CONCEPT OF DRUG INTERACTION

Singh Nidhi*
Department of Pharmacognosy, JSS College of Pharmacy, Ooty, Tamil Nadu, India

Article Received on: 19/04/12 Revised on: 16/05/12 Approved for publication: 20/06/12

*Email: nidhi.jssooty@yahoo.com

ABSTRACT

Drug interaction is an increasingly important cause of adverse reactions (ADR), and is the modification of the effect of one drug (object) by the prior or concomitant administration of another drug (precipitant drug). Drug interaction may either enhance or diminish the intended effect of one or both drugs. For example, severe haemorrhage may occur if warfarin and salicylates (aspirin) are combined. Precipitant drugs modify the object drug's absorption, distribution, metabolism, excretion or actual clinical effect. Nonsteroidal anti-inflammatory drugs, antibiotics and, in particular, rifampin are common precipitant drugs prescribed in primary care practice. Drugs with a narrow therapeutic range or low therapeutic index are more likely to be the objects for serious drug interactions. Object drugs in common use include warfarin, fluoroquinolones, antiepileptic drugs, oral contraceptives, cisapride and 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors. Many other drugs, as act as precipitants or objects, and a number of drugs act as both. The aim of present review is to throw light on the concept of drug interaction.

Key words: Drug, Administration, Pharmacokinetics, Pharmacodynamics, Synergism, Antagonism.

INTRODUCTION

Drug interaction refers to modification of response to one drug by another when they are administered simultaneously or in quick succession. The modification is mostly quantitative, i.e. the response is either increased or decreased in intensity, but sometimes it is qualitative, i.e. an abnormal or a different type of response is produced. The possibility of drug interaction arises whenever a patient concurrently receives more than one drug, and the chances increase with the number of drugs taken. Today, with the increasing availability of complex therapeutic agents and widespread polypharmacy, the potential for drug interaction is enormous. In other words, phenomenon of drug interaction is defined as when the effects of one drug is changed by the presence of another drug, food, drink or an environment chemical agents. The net effect of the combination may be -

- Synergism or additive effect of one or more drugs
- Antagonism or subtractive effect of one or more drugs
- Alteration of effect of one or more drugs or the production of idiosyncratic effects.

It is important to know the difference between a drug interaction and a side effect. A side effect, also known as an adverse effect, is caused by a single drug. Side effects can occur with the normal use of a drug and sometimes can be predicted and treated. A side effect, if severe enough, may require doctor to stop the drug or lower the dosage. An example of a side effect is the drowsiness caused by certain antihistamines. A drug interaction is caused by two or more drugs, foods, or other substances taken by the same person. A drug interaction may require your doctor to stop one or more of the drugs.

Types of drugs most likely to be involved in clinically important drug interactions

- Drugs with narrow safety margin, e.g. aminoglycoside antibiotics, digoxin, lithium.
- Drugs affecting closely regulated body functions, e.g. antihypertensives, antidiabetics, anticoagulants.
- Highly plasma protein bound drugs like NSAIDS, oral anticoagulants, sulfonylurease.

- Drugs metabolized by saturation kinetics, e.g. phenytoin, theophylline.

<table>
<thead>
<tr>
<th>S.No</th>
<th>Precipitant drug*</th>
<th>Object drug*</th>
<th>Likely interaction and comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NSAIDS</td>
<td>Ciprofloxacin and other Fluoroquinolones</td>
<td>Enhanced CNS toxicity, seizures; Avoid concurrent use.</td>
</tr>
<tr>
<td>2</td>
<td>Chronic alcoholism</td>
<td>Paracetamol</td>
<td>Hepatotoxic dose of paracetamol is reduced; doses ≤ 3 g/ day are safe.</td>
</tr>
<tr>
<td>3</td>
<td>Lidocaine</td>
<td>B-blockers Quinidine and other antiarrhythmic drugs</td>
<td>Enhanced bradycardia and hypotension; Avoid concurrent use. Exaggerated cardiac depression, precipitation of arrhythmias; Avoid concurrent use.</td>
</tr>
<tr>
<td>4</td>
<td>Aspirin</td>
<td>Spironolactone</td>
<td>Reduce K+ conserving action due to decreased tubular secretion of canrenone (active metabolite of spironolactone); Avoid concurrent use.</td>
</tr>
</tbody>
</table>

*Precipitant drug* is the, which alters the action/pharmacokinetics of the other drug
*Object drug* is the drug whose action/pharmacokinetics is altered

Examples of some nonprescription drugs that may have important interactions

People start using non-prescription drugs whenever they feel themselves to be uncomfortable, and these drugs are not only available in pharmacies but also in grocery stores and convenience stores. So it’s better and safe that before using such non-prescription drugs people must be aware of its interactions.

*Email: nidhi.jssooty@yahoo.com*

INTERNATIONAL RESEARCH JOURNAL OF PHARMACY
www.irjponline.com
ISSN 2230 – 8407

Review Article

Singh Nidhi IRJP 2012, 3 (7)
Sometimes a patient is not satisfied by one doctor and may consult other doctor without informing about the consultation of the first doctor.

Irrational polypharmacy, concurrent use of prescribed and non-prescribed drugs

A patient may take drugs like Aspirin, antacid which are available without physician’s prescription. If such patients are on other drugs prescribed by physician for example digoxin or tetracycline, the drug interaction may occur.

Patient’s non compliance

Sometimes patient does not comply with the instructions given by the physician and may take food material which is being prohibited. For example cheese with monoamine oxidase inhibitors, this may result to severe hypertension crisis.

Types of drug interaction

Depending on the type of the effect produced, drug interaction may be classified as inhibiting drug interaction, potentiating drug interaction or modifying drug interaction.

Inhibiting drug interaction: An inhibiting interaction partially or completely prevent a drug from exerting its action thus diminishing its effect in the patient. Antagonism, a type of inhibiting interaction occurs when a drug with a given activity is blocked by a drug with a nullifying action e.g.

- Amphetamine and barbiturates
- Morphine and naloxone
- Adrenaline and propanolol

Potentiating drug interaction: A potentiating interaction enhances the toxic or therapeutic effects of a drug in patients. Synergism, supra-addition, modification, absorption, distribution, metabolism and excretion of drug or modification of the drug action at receptor or sites may be involved.

Synagris, a type of potentiation, occurs when the combined effect of two or more drugs, acting simultaneously is greater than the sum of the individual effects produced when each drug is administered alone e.g.

- Levodopa and carbidopa
- Sulfonamide and trimethoprim
- Isoniazid and rifampicin

Modifying drug interaction

Factors responsible for drug interaction

- Insufficient knowledge: Inadequate understanding of the pharmacokinetics and pharmacodynamics of the drug may lead to drug interaction.
- Dietary factors: Constituents of an individual’s diet including food stuff-vegetables which may interact with certain drugs.
- Physiology of the individual: Factors such as age, sex, weight and genetic abnormalities influence the occurrence of drug interaction.
- Presence of disease states: Pathological conditions like liver disease, kidney damage or altered enzyme systems may affect the handling of drugs by the body and lead to adverse drug interaction.

Regular medication drugs likely to be involved in drug interaction

1. Antidiabetics
2. Antihypertensives
3. Antianginal drugs
4. Antiarthritic drugs
5. Antiepileptic drugs
6. Antiparkinsonian drugs
7. Oral contraceptives
8. Anticoagulants
9. Antiasthmatic drugs
10. Psychopharmacological agents
11. Antipeptic ulcer drugs
12. Corticosteroids
13. Antitubercular drugs
14. Anti-HIV drugs

Mechanism of drug interaction

Drug interactions can be broadly divided into pharmacokinetic and pharmacodynamic interactions.

Pharmacokinetic interaction: Pharmacokinetic interactions are those which can affect the process by which drugs are absorbed, distributed, metabolized or excreted.

Pharmacodynamic interaction: Pharmacodynamic interactions occur due to modification of the action of one drug at the target site by another drug, independent of a change in its concentration. This may result in an enhanced response (synergism), an attenuated response (antagonism) or an abnormal response.

Synergistic interaction – If two drugs with similar pharmacological effects are given together, the effects can be additive. Although not strictly drug interactions, the mechanism frequently contributes to adverse drug reactions. For example, the concurrent use of drugs with CNS depressant effects, such as antidepressants, hypnotics, antiepileptics and antidepressants, may lead to excessive
drowsiness; yet such combinations are frequently encountered.

### Drug Interaction Table

<table>
<thead>
<tr>
<th>Drug</th>
<th>Combined drug</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin</td>
<td>Paracetamol</td>
<td>Synergistic action as analgesic/antipyretic</td>
</tr>
<tr>
<td>Nitrous oxide</td>
<td>Ether</td>
<td>Positive effect as general anaesthesia</td>
</tr>
<tr>
<td>Ephedrine</td>
<td>Theophylline</td>
<td>Synergism as bronchodilator</td>
</tr>
<tr>
<td>Sulfadiazine</td>
<td>Sulfamethazine</td>
<td>High antibacterial activity</td>
</tr>
<tr>
<td>Glipizide</td>
<td>Metformine</td>
<td>Beneficial hypoglycaemia occurrence</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>Propranolol</td>
<td>Additive action and propranolol decreases sympathetic activity</td>
</tr>
<tr>
<td>Minoxidil</td>
<td>Nifedipine</td>
<td>Additively cause arteriolar dilation</td>
</tr>
<tr>
<td>Losartan</td>
<td>Captopril</td>
<td>Both act as synergism to cause hypotension</td>
</tr>
<tr>
<td>Isoniazid</td>
<td>Pyridoxine</td>
<td>One of the therapeutically applied combinations</td>
</tr>
</tbody>
</table>

### Antagonistic interaction

It is to be expected that a drug with an antagonist action at a particular receptor type will interact with antagonists at that receptor.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Combined drug</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atropine</td>
<td>Acetycholine</td>
<td>Both the drug diminished each other’s effect</td>
</tr>
<tr>
<td>Epinephrine</td>
<td>Propranolol</td>
<td>Competitive antagonism occurs</td>
</tr>
<tr>
<td>Dopamine</td>
<td>Acetycholine</td>
<td>Antagonism to each other in case of Parkinsonism</td>
</tr>
<tr>
<td>Androgen</td>
<td>Danazol</td>
<td>Danazol-compelotely inhibit androgen</td>
</tr>
<tr>
<td>Megestrol</td>
<td>Mifepristone</td>
<td>Mifepristone antagonised Mifepristone efficacy</td>
</tr>
<tr>
<td>Flumazenil</td>
<td>Alprazolam</td>
<td>Flumazenil antagonised Alprazolam activity comparatively</td>
</tr>
<tr>
<td>ADH</td>
<td>Furosemide</td>
<td>Competitive antagonism happens</td>
</tr>
</tbody>
</table>

### Centers for Getting Information about Drug Interaction

Following are good places to get information about drugs, including drug interactions:

- **Pharmacist**: Most accessible. Also, pharmacists have the greatest knowledge about interactions.
- **Doctor**: A good source, but often not available and not as knowledgeable about interactions.
- **For prescription drugs**: Look at the label and any accompanying information, such as brochures or fact sheets given with the prescription.
- **For over-the-counter drugs**: Look at “warnings” or “drug interaction precaution” section on label. It often will say which drugs or foods may interact with the product or which drugs or foods to avoid.
- **Patient-oriented sources**: Listed below are some examples of drug information books written for the public.

- The Complete Drug Reference, published by Consumer Reports.

### Important Tips for Avoiding Drug Interaction

- With each visit to the doctor, inform him or her of all the medications (including prescription drugs, OTC drugs, home remedies, and herbal medicines) that you are taking.
- Get all prescriptions filled at the same pharmacy.
- Read the drug labels very carefully.
- Read directions, warnings, and interaction precautions printed on all medication labels.
- Take only drugs prescribed for you.
- Have your medications thoroughly reviewed by your doctor or pharmacist once a year.
- Know what to do if you have new symptoms or side effects. Know whom to contact and how to reach them.
- Take medicine with a full glass of water.
- Don’t stir medicine into your food or take capsules apart unless directed to do so.
- Don’t take vitamin pills at the same time you take medication without checking first with your doctor or pharmacist.
- Don’t mix medicine into hot drinks.
- Never take medicine with alcoholic drinks.
- Don’t stop taking a drug without checking with your doctor.
- Don’t keep old or expired medicines in your medicine cabinet.
- **Don’t be afraid to ask questions.** This is the most important tip of all and cannot be stressed enough!

### Conclusion

Present review concludes that people should possess sound knowledge of drug interaction before using a particular drug or two or more drugs at a same time, in order to have safe medication. There are many drugs which commonly involve in interaction process and their harmful effects are also discussed.

### References

4. Chris Raich, Pharm. D. candidate; Marie Abate, Pharm. D. Teri Dunsworth, Pharm. D., WVU School of Pharmacy , Drug Information Center, West Virginia University Extension Service.