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CONCEPT OF DRUG INTERACTIONS IN AYURVEDA

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ABSTRACT
A Drug interaction is a situation in which a substance (drug/food) affects the activity of a drug when both are administered together. Drug interaction can have reduction / enhancement in therapeutic effects or increase in the adverse effects of the drugs. Drug safety is a very basic and fundamental concept of medical practises. Therefore the systematic knowledge of drug interaction in particular on the level of absorption, elimination, transport and drug metabolism may help to prevent adverse effects. Though Ayurveda is an ancient science, scholars had the knowledge of drug interactions and was expressed in different contexts like Pathyapathya along with the drug (Diet), Aushadhasevanakala (Time of drug administration), Anupana/Sahapana (Vehicle), Virudhaahara/aushadha (incompatibility), Prativishadravyas (Antidote). In this article an attempt was made to highlight these different areas of drug interactions.

KEYWORDS: Drug interaction, Pathyapathya, Aushadhasevanakala, Anupana, Virdhhaahara, Prativisha.

INTRODUCTION

Many problems in pharmacotherapy result due to drug interactions. Drug interaction is a consequence in which the effects of one drug are altered by prior or concurrent administration of drugs or food. This results in synergistic (enhanced) or antagonistic (decreased) effects may be harmful or beneficial.[1] These interactions may occur due to accidental misuse or due to lack of knowledge about the action of ingredients involved in the relevant substances.

These interactions may occur either due to pharmacokinetic or pharmacodynamic reasons. When the absorption, distribution, metabolism and excretion of one drug are affected by another drug then that is said as pharmacokinetic interaction. Pharmacodynamic drug interaction includes alteration of pharmacological action of the drug. A drug showing opposite pharmacological action on the same physiological system is known as antagonistic effect or antagonism. A drug showing some pharmacological action on the same physiological system is known as synergistic effect or synergism.[2]

Like drug, foods are not tested as comprehensively so they may interact with prescription or over the counter drugs. Drug interactions can produce negative effects in safety and efficacy of the drug therapy, as well in the nutritional status of the patient. Like food, drugs taken by the mouth must be absorbed through the lining of the stomach or the small intestine. Consequently, the presence of food in the digestive tract may reduce the absorption of a drug. Often such interactions can be avoided by taking the drug one hour before or two hour after eating. Therefore it is advisable for the physicians to give proper instructions to the patients to obtain maximum benefits with least food drug interactions.

DIFFERENCE BETWEEN DRUG AND FOOD

In Vedic science food and drug both are considered as Bheshaja, where food is named as Ayushyani, means the one which used for the prolongation of lifespan.[3] According to Charaka Samhita whatever substances are found in the nature are also found in the body. Thus man is said to be a miniature form of nature. Deficit of these substances in the body can be corrected by using them from nature to nourish him as a food and treat the diseases as a medicine. But for the food only herbal and animal origin safe substances are taken into consideration as a source, for the preparation of medicine along with these two sources, importance is also given to mineral origin substances. Hence the shloka“nanaushadhibhutamjagathikinchitdravyamupalabhyate”.[4] Food is said as rasa predominant means they were rich in primary metabolites like carbohydrates, proteins, fat, minerals and vitamins. Classically it is mentioned as “shadrasopetammadhuraprayaha” Whereas medicine is predominant of veerya i.e. secondary metabolites like alkaloids, glycosides, tannins etc., they exert a physiological and therapeutic effect. Here selection of rasa of medicine depends on vitiation of

dosha in that particular disease. Other difference between food and medicine is in quantity (dose). In case of food quantity depends on the state of agni, but medicine dose is fixed on the basis of many factors like kala, agni, vaya, bala, prakruti, dosha, desha and kosta.[5] In the condition of disease, patient should be under proper diet (pathyaahara), where quantity is mentioned as one fourth of the normal food that he is consuming in healthy state.

CONTEXTS OF DRUG INERACTION

Though Ayurveda is an ancient science, scholars had the knowledge of drug interactions in detail at that period and it was expressed in different contexts like Pathyapathya along with the drug(diet), Aushadhasevanakala (time of drug administration), Anupana/Sahapana(vehicle), Virudhaahara/aushadha (incompatibility) and Pratvishadravyas(antidote).

In drug interaction food /drug affects the activity of the main drug, when both are administered together. Accordingly drug interaction is classified as drug and drug interaction and drug and food interaction. Pathyapathya and Aushadhasevanakala these two comes under drug and food interaction, whereas Anupana, Virudhaaushadha, Prativisha are drug and drug interactions.

DRUG AND FOOD INTERACTION

Pathyapathya

Pathya can be defined as small quantity of food which does not interfering with the normal functioning of the srotas(channels) and that is appealing to the mind.[6] This means with this food, drug provides better therapeutic effectiveness through proper absorption and assimilation and also it does not produce antagonistic or harmful effect by interacting with the food. Apathya is one such a food that interferes with normal pharmacokinetics of the drug hence lesser ability to produce the action. For example, a group of drugs called Kakarastakagana (Kushmanda, Karkati, Kalinga, Karavellaka, Kusumbha, Karkota, Kadali, Kakamachi) are said to beapathya along with medicines prepared with Parada(Mercury) as it has got laxative property; it makes the excretion of drug early without giving proper time for absorption. Hence the same drugs of Kakarastaka are also said as antidote for Mercury poisoning. Along with Parpatikalpana, amlarasadravya(sour) and guda(jaggery) are said to be apathy, as they have got sara(laxative) property which will increase the motility of intestine hence no desired effect. Kshara(alkaline) and amla(sour) substances are said as apthya along with Abhrakabhasma. Abhrakabhasma has got madhuravipaka and these apathyas have opposite properties, hence they may inhibit or produce untoward effects on the body. Intake of Shilajitu along with Kulatha is said as “athyantaviruddha” (absolutly opposite) means interaction of these might produce antagonistic or toxic effects on the body due to complex formation. Hence the proper knowledge about the pathyapathya along with the drug is very essential to get the desired results from the drug. Masha (Blackgram) is said as apathya along with Lohabhasma. The same is accepted by modern physicians as it contains oxalic acid and phytates which reduces the ability of the body to absorb iron. Ashwini Ambalpady has worked on the topic “An experimental evaluation of impact of Masha as an apathya in the haematinic activity of Loha bhasma”.[7] Wherelohabhasma was administered in Albinorats along with Masha and response observed is compared with control group. Final result showed significant decrease in the haematological values in the group, where Loha Bhasma was given along with Masha as a food.

Aushadhasevanakala

According to Ayurveda classics, a healthy person should have food twice in a day i.e morning and evening. The food that is in the course of a process of digestion should not get mixed with the food in a different stage of digestion, hence it is advised so. Oushadhasevanakala i.e time of drug administration has got greater importance in the treatment of a disease. This has to be prescribed taking into consideration of time of food intake, involvement of doshaand area of the body which is to be affected in the particulardisease. Also physician should see the strength of disease and patient. As per Acharya Sushruta[8] aushadhasevanakalas are 10 in number. Acharya Vriddha Vagbhata added one more for this as nishi.[9] Among that abhakta, antarabhakta and nishi are the three times where drug is administered in empty stomach. Abhakta means in the morning after complete digestion of food indicated in kapha and pittaja diseases, whereas in case of antarabhakta drug is taken in between the meals after digestion of morning food. Evening food is given after digestion of medicine. Similar thing is followed in case of night and morning food. This time is indicated in diseases of vyanavayu. Nishi means night at the time of sleep that means after digestion of evening food and is indicated in the diseases pertaining to urdhwajatru(above the clavicle). As in all the three times drugs are administered in empty stomach drug will remain more concentrated without the contact of food hence the quick therapeutic effect. The same is said in Sushrutasamhitaas“veeryadhikambhavatibheshjamannah eenamhanyat tadamayamasamshayamaashu”.[8] But it should be followed in those patients have the ability to tolerate the potency of the drug. According to modern concept in the fed state bioavailability of the drug reduces, results in risk of treatment failure due to chelation of drug with the components of food or by the direct interaction between the drug and certain food components. In remaining all types of aushadhasevanakalas, drug is administered before, after, in between or along with the food. It mainly depends on the type of vatadosha affected as well as area of the body where the drug action is required. It says that food restricts action of drug to particular area of the body. If the drug is taken before food its action is limited to lower parts of the body. If it is after food, action of drug is restricted to upper parts of the body. Drug administered in between the food produces action only in the kosta.

For example in case of mutravarodhajanyavyadhi, Avapeedakasarpi was advised before food as there is vitiation of Apanavata and disease is limited to lower parts of the body. The word avapeedaka implies the meaning of either peedana(pushing down) of doshas or peedana of food. In Bahushosha, Kalyanakaghrita was advised after food. Guda Hareetaki given in abhaktakala is useful in Arshas and at pragbhakatakala it is useful in Udararoga. Advantages of drug and food interaction is said as bhojanavritaannagunas by Sushruta as "sheeghramvipakmupayatibalamnahimsyadannavrutamn a cha muhurvadanannireti".[8] With food, drug digestion becomes fast, more drug tolerance due to drug dilution and prevents vomiting of drug due to food coverage. As per modern concept concomitant food intake may result in an increase in drug bioavailability either because of food induced increase in drug solubility or because of the secretions of gastric acid or bile in response to food intake.

DRUG AND DRUG INTERACTIONS

Anupana/Sahapana

In the text Rasatarangini, anupana is defined as a medicine having similar therapeutic action as that of main drug and when given together enhances the therapeutic efficacy of the main drug.[10] So this is a kind synergistic drug and drug interaction and is of pharmacodynamic variety. For instance Shwetaparpati and Badarshmapisti both are indicated in Mutrashmari(urinary calculai). Enhanced efficacy is observed inboth when they administered with Kadalikandaswarasa(juice of root of banana plant) as anupana. One study was carried out by Shweta on anupana with the topic "An experimental evaluation of role of anupana in the purgative action of Ichchabhedi rasa w.s.r. to sheeta and ushna jala".[11] As per classical reference anupana of Ichchabhedi rasa is cold water. In this study Ichchabhedi rasa was given in two groups of Albino rats with cold and hotwater respectively and results were observed. Maximum purgation was observed in a group with cold water anupana, whereas hot water showed minimum purgation. This says about how the anupanachanges the therapeutic efficacy of the drug through ineraction. Anupanahelps producing target specific action. For instance, Kajjali has got therapeutic action on almost all the diseases, but with specific anupana it becomes more target specific. Makaradwaja is useful in Jwara(fever) when given with Ardhrakaswarasa and in Rakatpitta(bleeding disorder) with Vasa swarasa. Pravalabhasma is affective inShushkakasa(dry cough) with sharkara as anupana, but in Kaphajakasa(productive cough) it is more affective with madhu. In case of Mutrakrichra (difficulty in urination) same Pravalabhasma is given with tandulodaka(water obtained by washing rice). In Pradara it is given with milk. Better and quick action of medicated ghee will be obtained with hot water as anupana, as it helps in easy disintegration of the ghee hence quick absorption. This is a kind of pharmaco kinetic interaction. Anupanaalsohelps in rectifying the untoward effect of some of the medicines. For exampleushnaveerya (heat generating property) of Rasasindhura, Makeradwaja, Sameerapannga rasa, Mallsindhura is nullified by administering them with Pravalabhasma and milk, which is of sheetaverya(cold property) and madhuravipaka respectively. It is safe to administer of Asava/Arista with water as it reduces gastric irritation because of dilution.

In the same text Rasatarangini[10], definition of Sahapana is mentioned as a medicine, when it is given along with the main drug it helps in the easy disintegration and assimilation of main drug. Again this also a kind of drug and drug interaction and is of pharmacokinetic variety.

Virudhaahara/aushadha

When two or more drugs are combined, Virodha (incompatibility) is the most important point to be kept in mind. Acharya Charaka[12] has described it in detail in the context of diet. For the practical purposes, in relation to drugs the following may be useful. Those are (i) manavirodha(quantitative incompatibility) example: honey and ghee in equal quantity, (ii) gunavirodha(chemical incompatibility) example: milk and salt, (iii) karma virodha (pharmacological incompatibility) example: Dhataki and Danti. All these examples says about antagonistic drug and drug interactions and it might be toxic to the body, hence the disease manifestation. If consideration is given to the aetiopathogenesis of different diseases as per Ayurvedic concepts one of the most frequently quoted cause for triggering patho-physiological events in majority of the disease condition is the viruddhaahara. Hence the physician should critically examine the compatibility of the food of the patient with the drug to avoid the manifestation of complications. Shweta worked on this concept with the title "Experimental evaluation of toxicological implication of the combination of Kadaliphala and Goksheera w.s.r. to the concept of Samyoga viruddha[13]". Study was conducted for a period of 28days. In the antioxidant study the individual samples of kadaliphala and milk showed presence of high levels of antioxidants. Whereas in the combination showed reduced levels of antioxidants. Histopathological study has shown moderate mayocarditis in the section of heart, micro fatty changes in the liver, moderate increase in the white pulp portion of spleen. Kidney function test has shown significant elevation in the serum urea level andit might be due to excessive catabolism of bodily proteins. Decrease in food conversion ratio indicates hampered absorption and assimilation of the taken food by the rats.

Prativisha

Prativisha (antidote) can be defined as an agent used to neutralize or counteract the efficacy of a poison. In case of mercury poisoning Shudha Gandhaka along with ghee and milk is said as prativisha as Gandhaka has got laxative action with ghee and milk has got demulcent action. This is a kind of pharmacokinetic interaction as it interferes with the absorption of mercury. Excessive

dehydration due to the intake of Kampillaka can be corrected by giving decoction of Babbulamulatwak with Jeera, because of opposite actions like sthambhana and grahi respectively. Shilajitu toxicity can be corrected by administering Maricha along with ghee through neutralization. In case of Haratala poisoning Kushmandaswarasa is given along Jeeraka and madhu. Kushmandacontains calcium, phosphorous, iron, sodium; potassium. Calcium is antagonist of arsenic, phosphorous interferes with arsenic function and iron, sodium, potassium forms insoluble precipitate. All examples are for antagonistic pharmacodynamic interactions. Shanker did work on the concept of prativisha with title "An experimental study on the antidote effect of chitrakapatrakalka along with navaneeta in Kupeelu poisoning".[14] Reversal of hematological, biochemical and histopathological changes induced by Kupilu seed poisoning can be considered as strong evidence for the antidotal effect.

CONCLUSION

To conclude, the oral route of drug administration presents numerous challenges to patients in predicting the outcome of their medications, because of all the different medications, food, liquid and other factors involved with it. Medicine can treat many health problems; however they must be taken properly to ensure that they are safe and effective. Ayurvedic medicines are now available in the market as over the counter products. Today people use prescription and non-prescription medicine along with Ayurvedic medicine for quick relief from ailments. Safety aspect of this kind of administration is still questionable. Many of these medicines can interact with Ayurvedic medicines; can cause either potentially dangerous side effects or reduced benefits from the medication. Therefore it is advisable for the patients to follow the physician's instruction to avoid the serious side effects during medication because of drug interactions. Acharya Charaka[15] has clearly mentioned that, an effective medicine can prove to be a fatal poison if it is used injudiciously and a strong poison to be very effective medicine with judicious use.

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