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DRUG INTERACTIONS BETWEEN AYURVEDIC AND ALLOPATHIC MEDICINES-A REVIEW

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ABSTRACT

Drug interaction is any modification of response of one drug by simultaneous administration of another drug. The interactions may be either synergistic or antagonistic. Use of Ayurvedic drugs and allopathic medications concomitantly has led to potential chances for interactions between the drugs of two systems. This paper deals with the drug interactions of some commonly used Ayurvedic and Allopathic drugs. *Guggulu* is known to interact with hypolipidaemics, anticoagulants, antihypertensives and thyroid medications. Garlic interacts with anticoagulants, NSAIDs by anti platelet activity. *Aswagandha* may potentiate the effects of barbiturates. Concomitant use of castor oil reduces the efficacy of antiarrythmic drugs, diuretics, fat soluble vitamins and antihistamines. *Yashtimadhu* increases potassium loss and so prolonged use with thiazide and loop diuretics may be harmful. Other examples include the interactions of herbs like *Tulsi* with paracetamol, *Methika*, *Meshasringi* etc. with antidiabetic drugs, *Jatamamsi* with benzodiazepines, berberine in *Daruharidra* with hypolipidaemic drugs and *Vasa* with theophylline. Proper knowledge of drug interaction can be useful. For example Risorine, an anti-tuberculosis drug has been developed on the basis of synergistic interactions of piperine from *Pippali* with rifampicin. Important mechanisms involved in ayurvedic- allopathic drug interactions are alteration of absorption and induction or inhibition of cytochrome systems. The methods to avoid these interactions include taking a detailed drug history before prescribing, correct timing of medications, identifying risky patients and risky drugs and proper regulation in the sale of medications. To conclude what

becomes important is creating a detailed database about clinically relevant interactions of Ayurvedic and Allopathic drugs.

KEYWORDS: Drug interaction, Ayurvedic, Allopathic.

INTRODUCTION

Use of alternative systems of medicine is at rise globally. Ayurveda, the oldest herbal system of medicine is the most commonly practiced alternative system in India fulfilling the medical needs of 80% of the population.[1] Many a times people tend to use more than one system medicine simultaneously. In a study conducted in Australia, 50% of people reported that they used alternative therapy along with conventional medicine.[2] For example, in Kerala, people prefer allopathic medicines for emergency conditions and Ayurvedic medications for chronic ailments like arthritis. Regardless of the system of medicine, it's an acknowledged fact that every drug, Ayurvedic or allopathic, has constituents in them that has the potency to affect metabolism. These chemical constituents may interact with each other. These drug interactions can affect the end result of either drug countering the effects or enhancing of the other drug, and at the end producing a better or worse, but certainly different outcome of the singular parts in their action. Some of the interactions may not be clinically relevant and some others may be beneficial for betterment of pharmaceuticals. So all the possible drug interactions should be listed out and important ones should be established. But there is a severe deficiency in studies reporting these types of interactions. This paper attempts to review major Ayurvedic- allopathic drug interactions.

METHODOLOGY

The study was a literary review study and a general Google search was done. The keywords used were 'interaction', herb-drug interaction' and interactions of individual drug.

RESULT

Drug interactions-Definition

Drug interactions result from the use of two or more drugs simultaneously. It is the modification of response to one drug by another when they are administered simultaneously or in quick succession.[3] This may lead to enhanced or diminished effect that may be useful or harmful. The action of one drug is affected by the other drug either quantitatively i.e. increased or decreased intensity of action or qualitatively, i.e. an abnormal or a different type of response is produced.

If any new symptom arise during treatment in a person receiving multiple medications and if more than one drug in this medication list is capable of causing the same new symptom, then the physician should always consider the scope of drug interactions. All drug treatment should be reviewed, if the clinical condition of a severely ill or elderly patient changes. A physician who is giving medicines to a patient already receiving treatment from another doctor or another system of medicine should be constantly alert to the possibility of drug interactions.

The physician should be aware of drugs prone to interaction and patients in whom interaction may occur. He should be cautious while administering two drugs with same pharmacological property, while combining drugs that affect the vital process in the body, drugs showing dose dependent toxicity, drugs whose loss of effect leads to breakthrough of disease. The patients more prone for drug interactions are elderly patients receiving many drugs, patients with unstable disease like epilepsy, patients with liver or kidney damage, patients receiving treatment for very serious condition and patients receiving medicine whose variation in dose or properties of drug can lead to death.[4]

When two or more drugs are given simultaneously or in quick succession, they may exhibit either synergism or antagonism. Drug interactions can be either synergistic or antagonistic. Synergism is when the action of one drug is facilitated or increased by the other. In a synergistic pair, both the drugs can have action in the same direction or given alone one may be inactive but still enhance the action of the other when given together. When one drug decreases or abolishes the action of another, they are said to be antagonistic. Usually in an antagonistic pair one drug is inactive as such but decreases the effect of the other. Of clinical significance is the unintended concurrent administration of synergistic or antagonistic pair of drugs with adverse consequences.

Mechanism of drug interaction

The mechanism of drug interaction is very complex and not completely understood. But it is generally considered that drug interactions occur due to pharmacokinetic or pharmacodynamic reasons.

A pharmacokinetic interaction means one drug altering the absorption, distribution, metabolism or elimination of other drug. The concentration of the drug at its site of action is altered by these types of interactions and as a result the intensity of response of the drug is

affected. For example *Aloe vera* a mild laxative reduces the intestinal transit time of orally administered drugs. This hinders the absorption of concurrently orally administered drugs. Drugs alter the absorption of other drugs by forming complexes with them in gut or by altering the gastric pH and thus decreasing the solubility of the other drug or by accelerating the absorption of other drug. Many drugs share the same transport system or protein binding sites and can interfere with the distribution of other drugs. Microsomal enzyme system especially cytochrome P450 have a major role in the metabolism of drugs. Synthesis of cytochrome P450 can lead to reduced efficacy of the drug. Agents like ethanol stimulate the synthesis of this enzyme system and can interact with drug metabolism. Drugs facilitate the excretion of concurrently administered drugs by increasing urine flow or by altering the pH of urine.

A pharmacodynamic interaction occurs in between drugs which act on the same target site. These 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. It mostly happens between drugs with same pharmacological activities on one system. For example *Sarpagandha* has synergistic effects when concomitantly used with other anti-hypertensive. These types of drug interactions mainly occur between drugs acting on the same receptor site or at different active receptors and thereby increasing or decreasing the response of one another.

Of all the mechanisms, the most important mechanisms involved in ayurvedic- allopathic drug interactions are alteration of absorption, for example laxatives and induction or inhibition of cytochrome systems, for example grape fruit juice, garlic, berberine of *Daruharidra*.

Drug interaction between Ayurvedic and allopathic drugs

The increasing popularity of alternative medicine has created a new situation-simultaneous use of medicines of more than one system of medicine. Ayurveda being the most popular alternative medicine in India, more and more Ayurvedic drugs are used by people simultaneously with allopathic medicines to treat the same symptom or any other symptom. Allopathic drugs for lifestyle diseases like diabetes, hypertension, thyroid medications are taken on daily basis and are lifelong. Simultaneously, patients take Ayurvedic medicines for arthritis, neurological complaints or skin diseases. And what is worse is that many Ayurvedic medicines are having over the counter profile than prescription medicine status. This creates an increasing chance for interactions between these drugs. Chances of interactions are more

with daily medication, medicines that affect vital functions and medicine with narrow therapeutic margin. Major herbs that are to be looked for interactions and the drugs with which they interact are given below.

Drug interactions involving *Guggulu* (*Commiphora mukul*)[5]

Guggulu is studied for interactions with hypolipidaemics, anticoagulants, antihypertensives and thyroid medications. *Guggulu* is well known for its hypolipidaemic property. Guggulusterone present in *Guggulu* lowers cholesterol by the following methods. It increases the rate of removal of cholesterol from the body, decreases the hepatic cholesterol biosynthesis and the ion exchange resin in the crude drug traps the bile acid containing cholesterol and thereby trapping it out of intrahepatic circulation. So *Guggulu* has synergistic effect when combined with hypolipidaemics. It potentiates the cholesterol and triglyceride lowering effects of hypolipidaemics. Thus it lowers the dose of the hypolipidaemic or eliminates the need of the drug. It should be used with caution when combined with warfarin and other anticoagulants, as it has antiplatelet activity and can increase the clotting time. It stimulates the thyroid gland and is especially useful where tri iodo thyronine (T3) levels are low. So it may alter the dosing requirements of thyroid medications. Guggululipid an active principle of *Commiphora mukul* when co-administered with propanolol, an antihypertensive or diltiazem decreases the bioavailability of these drugs. And also guggullipids is known to have anti-inflammatory activity and can reduce the dose of NSAIDs when used simultaneously.

Drug interaction involving *Rasona (Allium sativum)*

Rasona interacts with anticoagulants like warfarin and NSAIDs by decreasing platelet aggregation activity and may lead to bleeding tendencies. It may also interact along with high doses of alpha tocopherol that is vitamin E. It is reported to change pharmacokinetic variables of paracetamol, decreases blood concentrations of warfarin and produces hypoglycaemia when taken with chlorpropamide.[6] *Rasona* reduces the plasma level concentration of saquinavir, antiretroviral drug used in HIV therapy and can also interact with other protease inhibitors.[7]

Drug interactions involving *Aswagandha (Withania somnifera)*

Aswagandha has anxiolytic and mild sedative property and may potentiate the effects of barbiturates and sedatives when used simultaneously. The drug has additive effect when used in combination with diazepam. The combination when used in status epilepticus was able to

reduce significantly the effective dose of diazepam and offer complete protection with no subsequent mortality.

Drug interaction involving *Sunti (Zingiber officinale)*

Sunti can interact with anti-inflammatory medications such as ibuprofen. It can also interact with aspirin, warfarin, heparin and other drugs that effect bleeding tendencies or platelet count. The anti-inflammatory action of *Sunti* is thought to be due to the inhibition of prostaglandin release and may act in the similar way as NSAIDs, which interfere with prostaglandin biosynthesis. *Sunti* inhibit platelet aggregation and reduces platelet thromboxane synthesis and so can interfere with medications like anticoagulants.

Drug interaction involving *Jatamamsi* (*Nardostachys jatamamsi)*

Jatamamsi is to be given cautiously in patients on benzodiazepine or any other sedative medicine. It is also to be given with caution with anti hypertensive medicine as it may have additive effect.

Drug interaction involving *Yashtimadhu (Glycyrrhiza glabra)*

Glycyrrhizin in *Yashtimadhu* decreases plasma clearance, and increases plasma concentration of prednisolone and thus its action is enhanced. It also causes hypertension, oedema and hypokalemia when simultaneously used with oral contraceptives. It is reported that oral contraceptive use may increase sensitivity to glycyrrhizin. Women are reportedly more sensitive than men to adverse effects of *Yashtimadhu.* It should not be administered for prolonged time with thiazide and loop diuretics because it increases potassium loss.

Drug interaction involving alcohol

Arishtas and asavas are major dosage forms used in Ayurveda. They contain varying range of alcohol content. Alcohol is known to interact with aspirin and NSAIDs and cause increased risk of gastric mucosal damage and gastric bleeding. Many medications cause an unpleasant hypersensitivity to alcohol called “disulfiram effect”. Examples of such medications are antibiotics like metronidazole and tinidazole, sulfonylureas like tolbutamide etc.

Other examples of Ayurvedic- allopathic drug interactions

Concomitant use of castor oil (*Ricinus communis*) reduces the efficacy of antiarrythmic drugs, diuretics, fat soluble vitamins and antihistamines.[8] As it contains L-dopa, *Kapikachu (Mucuna pruriens)* may potentiate the action of anti parkinson’s medicine. *Bhanga (Cannabis*

sativa) have additive effects with barbiturates potentiating its depressant action. It should be used cautiously with antihistamines, phenothiazines and benzodiazepines. *Tulsi (Ocimum sanctum)* has been reported as hepatotoxic in rats with glutathione depleted liver. So concurrent use with paracetamol which depletes glutathione may be harmful. Piperine in *Pippali(Piper longum)* increases the concentration of phenytoin, propanolol and theophylline.[9] Other examples include the interactions of herbs like *Methika (Foeniculum vulgare), Meshasringi(Gymnema sylvestre)* etc. with antidiabetic drugs, berberine in *Daruharidra (Berberis aristata)* with hypolipidaemic drugs like statins and *Vasa* (*Adathoda vasica*)with theophylline, a bronchodilator.

Benefits of drug interactions

Proper knowledge of drug interaction can have radical effects in future pharmaceuticals. For example Risorine, an anti-tuberculosis drug manufactured by Cadila combines rifampicin and piperine. This has been developed on the basis of synergistic interactions of piperine from pippali with rifampicin. It contains almost sixty percent less dose of rifampicin than usual.[10]

Women being treated for polycystic ovary syndrome with spironolactone has side effects of diuresis, low blood pressure, volume depletion. Studies shows that these side effects can be reduced by combining spironolactone with *Yashtimadhu.* In patients of PCOS the mineralocorticoid properties of *Yashtimadhu* can reduce the prevalence of side effects related to the diuretic activity of spironolactone. Studies also showed that the combination of *Yashtimadhu* and spironolactone reduced the prevalence of metrorrhagia in studied population.[11]

Methods to avoid drug interaction

Today when more and more people are using one or more systems of medicine for same or different diseases, drug interactions can happen. There are no fool-proof methods to avoid these interactions as there mechanisms are ill-understood and complex. But based upon the present knowledge we can devise some basic necessary steps towards preventing this issue.

They include

- Taking a detailed history of all the drugs used by an individual before prescribing
- Correct timing of medications.
- Administer drugs with caution in elderly patients and patients with kidney and liver damage

- Be careful while combining drugs with same pharmacological property and drugs that affect vital process in body and drugs having narrow therapeutic index.
- Strict regulation on the sales of Ayurvedic medications as many of it are taken without prescription of a registered practitioner.
- Identify drugs that are possible candidates for interaction.
- Create database about clinically relevant drug interactions.

CONCLUSION

The increasing popularity of Ayurveda has led to the concurrent use of the medicines in the system with allopathic medicines. The free availability of even single drug choornas as over the counter medicine and its irrational use at any time concurrently with any medicine has increased the chance of drug interactions. A detailed study on the possible candidates of Ayurvedic and allopathic drugs which may interact with each other is needed and it should be established by experimental studies. Also the beneficial combinations can be found out and used for removing the side effects of or decreasing the dose of important drugs. To conclude what becomes important is creating a detailed database about clinically relevant interactions of Ayurvedic and Allopathic drugs and making awareness about these types of interactions so that the patient's life will never be at risk.

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