction is basis of this type. Negative impact on patients mind is driving force of treatment. Negative impact of current therapy so crafting faith on alternative one is motive of nocebo effect.

NCCIH classification-

Alternatives are generally given to avoid multiple therapies it may consist replacing the drug with another drugs having same effect which gives same therapeutic effect without any drug interaction for ex. When erythromycin cause hazardous effect azithromycin is better option.

National centre on complementary and integrative health

The NCCIH classification system is -

Whole medical systems: cut across more than one of the other groups; examples include traditional Chinese medicine, naturopathy, homeopathy, and Ayurveda

Mind-body interventions: explore the interconnection between the mind, body, and spirit, under the premise that the mind can affect "bodily functions and symptoms"

·Biology"-based practices: use substances found in nature such as herbs, foods, vitamins, and other natural substances. (Note that as used here, "biology" does not refer to the science of biology, but is a usage newly coined by NCCIH in the primary source used for this article. "Biology-based" as coined by NCCIH may refer to chemicals from a nonbiological source, such as use of the poison lead in traditional Chinese medicine, and to other nonbiological substances).

Manipulative and body-based practices: feature manipulation or movement of body parts, such as is done in chiropractic and osteopathic manipulation.

Energy medicine: is a domain that deals with putative and verifiable energy fields:

Biofield therapies are intended to influence energy fields that, it is purported, surround and penetrate the body. No empirical evidence has been found to support the existence of the putative energy fields on which these therapies are predicated.

Bio electromagnetic-based therapies use verifiable electromagnetic fields, such as pulsed fields, alternating-current, or direct-current fields in an unconventional manner.[11]

Patient counselling

Patient counselling or patient education can minimise the drug side effects. Patients should be aware of side effects of drugs which plays important role with the patient having habit of smoking or alcoholism.

Some principles of patient counselling

Patients instruction and data on wellbeing condition and medication treatment; the training part included medicine advising on every single endorsed prescription, inhaler method evaluation, verbal instruction, symptoms of medications, and arrangement of composed asthma instruction materials.

Examination of release prescription with preadmission regimens and compromise of disparities with the therapeutic group's assistance

Screening of past medication related issues, including no adherence, absence of adequacy, and reactions

Audit of signs, bearings for use, connections, significance of AM routine and potential unfriendly impacts of each release prescription with the patient, and talked about noteworthy discoveries with the restorative group.[5]

Techniques of patient counselling

Stage I: Medication data exchange, amid which there is a monolog by the drug specialist giving essential, brief data about the sheltered and appropriate utilization of prescription.

Stage II: Medication data trade, amid which the drug specialist answers questions and gives point by point data adjusted to the patients' circumstance.

Stage III: Medication instruction, amid which the drug specialist gives exhaustive data with respect to the best possible utilization of meds in a shared, intuitive learning background.

Stage IV: Medication advising, amid which the drug specialist and patient have a point by point discourse proposing to give the patient direction that improves critical thinking aptitudes and helps with appropriate administration of restorative conditions and successful utilization of medicine.[4]

Enzyme induces and enzyme inhibitors are agents which can increase or decrease the metabolism of drug and subsequently the drug effects. Common enzyme inducing agents are barbiturates, alcohol and phenytoin while enzyme inhibitors are chloramphenicol, sulphonamide, metronidazole etc.

CYP are main enzymes which present throughout the body which are responsible for enzyme inhibition and inducer. Individual therapy is type of therapy that is unique to individual this type of medications are common with alternative therapies like Ayurveda, homeopathy and aromatherapy. Another type of drug interaction management is case based studies. It consist screening, evaluations and management. Generally, drugs with known side effects are less tend to prone to hazardous effects because preventive care can be taken.

The cytochrome (P450 or CYP) isoenzymes are a gathering of heme-containing catalysts installed essentially in the lipid bilayer of the endoplasmic reticulum of hepatocytes, it partakes in the digestion of numerous medications, steroids and cancer-causing agents.[20]

In man there are around 30 CYP proteins which are in charge of medication digestion and these have a place with families 1– 4. It has been evaluated, nonetheless, that 90% of medication oxidation can be credited to six principle compounds: CYP 1A2, 2C9, 2C19, 2D6, 2E1 and 3A4 [6]. The most huge CYP isoenzymes regarding amount are CYP3A4 and CYP2D6. CYP3A4 is found in the liver as well as in the gut divider, where it might fill in as an essential resistance instrument. The majority of medications following up on the CNS (Central Nervous System), except for unpredictable analgesic specialists, are processed by this compound.[8]

Screening

Screening is the process which include classification of effects like mild, moderate, severe or lethal. When effects like mild or moderate normal precautions prove useful but when conditions become severe hospitalization is must.

Pharmacy automated drug interaction screening (PADIS) framework is portrayed which identifies conceivable medication cooperation's by screening tolerant medicine profiles. The information base contains around 24,000 medication cooperation mixes of medications advertised in the U.S. and furthermore remote and investigational drugs that have been involved to cause tranquilize cooperation's. It is refreshed on a month to month premise. The PADIS framework works as a bunch run program which screens all patient drug profiles on an everyday plan. A patient medication collaboration profile is printed by the PC for use by the drug specialist to recommend elective treatment to the doctor. The PC recognizes potential medication cooperation's in roughly 9% of the patients every day at the 635-bed doctor's facility at which the framework was created. [7]

Evaluation of drug interaction

Comprehension of digestion, transport, and drug– sedate associations is basic to the advantage/hazard evaluation of a medication.

• Using a coordinated methodology, joining in vitro and in vivo digestion and transport concentrates to explain the hidden mechanisms and to evaluate the potential for medication connections can lessen the number of studies needed and optimize our knowledge.

• Utilization of PBPKmodels in prediction of multiple drug interactions or various hindrance can help illuminate further clinical examinations.

• Therapeutic protein– tranquilize connections should be assessed dependent on robotic comprehension, potential outcomes of mix treatment, and past encounters of known components of associations.

• The clinical criticalness of drug– sedate connections ought to be deciphered dependent on all around characterized introduction reaction information and examinations.

• Classification of CYP inhibitors and substrates can help in the examination structure and cross-marking of medications.

• Drug– tranquilize cooperation data ought to be properly set in the naming. With enhanced comprehension of the sub-atomic bases of drug– sedate cooperation's and the interchange of different inherent and extraneous elements influencing these communications, dangers related with drug– medicate associations can be evaluated and figured out how to limit untoward impacts.[13]

Acute poisoning is an emergency medicine that is common in many countries and contains many chemicals and medicines. The exact spread of this problem in our country is still unclear, but it is estimated that between 1 and 1.5 million cases of poisoning occur annually and more than 50,000 people die. The purpose of this article is to familiarize the doctor with the various steps necessary for the effective treatment of acute poisoning.

To effectively manage the victims of acute poisoning, five additional steps are needed. These include:

- Early resuscitation and stabilization
- Diagnosis of point types
- Non-specific treatment
- Special treatment
- Auxiliary therapy[16]

Guidelines for pharmacist for avoiding drug interaction

Defining a prescription treatment plan: choosing, starting, altering, or overseeing drug treatment.

Observing and assessing the patient's reaction to treatment, including wellbeing and adequacy

Playing out an extensive prescription audit to distinguish, resolve, and avert medicine related issues, including unfriendly medication occasions.

Reporting the consideration conveyed and imparting basic data to the patient's other essential consideration suppliers.

Giving verbal instruction and preparing intended to upgrade persistent understanding and suitable utilization of his or her meds.

Giving data, bolster administrations, and assets intended to improve understanding adherence with his or her treatment.

Planning and incorporating medicine treatment the executives benefits inside the more extensive human services the board administrations being given to the patient.

Give human services experts an entire rundown of the majority of the medications that you are utilizing or include utilized inside the most recent couple of weeks. This ought to incorporate over-the-counter prescriptions, nutrients, nourishment enhancements, and homegrown cures.

Educate medicinal services specialists when drugs are included or suspended.

Illuminate social insurance professionals about changes in way of life (for instance, work out, diet, liquor consumption).

Get some information about the most genuine or successive medication cooperation's with the drugs that you are taking.

Since the recurrence of medication associations increments with the quantity of drugs, work with your human services professionals to wipe out pointless prescriptions. [12]

SUMMARY

Various case studies, research papers, and reviews have been published till today on drug interaction management. Drug interaction is most common problem occurs with drugs. This article provides a brief review on drug interactions and role of pharmacist in its management. This article also focuses various guidelines, screening process and evaluation methods for managing drug interaction.

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