

CONCEPTUAL STUDY OF GARAVISHA WITH SPECIAL REFERENCE TO ADVERSE EFFECTS OF CARBOPLATIN

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ABSTRACT

In Ayurveda the *Gara visha* is considered to be as one of the form of *Kritrim visha*. *Agad tantra* which is one of the branch of *Ashtang Ayurveda* has given more emphasis over *Garavisha* (Artificial poisons) as well as natural poisons ie. *Sthavar* and *Jangam* visha. It is formed by combination of two or more than two poisonous or non-poisonous drugs, which ultimately affects the whole body by vitiating all the *doshas*, *dhatus* and *srotas* in the body. Detailed explanation of the *Garavisha* i.e. its definition, sign and symptoms, mode of administration and treatment has been described in our *Samhitas*. Cancer is second leading cause of death and it is one of the Global burden. Most Cancers diagnosed in late stage so Chemotherapy is choice of treatment. It includes immunosuppressive drugs which help

to prevent the growth of the cell but damage the healthy cell. Carboplatin is anti-cancer cytotoxic drug used in Chemotherapy. Long exposure to Chemotherapeutic drugs produces the toxicity which will be correlated with the concept of *Garavisha* in *Ayurveda*. As the toxogenesis and symptoms of *Garavisha* mentioned in ayurved is quite similar to drug toxicity. Hence *Chikitsa sutra* of *Garavisha* will be applied for the cumulative toxicity which is produced by chemotherapeutic drug (Carboplatin) which is used during chemotherapy. This article review based on the concept of *Garavisha* which can play significant role in adverse effects of Carboplatin and *ayurveda* can provide effective management also. It is burning

issue of this era because Cancer is most prevalent life threatening disease.

KEYWORDS:- Garavisha, Carboplatin, Chemotherapy, Cumulative toxicity.

INTRODUCTION

Cancer is second leading cause of death and it is one of the global burden. Cancer is uncontrolled division of abnormal cells, anywhere in body. Cancer is caused by mutation of DNA About 1 of 6 deaths caused worldwide due to cancer. Most common cases of cancers are breast prostate stomach, skin lung, liver, colorectal.^[1] In 2022, 1,918,030 new cancer cases and 609,360 cancer deaths are projected to occur in the United States, including approximately 350 deaths per day from lung cancer, the leading cause of cancer death.^[2] Tobacco related Oral cancer common in males and cervical cancers in females. In management of cancer various therapies are used such as surgery, immunotherapy, biological therapy, radiation therapy, photodynamic therapy. Chemotherapy is most commonly used in the treatment of cancer. It includes immunosuppressive drugs which help to prevent the growth of cells but also damages the healthy cells.^[3] Platinum coordinator complexes include the drug Cisplatin and Carboplatin.

Carboplatin is anti-cancer cytotoxic drug used in chemotherapy. It affects bone marrow and developing cells in it. Carboplatin is widely used and second generation chemotherapy drug. It is cytotoxic drug and effective in various cancers and preventing the growth of neoplasm. It causes damage to DNA in developing cell of Bone Marrow and leads to destruction of cells and resulting in bone marrow suppression.^[4]

Garavisha is prepared artificially by mixture of various substances to produce various diseases. *Kritrimvisha* is called as *Garavisha* according to *vagbhatta*.^[5] *GaraVisha* means the *Dravya* (substance) causes *Vishaad* (sorrow or depression) is also known as *Visha*. *Laghu ruksha, aashu, vishad, vyavayi, tikshna, vikaashi, sookshma, ushna, anirdeshya rasa* are the ten qualities of poisonous drugs.^[6] So substance which when administered, inhaled or ingested capable of acting deleteriously on human produces ill health. Poison may be synthetic, mineral, vegetable or of animal origin *Garavisha* is them.^[7] Ayurveda has elucidated *Garavisha* as non-natural poison. Wonderful concept of *Garavisha* explained by Ayurveda. Today man is commonly unprotected to these artificial poisons which are primed combination of poisonous and non-poisonous substances. Hence it is the need of the hour to be correctly about all the potential toxins which we are exposing unknowingly, *Garavisha* is

often consumed unintentionally, Hence the person doesn't feel anything proximately and even delayed onset of symptoms makes treatment bit difficult. In the diagnosis of *Garavisha*, *darshana*, *sparshana*, *prashna* has basic *rogi parikshan* mention in *Ayurveda*. *Sanshodhan* is half treatment in *Ayurveda*, without *sanshodhan* treatment of *Garavisha* is not possible. Copper dust with honey which is good stomach cleanser mentioned by *Acharya Charaka* in the treatment of *Garavisha*. Gold quickly destroys all kind of poison which may be natural or artificial in origin. *Virechana* also helps the body to remove the *prakropit doshas* and cleans the body. *Ayurveda* play an important role in management of *Garavisha*. [Pandit Kashinath Shatri 2011]

AIM AND OBJECTIVES

Aim

1. To study the correlation of *Garavisha* with adverse effects of Carboplatin.

OBJECTIVES

1. To study the *Garavisha* in detail.
2. To Study the adverse effects of Carboplatin in Chemotherapy.

MATERIALS AND METHODS

The study based on the literature review of relevant ayurvedic text with commentary necessary and valid interpretation.

The description of Carboplatin drug is obtain by searching various medical research database like Pubmed, Google scholar and other natural Database.

Garavisha

Nirukti

The 'Gara' word is derived from the root word *gru* with suffix *ach* which means to digluted or could be digluted which generally indicates the liquid form.^[8] From one aspect this word (*Gara*) meaning also come as poison.^[9]

Paribhasha

CHARAK SAMHITA

Gara is a toxic combination of poisonous or non-poisonous substance and which exerts toxic effect after interval of some time and as such does not kill the patient instantly. In addition to *sthavar* and *jangamvisha* there is one another type of poisons which is called *Garavisha*. It

creates many disease, *Garvisha* are not to digested they take long time to digest hence they are not fatal.^[10]

SHUSHRUT SAMHITA

The pulverized bodies of insect poisoning, as they do, the characteristic features of *Dushivisha* or enfeebled poison [laying inherent in human system] is turned into a *Gara* or chemical poison if administrated internally with any medicine or externally with any plaster/lepa.^[11]

VAGBHATA SAMHITA

Combination of parts of body and excreta of different animals, incompatible drugs, ashes and poisonous substance of mild potency is known as *Garavisha*.^[12]

Vagbhatta classified poison into two types.

One is the *Akritrimvisha* [natural poison] and this subdivided into two i.e. *sthavara* and *jangam*. The other one is the *kritrimvisha* which is called as *Garavisha* [unnatural or chemically preparedpoison].^[13]

BHAVPRAKASH

Bhavprakash the *kritrimvisha* in different manner. The *kritrimvisha* is one which is prepared bynon-poisonous substance called as *Garavisha* and another which is prepared by poisonous substance is called as *Dushivisha*.^[14]

YOGRATNAKAR

Yogratnakar also classified the *kritrimvisha* in two one which is prepared by combination of twopoisonous substances called *Dushivisha*. And other which is prepared by combination of two non-poisonous substances called as *Garavisha*.^[15]

SHARANGDHAR SAMHITA

Sharangdhar classified *KritrimVisha* in to two types, one of them is *Garavisha* and other is *Dushvisha*. *Dushvisha* is prepared by the combination of two poisonous substances and *Garavisha* is prepared the by combination of two non- poisonous substances.^[16]

MADHAVNIDANA

Madhavnidhana classified *Samyogajvisha* in to two types, one is *Kritrimvish* which is prepared by poisonous substance and other is *Garavisha* which is prepared by nonpoisonous substance.^[17]

CHAKRAPANI

In his commentary he described the *Samyogajvisha* is one of two types one which is prepared by non-poisonous substance called as *Garavisha* and another one which is prepared by poisonous substance called as *kritrimvisha*.^[18]

Symptoms / Lakshana of *Garavisha* Acharya charak^[19]

-*Pandu* (pallor skin)

-*Krishna*

-*Madagni*

-*Adhman*

-Fever

-Edema on hands and feet

-*Grahani*

-*Rajyakshma*

-*Gulma*

-*Udarrog*

-In dreams he mostly sees cats, jackals, moongoos, monkey, dried rives and trees.

-In dreams having lost his sense organs, he sees himself as fair complexion or devoid of ears and nose.

***Vagbhatta*^[20]**

-*Pandurog*

- *Udarrog*

-*Mandagni*

-*kaas, shwas*

-Edema

-*Adhman*

- Fever

-Increase the length of liver stomach & spleen

-*Dhatu kshaya*

***Yogratnakar*^[21]**

-*Pandu*

-*Krishna*

-*Mandagni*

- Laziness
- Heaviness
- Cough
- Dyspnea
- Loss of strength
- Edema
- Hemorrhage
- Yellow discoloration of eyes

Diagnosis

Clinical Examination account to *Ayurveda*

Trividha Pariksha [Banwari Lal Gaur, 2017]

It is unique concept in *Ayurveda* and it is play major roll to diagnose the disease which is *Darshan* (Inspection), *Sparshan* (Palpitation) *prashna* (Questioning).

1) Darshan

It is inspection done by netras(eyes) of physician which is nothing but visible sign of *Garavisha* which are paleness (*Pandu*), *Krushta*, Inflammation (*Shopha*) Which are evaluated by inspection which are major sign of *Garavisha*.

2) Sparshan (Palpation)

It is the process of using one's hand to check the body, especially while diagnosing a disease or illness. Liver, Spleen, Abdomen to detect the any organomegaly, ascites or swelling and tenderness.

3) Prashan (Questioning)

It is done by asking a questions to the patient about symptoms which is found in *Garavisha*.

Management of *Garavisha* in *Ayurveda*

1. Sansodhan Vaman

According to *Acharya Charak*, *Vaman* is given by Copper dust mixed with Honey is act as a good stomach cleanser. The main aim is to purify the blood and regulate the circulation because blood is main source of creation of disease. After *Hridaya* is detoxified, Colliodal powder of Gold (*I Shaana*) is given which destroys all kinds of poison and increase the appetite of patient.^[22]

Verechan

Nagdantayadi ghr̥it in 4gram will be given mixed with *trivrit kwath* 100ml which prepared by using its therapeutic dose 3-6 *mashe*. The *virechan vegas* will be countered and recorded.^[23] (Pandit kashinath shastri2011)

2. Sanshaman

Acharya Charak has mentioned *Amrit ghr̥ita* Twice in day.^[24]

Acharya Vagbhatt has mention *Murvadi yog* 250 mg twice a day for *Garavisha*. (Banwari lal Gaur 2007).

CHEMOTHERAPY

Chemotherapy is a drug treatment that uses powerful chemicals to kill fast-growing cells in your body. Chemotherapy is most often used to treat cancer, since cancer cells grow and multiply much more quickly than most cells in the body. Many different chemotherapy drugs are available. Chemotherapy drugs can be used alone or in combination to treat a wide variety of cancer. However, while the purpose of chemotherapy medications is to reduce your cancer symptoms and lengthen your life, the drugs can also have unwanted effects on your body. Chemotherapy can poison your body and lead to harm, and this is known as chemotherapy toxicity. Platinum compounds were introduced in the early 1970s as experimental agents following the observation that they inhibit bacterial cell division. Platinum compound included the drug Cisplatin, Carboplatin and Oxaliplatin.^[25]

CARBOPLATIN

It is less reactive second generation platinum compound and it is better tolerated. Nausea and vomiting is milder and is delayed - only infrequently limits the dose. Carboplatin is Platinum compound is being used in inhibition of the growth of the cancer. Mainly Carboplatin used DNA and proteins causes apoptosis and inhibition in that cell growth. It does not affect nephrotoxicity and peripheral neuropathy. It is administered as infusion into vein for at least 15 minutes. It is applicable in headache, breast, lung and ovarian cancers. The known side effect of Carboplatin are Bone Marrow suppression, weakness, nausea, vomiting and abdominal pain, temporary hair loss and Vision loss may occurs with high doses of Carboplatin. The dose limiting toxicity is Thrombocytopenia and less common leucopenia and Liver dysfunction may occurs. Because, of less plasma protein binding, it is rapidly eliminated by the kidney with plasma and 1/2 is 2-4 hours. It is primarily indicated in Ovarian Carcinoma of epithelial origin, and has shown promise in squamous carcinoma of

head and neck small cell lung cancer, breast cancer and seminoma.^[26] Hematological toxicity is dose limiting for carboplatin, with thrombocytopenia being a greater problem than leucopenia. Although carboplatin is not toxic to the kidney, renal function markedly affects the severity of carboplatin-induced thrombocytopenia. In chemotherapy drug act like a poison and they fall under the category of *Garavisha*, depending the potency of chemicals, they may act or cause any impairment after a break, from days to month.^[27]

While estimates of the overall incidence of carboplatin hypersensitivity vary, it is important to understand that the cumulative incidence of carboplatin hypersensitivity increases considerably in proportion to the number of cycles administered.^[28] Patients receiving five or fewer cycles of carboplatin were reported to have a 0.92% incidence rate of hypersensitivity, with the cumulative risk increasing to 19.5% among patients who have received eight cycles.^[29]

Adverse Effects Of Carboplatin^[30]

Common

Increase risk of infections

Breathlessness and looking pale

Tiredness and weakness during after treatment Feeling of being sick

Pain in different parts of body

Allergic Reactions Hairloss

Urine and Kidney Problems Diarrhoea

Numbness and tingling in in hands and feet Changes in your blood pressure Inflammation of Digestive system

Feeling very sleepy Fluid build-up (swelling)

Occasional

Loss of taste Tinnitus

Changes in heart rhythm and rate

Changes to the lung tissue that can cause cough and breathlessness

Constipation

Difficulty sleeping

Problems when you move or walk

Feeling worried or affecting the way you think about things

Fainting

Flu like symptoms, including fever, chills, headache, muscle or body aches, cough, sore throat,runny nose, and feeling tired.

Rare

Swelling in lower legs

Chest pain

Risk of developing a second cancer such as Acute Myeloid Leukemia (AML) Peeling and blistering of skin.

Cumulative toxicity

It is the undesirable impact produced by the assimilated poisons. Poisonous substance from totally diversified sources like food, medicine and external atmosphere could cause cumulative toxicity. This kind of poison primarily depends on absorption, biotransformation and excretion However cumulative toxicity is a predictable unfavorable reaction. Any drug can gather within the body if the speed of administration is higher than the rate of elimination. This means if a drug is excreted slowly, its perennial administration could build up a sufficiently high concentration within the body to supply toxicity.^[31] Rechallenge with platinum-based combination regimes is commonly limited by the risk of cumulative long-term toxicities. Not all patients can continue with platinum at second-line or, indeed, further relapses due to loss of activity or toxicity-related issues including hypersensitivity, neurotoxicity, alopecia and ototoxicity. In particular, hypersensitivity reactions are a concern and have been reported in approximately 15-20% of women receiving the drug.^[32]

DISCUSSION

Due to changing life styles, people are exposing to many kind of poisons in their day to day life. This exposure is in the form of drinks, foods, cosmetics, drugs etc. In Ayurveda, *Charak* and *Vagbhata* both said that *Garavisha* produces various diseases like swelling, anemia etc which can be compared with adverse effect of Carboplatin drug which is used in chemotherapy. *Pandu* is correlated with changes in heart rhythm and thrombocytopenia, *Mandagni* is correlated with loss of appetite, loss of taste. *Jwara* is correlated with flu like symptoms including fever with chills, headache, loss of taste, pain in different parts of body, *Grahani* is correlated with inflammation of Digestive system, diarrhea, loss of appetite. *Dhatu kshaya* is correlated with tiredness and weakness during and after treatment, feeling of being sick, increase risk of infections, looking pale. *Rajyakshma* can correlate with looking pale, changes in lung tissue, Dyspnea, cough and breathlessness. Some Psychological

symptoms in *Garavisha* are correlated with feeling worried, depression, feeling very sleepy i.e. the some psychic adverse effects of Carboplatin.

CONCLUSION

Garavisha is Artificial Poison, which is the wonderful concept explained by *Ayurveda*. *Garavisha* tends to accumulate in the body and symptoms are produced due to vitiated *Kapha*. *Vaman Chikitsa* is employed for removal of accumulated poison in GIT and detoxification of body in *Garavisha*. The possibility of exposure of toxins due to using many chemotherapeutic agents act like cumulative poison which can be correlated with concept of *Garavisha* in *Ayurveda*. In *Ayurveda*, Management of *Garavisha* is explained very nicely which helps body to detoxify. *Chikitsa Sutra* of *Garavisha* can be applied for better management of chronic toxicities of such chemotherapeutic drug Carboplatin. From Discussion, we can conclude that *Garavisha* deteriorate the well being of individual and produces symptoms after long time period and due to it's nature of being *Kalantar vipaki* which can be correlated with the adverse effects of Carboplatin Drug. The article aims to understand the concept of *Garavisha* and relation of *GARAVISHA* with adverse effects of Carboplatin Drug in chemotherapy. For this further study is needed in future.

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