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Dushivisha In Chemotherapy Induced Toxicity: Recognising The Usual Suspects

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ABSTRACT: -

Visha (Poison) is a substance that causes vitiation of seven dhatus on ingestion and can also leads to death. Synthetic toxins, pharmaceutical medications, etc are few of the toxins that can enter the body and turning into *visha* if they aren't completely cleared out of the body. In Ayurvedic texts, it is called *Dushivisha* (cumulative toxin*).* Cytotoxicity is an undesired response to drug delivery in which the drug or an active metabolite causes significant cell damage. Chemotherapy, a cancer treatment in which antineoplastic cytotoxic medications accumulate in the body rather than being completely removed, causes toxicity with signs and symptoms comparable to *Dushivisha*.

KEYWORDS: - *Dushivisha*, cumulative toxicity, chemotherapy toxicity, latent poison.

INTRODUCTION: -

One of the most significant health problems that is becoming worse is toxicity. It is an inherent potential or capacity of a substance to cause adverse effects in a living organism. A toxic substance cause damage if administrate in a very small amount but a substrate of toxicity will not produce until and unless the amount is large enough. Variety of medicines in form of chemotherapeutic drugs are being consumed in cancer through a variety of means. When favourable condition comes, it is then accountable for the delayed or cumulative toxicity which referred as *Dushivisha* (latent poison).

Thus, *Dushivisha* refers to denatured poisons, or poisons that do not completely expelled from the body. According to *Aacharya Sushruta*, a poison that is vitiated by habitat, season, food, and *diva-swapna* (after noon sleep) that vitiates the *dosha, dhatus* is known as *Dushivisha*. A component of *sthavar* (plant poisons), *jangham* (animal poison), or *kritrimVisha* (artificial poison) that is not eliminated from the body, but whose potency is reduced by the effects of *aatap* (sunlight), *vayu* (air), *vyavayi*, and *vikasi*, this cumulative poison remains in the body.

Dushivisha refers to any toxin that lacks some of the ten potent inherent properties of *visha* or having mild potency of all its ten properties, is incapable of producing acute signs of toxicity. It reaches a hidden or latent stage that is responsible for the cumulative toxicity & delayed action in the body and produces symptoms of *Dushivisha* whenever any triggering factor comes. Its *alpa-veerya* (mild potency) does not

prove fatal for an individual and as it gets enveloped by the kapha, so it resides in the body for many years in *avyakata avastha* (latent phase) without producing any fatal symptoms.

AIM AND OBJECTIVE: -

- To describe *Dushivisha* from ayurvedic perspectives.
- To describe chemotherapy induced cytotoxicity (CIT) from modern perspective
- To explore the correlation between the toxic effects of chemotherapy (CT) and *Dushivisha*

MATERIALS AND METHODS: -

materials include ayurvedic scriptures (*Charaka Samhita, Ashtanga Hridaya),* modern textbooks, medical journals and published research papers. The study is a review based on the literature from both ayurvedic and modern texts.

Triggering factors of *Dushivisha* -

Dushivisha, which already exists in the body, is exacerbated by *dushita desha* (polluted land), kala (deranged seasons), anna (toxic food), and *diwaswapna* (daytime sleep). *Dalhana*, the commentator, has provided a complete explanation for these symptoms. *Dushita desha*: is defined as a wet, watery, or humid area with high winds, cold temperatures, and rain. This land (*Anupa Desha*) aggravates the *visha*. *Dushita kala*: Sheet Anila (cold wind), summer days, *durdina* (cloudy days) both contribute to the aggravation of *visha*. Rain wets the body (*klinna*), and cold air hampers the digestive fire (*pachaka-agni). Dushita anna:* Certain foods, such as s*ura* (alcoholic preparations), *kulathi* (horse gramme) and *tila* (sesame oil), are *vidahi, teekshna dravyas* that aggravate the *Dushivisha*.

Anger, excessive sexual behaviour, exercise, also have an impact on both the body and the mind are capable enough to aggravate *Dushivisha.*

***Purvarupa* (Prodromal symptoms):** *Nidra* (Excessive sleepiness), *guruta* (heaviness of body), *vijrambha* (yawning), *vishlesh* (laxity of joints), *romaharsha (*horripilation), *angamarda* (body pain).

***Lakshana* (Symptoms)**: *Atisaar* (Diarrhoea), t*vaka vaivarnya* (Altered complexion), *mukha daurgandhya* (Foul smell from mouth*), virasta* (altered taste), *trishna* (excessive thirst), *murchha* (Syncope), *chhardi* (Vomiting), *swarvaikrutya* (Hoarseness of voice), *dushyodar* (Ascites).

Other symptoms include: *Avipaka* (indigestion*), arochaka* (Anorexia), *mandala, kotha* (appearance of red patches over the body), *dhatukshaya* (depletion of dhatus), *hasta- paad shotha* (Oedema on extremities), *vishamjvara* (intermittent Fever), *unmada* (Insanity), *anaha* (Distention), *shukra kshaya* (Oligospermia) and various other abnormilties.

As per *Acharya Charaka*, *Dushivisha* primarily vitiates *rakta* (blood), which causes *kitibha and kotha utpatti* (skin disorders) in the body. According to *Dhatu* that is contaminated by *Dushi visha*, its *Lakshana* (symptoms) varies:

- *Rasa Dhatu*: *Aruchi, Ajirna*
- *Rakta Dhatu: Kushtha, Visarpa* (Herpes)
- *Mamsa Dhatu: Mansarbud* (Tumour)
- *Med Dhatu: Med Granthi* (Lipoma)
- *Asthi Dhatu: Asthi-dantadi vikara* (Osteological changes)
- *Majja Dhatu: Tamo-darshana* (Blurred vision, blackouts)
- *Shukra Dhatu: Klaibya* (Infertility)

Upadrava* (complications) of *Dushivisha: *Jwar* (fever), *daha* (burning sensation), *hikka* (hiccup), *anaha* (distension of abdomen), *shukra kshaya* (decrease in sperm count, *shotha* (inflammation), *atisara* (diarrhea), *murchha* (fainting), *hridroga* (cardiac manifestation), *unmada* (insanity), *kampana* (tremor).

Concept of *Dushivisha* in chemotherapy induced cytotoxicity -

Cytotoxicity is the noxious and unintended response following the administration of a drug where the drug or an active metabolite causes serious damage to the cells. Such toxicity is commonly seen in cancer people undergoing chemotherapy treatment. Cancer is a disease in which some of the body's cells grow uncontrollably and spread to other parts of the body. It is Failure of genetic mechanism (mutation in genes) that controls the growth and proliferation of cells. Its etiology is usually linked to environmental, dietary and lifestyle factors. However, a person's inherited genetic background also may strongly contribute.

Chemotherapy is a crucial cancer treatment strategy. However, it is commonly associated with side effects which usually a reflection of their mechanism of action. Despite its therapeutic effects, it has several adverse impacts that greatly reduce quality of life. The initial few dosages Chemotherapy function as therapeutic doses, destroying cancerous cells. Most chemotherapy drugs show activity in rapidly multiplying cells. They cannot distinguish between cancer and healthy cells so they tend to affect healthy normal rapidly multiplying cells, e.g., bone marrow, GI tract, hair follicles. Its subsequent doses accumulate in the body and cause significant damage to healthy organs too, so the body fails to clear excess medications and some of its components remain in the body, continuing to harm body when concentration is highest, resulting in a formation of *visha* (latent poison). The accompanying signs and symptoms will be consistent with the *Dushivisha.*

Many chemotherapy medicines are utilised in the treatment, such as alkylating agent (e.g. cisplatin), antimetabolites (e.g. Capecitabine), Mitotic spindle agents (e.g. Paclitaxel), folic acid antagonist, pyramidine antagonist, cytotoxic antibiotics, taxanes, Miscellaneous agent (e.g. Methotrexate), immunomodulators (e.g. Thalidomide) etc.

Pathophysiology of Chemotherapy induced toxicity in Ayurveda -

The chemotherapy (CT) qualities are comparable to the properties of *visha* but contrary *to Oja* (a subtle component in a healthy body that provides strength). The CT medicines are administered via two routes: parenteral (I/V, I/M, S/C, I/D) and oral. When given parenterally, the CT medication is blended with *rasa-raktadi dhatu*. When taken orally, it mixes with *anna-rasa* and forms *rasa dhatu*. The *Adhya dhatu* (nearest) is simply *rasa*, therefore when the *koshtha* becomes contaminated with *Dushivisha*, it always manifests in rasa dhatu, resulting in *rasa dushti*. *Prinana or poshana* (nutrition*) karma* is performed by the *rasa dhatu*, hence if it is not pure, it will not perform its *prinana karma* adequately. *Sharir bala* (physical strength) and *satva bala* (mental strength) will be significantly lowered. The *Agni* (digestive strength and metabolic rate of body tissue) and *Oja* are responsible for the body's viability. CT causes an imbalance of *Agni and Vata Pitta doshas*, resulting in the formation of *ama* (partially digested), decreased *dhatu Agni* (the metabolic rate of dhatu), and the undesirable effect of CT in *dhatu (dhatukshaya, dhatupaka), updhatu, mala, and indriya*, and because there is already *ojakshaya* by malignant cells, it is exacerbated by CT agents, resulting in advanced *ojovikriti*. With cancer and their treatment effect, there is considerable *Oja kshaya* in the subject. In cancer patients, post-chemo, post-radiation, *Sharira bala* (physical strength) and *Satva bala* (mental strength) will be much reduced.
Acharya Charaka has mentioned in ch.su.23 that *Dushivisha* primarily vitiates *rakta* (blood), leading to *rakta dushti* (blood disorders) which causes *kitibha* and *kotha utpatti* (skin disorders) in the body.

Table 1: Shows various toxicity due to chemotherapeutic drugs:

S.NO.	Immediate toxicity (Occurs within few min to hrs)	Delayed toxicity (Occurs within days to weeks)	Late toxicity (Occurs within years)
1.	Allergic reaction	Delayed onset of emesis	Ototoxicity
2.	Burning sensation at site of infusion	Fatigue	Memories difficulties
3.	Urine discolouration,	Myelosuppression	Sexual dysfunction
4.	Acute emesis, etc	Mucositis	Secondary amenorrhea
5.		Diarrhoea or Constipation	Sterility
6.		Reduced appetite	Cardiotoxicity
7.		taste alteration	Pulmonary fibrosis, etc
8.		Alopecia	
9.		Peripheral neuropathy	
10.		Dry skin or pigmentation	
11.		Nail changes	
12.		Fluid retention	
13.		Musculo-skeleton pain	
14.		Nephrotoxicity	
15.		Hepatotoxicity, etc	

Table 2: Shows the symptoms of chemotherapy induced toxicity as per ayurveda text and contemporary science:

S.No.	Sign & symptoms	*Dushivisha*	Chemotherapy toxicity symptoms
1.	*Vishlesh* (looseness of joints)	✓	✓
2.	*Harshathvangmarda* (tingling or diffuse pain in body)	✓	✓
3.	*Avipaka* (indigestion)	✓	✓
4.	*Vairasya* (loss of taste)	✓	✓
5.	*Mandal kotha* (appearance of round patches & rashes on skin)	✓	✓
6.	*Dhatukshaya* (depleted tissues)	✓	✓
7.	*Paad-kara-asyashopha* (swelling of hands, feet & face)	✓	✓
8.	*Chardi* (vomiting)	✓	✓
9.	*Atisar* (diarrhoea)	✓	✓
10.	*Vaivarnya* (discolouration of skin)	✓	✓
11.	*Pravradha prabala Trishna* (profound thirst/dryness of mouth)	✓	✓
12.	*Anaha* (flatulence)	✓	✓
13.	*Kshpyet shukram* (reduced fertility)	✓	✓
14.	*Kushtha vikara* (skin disease)	✓	✓
15.	*Dushya-udar* (hepatotoxicity)	✓	✓
16.	*Vibhanda* (constipation)	✓	✓
17.	*Arochaka* (loss of interest in food)	✓	✓
18.	*Dhvast shiro-ruhaango* (loss of hair of head & body)	✓	✓
19.	*Vishada* (depression)	✓	✓

➢ **Treatment modalities mentioned in classical text: -**

The drug-induced toxicity results in building up of *Dushivisha,* as well as vitiation of *vata-pitta dosha* and *rasa- raktadi dhatu*. Treatment comprises of *shaman and Rasayana Chikitsa* (rejuvenation). As the body is already deprived with *rasa-raktadi dhatus*, *shodhan chikitsa* (detoxification) like *vamana and virechana* are not recommended; however, after the *bala* (strength) has been established in the body, *shodhana* can be performed.

To eliminate toxins from the body, the first step should be to restore *pachaka-agni* (digestive fire) and *dhatwa-agni* (cellular metabolism), which also promotes regeneration of healthy tissues. *Deepana (of agni*), *pachana* (of toxins), *vata-pitta shamana*, *rasa-rakta prasadana*, and *kapha* and *oja vardhana*, all lead to increase in *vyadhishamatva* (immunity) and *bala* (strength).

- **Shamana chikitsa**: *Phyllanthus emblica, Withania somnifera, Glycyrrhiza glabra, Santalum album, Commifora guggulu, Tinospora cordifolia, Curcuma longa, Zingiber officinale, Piper longum*: are some of the drugs that possess antioxidant, antimutagenic, immunomodulatory, and anabolic properties that helps in reducing chemotherapy toxic effects and to repair damaged tissues and cells.
- ***Rasayana* (Rejuvenating drugs)**: *Chyavanaprasha, pippali rasayana, shatavari rasayana, amalaki rasayana, ashwagandha rasayana, guduchi ksheera, brahma-rasayana* to gain bala (body and mental strength). *Go-ghrit* is an excellent choice because it has both *rasayana* and *vishahara* (anti-toxic) properties.
- ***Agada-pana* (Anti-toxic drugs)**: *Dushivishari agada, ajeeta agad, bilwadi agad, sanjeevana agad, kshar agad, dashanga agad, champaka agad, pippalyadi agad,* and others.
- **Medicated Food**: Medicated *yusha* (lentil soup), *takra* or medicated buttermilk (e.g. *panchkola takra*), medicated *aja ksheer* (goat's milk) and *mamsa rasa,* medicated *ghee* (e.g. *shatapala ghrit, kalyanaka sarpi and bhrami ghrita*) are also recommended.
  All these treatment measures help in repair the damage which chemotherapy has done to body and also to prevent further damage if it happens.

DISCUSSION: -

The *visha Dravya* (poisonous substances) or CT agents are modified cytotoxic chemicals designed to target cancer cells; however, these agents also harm normal healthy tissues. The characteristics of CT agents can be interpreted in terms of *visha dravyas*. According to Ayurveda, the properties of *visha dravya* are *ruksha* (dry), *ushna* (hot potency), *tikshna* (penetrating), *sukshma* (entering into minute pores), *ashu* (quick action), *vyavayi* (spread in all over the body), *vikasi* (weaken the tissues), *vishada* (non-unctous), *laghu* (light), and *apaki* (indigestible). It aggravated *pitta* and *rakta* through its *ushna virya,* while its *ruksha guna* increased *vata. Tikshna* property disrupts the binding of vital organs; due to its *Sukshma guna,* it enters all organs. *Ashu guna* quickly kills tissues; its *vayayai* quality spreads throughout the body; *vikasi guna* loosens and dissolves the *dosha, dhatu*, and *mala*. Because of its *vishada guna*, it does not cling to any area; because of its *laghu guna*, it is tough to treat; and because of its *apaki guna*, it is difficult to expel it from the body and cause problems for a long time. Some *visha dravyas* do not have enough potent properties to cause acute or sub-acute toxicity and some have potent *vyavayi, vikasi and ashu guna* to cause sudden death. Chemotherapy drugs cause delayed or cumulative toxicity comparable *to dushivisha dravayas* as they are not potent enough to cause sudden death.

RESULTS: -

Upon entering the body, all forms of toxins - whether from mineral, animal, or synthetic, sources undergo a transformation into *Dushivisha*. As a result, the cumulative toxic effects of chemotherapy exhibit symptoms that align with the classical descriptions of *Dushivisha* in Ayurvedic literature.

CONCLUSION: -

Owing to the preceding explanation, chemotherapeutic medications are considered *visha* as it possesses properties of *Dushivisha*. The aim of chemotherapy is to do maximum damage to cancer cells. But at the same time, healthy normal tissues get damaged hence producing cytotoxicity symptoms in body along with physical and psychological damage. All types of *visha* entering into body, be it *sthavara, jangama or kritrima visha* are transformed into *Dushivisha* in body. Hence the symptoms of cumulative toxicity due to frequent consumption of chemotherapy drugs are similar to the *lakshana of dushivisha* described in the Ayurvedic Samhita.

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