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REVIEW ARTILCE

REVIEW ON INTERACTION OF HERBAL MEDICINES WITH ALLOPATHIC MEDICINES

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Abstract

Whenever two or more drugs are being taken, there is a chance that there will be an interaction among these drugs. These interactions may increase or decrease the effectiveness or may cause serious fatal reactions. The likelihood of drug interactions increases as the number of drugs being taken increases. Therefore, people who take several drugs are at the greatest risk for interactions. It is quite common for a patient to seek herbal treatment while taking several prescription medications. Safety has become a major issue reasonably enough, patients want to know about compatibility and possible interactions when taking herbs and allopathic medicines simultaneously. Such specific questions, unfortunately, are often difficult to answer. This review discusses the issue of drug interactions and several ways to avoid them.

Key words: Herbal Drug, Ayurveda, Drug interaction, pharmacokinetics, pharmacodynamics, ADME interaction.

Introduction

During the last decade, an explosion in the consumption of herbal remedies has been witnessed. The vast majorities of these products are unlicensed and are not required to demonstrate efficacy, safety, or quality. Although herbs are often promoted as natural and therefore harmless, they are not free from adverse effects. A recent observational study indicates that herbal supplements are associated with adverse events that include all levels of severity, organ systems, and age groups. Recent examinations have indicated that as many as 16% of prescription drug users consume herbal supplements. Moreover, fewer than 40% of patients disclose their herbal supplement usage to health care providers and many physicians are

unaware of the potential for herb–drug interactions¹. Natural products are also liable to a great deal of variations even when standardized to one or more of their constituents such as source material, the method by which an extract is made will also affect its composition and thus its interaction potential. Certain foods and specific nutrients in foods, if ingested concurrently with some drugs, may affect the overall bioavailability, pharmacokinetics, pharmacodynamic, and therapeutic efficacy of the medications. The likelihood of drug interactions increases as the number of drugs being taken increases and it is estimated that if eight or more medications are being used, there is a 100% chance of interaction². The aim of this

article is to highlight the clinical interactions between herbal remedies and prescribed drugs.

Materials and methods

A drug interaction can be defined as an interaction between a drug and another substance that prevents the drug from performing as expected. This definition applies to interactions of drugs with other drugs (drug-drug interactions), as well as drugs with food (drug-food interactions) and other substances. One drug alters the rate or extent of absorption, distribution, metabolism or excretion of another drug. A change in the blood concentration causes a change in the drug's effect. Most of the possible interactions may be classified in two major categories: Pharmacokinetic and Pharmacodynamic interactions³.

Pharmacokinetic interactions are those that can affect the processes by which the drug increases or decreases ADME interactions⁴ i.e.

1. The Absorption of a drug into the body.
2. Distribution of the drug within the body.
3. Alterations made to the drug by the body (Metabolism).
4. Elimination of the drug from the body.

Absorption

- Depends on surface area of absorption (less in stomach and more in intestines)^{5,6}.
- Alteration in stomach HCL (HCL secretion α break down α absorption) e.g. avoid antacids with antibiotics which reduces the activity of antibiotic^{5,6}.
- Intestinal/Gut motility (Gut motility $1/\alpha$ absorption) e.g. *Capsicum annum* increases gut motility there by decreases absorption of aspirin^{4,7}.
- Blood flow to the site (blood flow α absorption) e.g. *Capsicum annum* increases blood flow to GIT absorption site^{4,7}.

Distribution

Distribution refers to the process in which herbs or drugs are carried and released to different parts of the body to exert their effect. Interactions occur during the distribution phase if the drug has a narrow range of safety index and is highly protein-bound. For example, Coumadin (warfarin) is an anticoagulant medication that is very highly bound to protein and has a very narrow range of safety index⁶. Some known examples that interact with Coumadin (Warfarin) include *Medicago sativa* (alfalfa), aspirin, ibuprofen, vitamin K and some types of tea, green leafy vegetables⁸. These items interact with Coumadin (warfarin) by either enhancing its effectiveness or thus leading to prolonged bleeding, or by decreasing its effectiveness and thus increasing the risk of blood clots in the vessels, both of which may be quite dangerous to the patient. This is why patients who are taking Coumadin (warfarin) need to be exceedingly cautious when taking herbs concurrently. (Intake of Vit k $1/\alpha$ effect of Warfarin)^{4,9}. Blood clotting times have been reported to double in patients taking Warfarin and garlic (*Allium sativum*) supplements (WHO1999). WHO states that ginger may affect bleeding times and immunological parameters owing to its ability to inhibit thromboxane synthase and to act as a prostacyclin agonist¹⁰.

Metabolism

Many drug interactions are due to alterations in drug metabolism. Most herbs and drugs are metabolized by the liver to inactive derivatives. The rate at which the liver metabolizes these herbs and drugs determines the length of time these herbs or drugs stay active in the body. If the liver were induced to speed up its metabolism, herbs and drugs would be inactivated at a faster pace and the overall effectiveness of ingested substances would be lower and vice versa^{5,6}. Although all the mechanism is undoubtedly relevant to interaction with herbal medicines, the main focus will be on the cytochrome p 450⁵ and drug transporter proteins. Drug metabolism goes in

the serum, the kidneys, the skin and the intestines but the greatest portion is carried out by enzymes that are found in the liver mainly cytochrome p 450^{11,12}. (Metabolism α enzymatic activity 1/ α effect of same drug or other drug) e.g. Rifampicin which increases liver metabolism and decreases the effect of oral contraceptive when used together, Grape juice (*Vitis vinifera*) inhibits cytochrome p 450 preventing midazolam, alprazolam to metabolise before entering blood stream^{4,11}.

Excretion

Drugs are eliminated from the body as an unchanged drug or changed by a process of excretion or converted to metabolite. Renal excretion the major route of elimination; affected by renal function and urinary pH, some drugs are eliminated in bile and other by body fluids^{5,6}. Loop diuretics (furosemide, bumetanide) increase excretion of potassium, magnesium, sodium, chloride, calcium and corticosteroids (prednisolone) decrease sodium excretion, resulting in sodium and water retention; increases excretion of potassium and calcium so that electrolyte imbalance should be monitored⁶.

Pharmacodynamic interaction

Pharmacodynamic interactions are those where the effects of one drug are changed by the presence of another drug at its site of action. Pharmacodynamic refers to the study of how drugs actually behave inside the human body²; one drug causes a change in patient response to another drug without altering that drug's pharmacokinetics⁴.

- E.g. Shankapushpi (*Convolvulus pluricaulis*) may decrease phenytoin levels as well as diminishes drug efficacy¹³.

Pharmacodynamic interactions refer to the fluctuation in bioavailability of ingested substances as a result of synergistic or antagonistic interactions between herb/drug molecules. Pharmacodynamic interactions are generally more difficult to predict and prevent than pharmacokinetic interactions^{4,6}.

Garlic (*Allium sativum*) and ginseng (*Panax ginseng*) should be discontinued at least seven days before surgery because both herbs have been reported to aggressive bleeding. *Ginkgo biloba* should be discontinued three days before surgery because it inhibits platelets aggregation causing bleeding^{4,11}.

Possible drug interactions^{4,7,11,14,15,16}

Herb	Drug	Interaction
<i>Aloe vera</i>	Digoxin and Thiazide	Increases cardiac toxicity
<i>Capsicum annum</i>	Hypoglycemic	May effect blood glucose levels
<i>Capsicum annum</i>	Theophyllin	May increase absorption
<i>Echinacea purpurea</i>	Warfarin	Decreases Warfarin metabolism
Garlic (<i>Allium sativum</i>)	Antihypertensive drugs	Herb may decrease BP
Garlic (<i>Allium sativum</i>)	Aspirin/Warfarin	Irreversible inhibition of platelet aggregation
<i>Ginko biloba</i>	Acetaminophen	Subarachnoid hemorrhage
<i>Ginko biloba</i>	Anticonvulsants	Increases seizures

Grape fruits (<i>Vitis vinifera</i>)	Calcium channel blockers	Increase oral bioavailability
Yashtimadhu (<i>Glycyrrhiza glabra</i>)	Loop diuretics	Sodium and fluid retention

Drug interactions are complex and chiefly unpredictable. A known interaction may not occur in every individual. This can be explained because there are several factors that affect the likelihood that a known interaction will occur. These factors include differences among individuals in their genes, physiology, age², lifestyle (diet, exercise), underlying diseases², drug doses², and the relative time of administration of the two substances. (Sometimes, interactions can be avoided if two drugs are taken at different times)

- Additive effects of alcohol and benzodiazepines¹⁷
- Beta-blocker given with beta-agonist⁹

Ways to prevent drug interactions

1. Best way to prevent is close monitoring of patient itself.
2. When therapeutic goals are not met, clinicians should ask questions about how and when drugs are being taken in relation to foods and nutritional supplements.
3. Give health care practitioners a complete list of all of the drugs that you are using or have used within the last few weeks.
4. Inform health care practitioners when medications are added or discontinued¹⁸.
5. Inform health care practitioners about changes in lifestyle (for example, exercise, diet, alcohol intake).
6. Ask your health care practitioners about the most serious or frequent drug interactions with the medications that you are taking since the frequency of drug interactions increases with the number of drugs used^{19, 2}, work with

your health care practitioners to eliminate unnecessary medications.

Discussion

Demand for herbal products worldwide has increased at an annual rate of 8% during the period of 1994–2001, and according to WHO forecast, the global herbal market would be worth \$5 trillion by the year 2050. As of today, Europe and the United States are two major herbal product markets in the world, with a market share of 41% and 20%, respectively.

The explosion in popularity of herbs dates to the Dietary Supplement Health and Education Act of 1994 (DSHEA), in which the FDA recognized herbal preparations as dietary supplements outside of its direct regulatory control. Supplements are permitted to have “structure–function” statements on their label stating only the product’s supposed physiological function²⁰.

The present paper includes various aspects of drug interactions commonly occurring knowingly or unknowingly which pose serious threat to human health due to limited scientific evidence from randomized, controlled trials to support the safety and efficacy of the majority of herbal products and represent an important issue to be tackled. It becomes very difficult to predict whether the combination of all these medications will lead to unwanted side-effects and/or interactions. It is imprudent to assume that there will be no interactions. On the other hand, positive herb-drug interactions having beneficial effects also need to be elucidated.

According to the scoring system described by Fugh-Berman and Ernst, 68.5% of the cases reported were classified as ‘unavailable’ (i.e. reports contained inadequate information to assess the likelihood of an interaction), 18.5%

were classified as 'possible' (i.e. reports provided some evidence for an interaction, but there may be other causes of the event) and 13% as 'well documented' (reports appeared to provide reliable evidence for an interaction)¹.

Lastly it is important for every physician to identify and monitor high risk patients those on multiple medications and marginal diets, and ask them about their use of herbs and provide education about potential herb-drug interactions.

Conclusion

With the increasing prevalence of the use of herbal products, and the fact that many consumers and patients are using herbal products in conjunction with conventional

medications, it is becoming increasingly important for health care providers to be aware of potential adverse effects and interactions. It is not uncommon for one patient to seek care from several doctors for an ailment. As a result, a patient may easily be taking multiple drugs, herbs and vitamins concurrently. On the other hand, it is just as unwise to abandon treatment simply for the fear of possible interactions therefore researchers should strive to fill the gaps in our present understanding of this problem. On the other hand, positive drug interactions having beneficial effects also need to be elucidated, where it should be possible to exploit the increased bioavailability of the drugs for reducing the dosage.

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