

Ayurvedic protocol for prevention and management of chronic toxicity of chemotherapy

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Abstract

Chemotherapy is a common treatment used for patients of cancer. Chemotherapy and its chronic toxicity have been mentioned in Ayurveda under the heading of *kshara-karma* and *kshara-vyapada* respectively. Even the properties and its mechanism of action of both chemotherapy as well as *kshara-karma* are similar in many aspects. Most of the chemotherapeutic agents produce *srotas vikriti* like *Ashthivaha Srotas* (Skeletal System), *Indriyavaha Srotas* (Sensory Organ), *Manovaha Srotas* (Psychological System), *Vatavaha Srotas* (Nervous System), *Pranavaha Srotas* (Respiratory and cardiovascular system), *Mutravaha Srotas* (Excretory System), *Annavaha Srotas* (Digestive System), *Sukravaha Srotas* (Reproductive System) and *Rasavaha Srotas* (Lymphatic System). Infertility, Cataracts and Cardiomyopathy has been found in both chemotherapy and *kshara-karma*. While some toxic effect like Osteoporosis, Avascular necrosis, Neuropsychiatric deficits, Cognitive decline, Neuropathy, hearing loss, pulmonary fibrosis, pulmonary hypersensitivity, decreased function of kidney, hypomagnesaemia, altered function of liver, premature menopause, Aplasia, myelodysplasia and Secondary Leukemia has been found only in modern science. It is due to probable using of most potent chemical therapeutic agent in modern science. *Nagabala, Baladi, Vijyasaradi, Triphala, Shankhpushpi ghrta, Aindra, Medhya, Neelkanth, Chyawanprash, Punarnava, Gokshuraka, Guduchiyadi, Shishukalpdrum ghrta* and *Lauhabhasmadi*, these are the *rasayana* described in the Ayurveda which will be useful to prevent chronic toxicity of chemotherapeutic agents like glucocorticoids, Vincristine, platinum, Taxanes Methotrexate, cycstarabine, Anthracycline, Trastuzumb, Bleomycin, Alkylating agents and miscellaneous drug. *Asthisanharadi churna, Panchatikta Ksheer Basti, Sukhavati varti, Mahatriphala Ghrita, Kalyanaka Ghrita, Amritaghya tailam, Soma Churna, Punarnavadi kvatha, Rohitakadi Vati, Kapikachhuadi churna, Phala Ghrita and Kharjuradi leha*, these are some ayurvedic formulations which will help to manage the *srotovaha vikriti* like *Ashthivaha Srotas, Indriyevaha Srotas, Manovaha Srotas, Vatavaha Srotas, Pranavaha Srotas, Mutravaha Srotas, Annavaha Srotas, Sukravaha Srotas and Rasavaha Srotas* respectively. Thus Ayurveda may play a major role to prevent and cure the chronic toxicity of chemotherapy during the management of cancer by using *Rasayana* and Ayurvedic formulations.

Keywords: chemotherapy, *kshara-karma*, toxicity, *vishakta*, ayurveda

Introduction

Chemotherapy is the use of any drug to treat any disease but the word chemotherapy means drug use for cancer treatment specially. Cancer is one of the leading causes of morbidity and mortality worldwide, with approximately 14 million new cases in 2012 [1], It is the second leading cause of death globally, and was responsible for 8.8 million deaths in 2015. Globally, nearly 1 in 6 deaths is due to cancer [2]. Though the chemotherapy plays a major role in the treatment of cancer but it gives potentially dangerous hazards which may be acute or chronic to the patient of cancer. American and Australian studies have shown that cancer survival rates after receiving chemotherapy can be as startlingly low as 2.1% [3]. Chemotherapeutic agents are not specific for cancer cells, however, and the side effects of treatment are a result of their antiproliferative actions in normal tissues such as the bone marrow, skin and gut. Most cytotoxic have a narrow therapeutic window or index and can have significant adverse effects. Considerable supportive therapy is often required to enable patients to tolerate therapy and achieve benefit. Myelosuppression is common to almost all cytotoxic. This not only limits the dose of drug, but also can cause life threatening complications [4].

The chemotherapy and its acute or chronic toxicity are not new for Ayurveda which described under the heading of *kshara-*

karma and *kshara -dosha* respectively. The standard operative procedure of *kshara-karma*, its indication, contraindication, properties and its *kshara-dosha* has been mentioned in Ayurveda in details along with some precautions measures of *kshara vyapada* (chronic toxicity) and management of its toxicity if occurred. But the principle of treatments and drugs mentioned for the toxicity of *kshara-karma* has been scattered. Even the current chemical agents use for chemotherapy, chronic toxicity, prevention and its management, we have to need to evaluate, elaborate and discuss in view of ayurvedic aspects which has been highlighted in this original fundamental research article.

Aims and objects

1. To elaborate, evaluate and discussions about chronic toxicity of chemotherapy as per ayurveda and modern science.
2. To elaborate, evaluate and discussions on pathophysiology (*srotas vikriti*) of chronic toxicity of chemotherapy in view of ayurveda.
3. To prepare an Ayurvedic clinical protocol for the prevention and management of chemotherapy in view of ayurveda.

Methodology

Thorough literary survey has been done to collect the relevant matters of this fundamental research. The main text of Ayurveda including *Brihatrayi*, *Laghutrayi*, its concern

commentaries and modern text book of medicine has been referred to collect, evaluate, elaborate and preparation of Ayurvedic clinical protocol for prevention and management of chronic toxicity of chemotherapy.

Result

Table 1: Chronic toxicity of chemotherapy drug on various organs [5] and its effect on *srotas*

DRUG	ORGAN	Chronic Toxicity	Clinical Features	<i>Srotas Vikriti</i> (Affected Systems)
Glucocorticoids	Bone	Osteoporosis,	Increased risk of bone fractures, acute and chronic pain	<i>Ashthi -Vaha Srotas</i> (Skeletal system)
		Avascular necrosis	osteonecrosis, cellular death of bone components	
	Eyes	Cataracts	blurry vision, loss of vision	<i>Indriya- Vaha Srotas</i> (Sensory- organ)
Methotrexate, Cytarabine	Brain	Neuropsychiatric deficits, Cognitive decline	Deficits in overall intelligence, mental illness.	<i>Mano- Vaha Srotas</i> (Psychological system)
Vincristine, platinum, Taxanes	Peripheral nerves	Neuropathy, Hearing loss	numbness, tremor, impairment of balance, and gait abnormality	<i>Vata- Vaha Srotas</i> (Nervous system)
Anthracycline, Trastuzumab	Heart	Cardiomyopathy	fatigue, shortness of breath, irregular heart beat and fainting	<i>Prana- Vaha Srotas</i> (Respiratory and cardiovascular system)
Bleomycin Methotrexate	Lung	Pulmonary fibrosis	Shortness of breath, particularly with exertion, Chronic dry, hacking coughing, Fatigue and weakness, Chest discomfort including chest pain	<i>Prana- Vaha Srotas</i> (Respiratory and cardiovascular system)
		Pulmonary hypersensitivity		
Platinum, others	Kidney	Decreased function, hypomagnesaemia	Oliguria or anuria	<i>Mutra- Vaha Srotas</i> (Excretory system)
Various	Liver	Altered function	Stomach pain, Nausea, Loss of appetite, Jaundice (yellow skin and eyes).	<i>Anna- Vaha Srotas</i> (Digestive system)
Alkylating agents, others	Gonads	Infertility, premature menopause	Abnormal sperm production or function, impair female fertility.	<i>Sukra- Vaha Srotas</i> (Reproductive system)
Various	Bone marrow	Aplasia,	Anemia, Pallor, Weakness, Lethargy	<i>Rasa- Vaha Srotas</i> (Lymphatic system)
		myelodysplasia,	Anemia, paleness (pallor), unusual bruising or bleeding, petechiae	
		Secondary Leukemia	Anemia, Easy bruising or bleeding, Paleness of the skin, Excessive fatigue, Bone pain	

The chemotherapy and chemotherapeutic agents have somewhat similar to *kshara-karma* and *kshara-dravya* (caustic alkalies) respectively, as their properties or its mechanisms of action and toxicity are similar. There are two types of *kshara-karma*, first is *Bahya parimarjana* (External application) and second is *Abhyantara parimarjana* (Internal application) [6].

a) ***Bahya parimarjana* (External application)** - It has indicated externally in *arbuda* (malignant tumour) and *granthi* (tumour) along with other diseases [7].

b) ***Abhyantara parimarjana* (Internal application)** - It has also indicated internally in *kafaja gulma* (abdominal tumour) as a chemotherapeutic agents along with other indication [8].

These drugs (*Kshara-dravya*) possesses the predominance of *katu* (pungent) *rasa*, *lavana* (salt) *rasa*, *tikshna* (penetrating)

and *ushna* (hot) in potency and causes *dahana* (burning), *pachana* (digesting), *avadharana* (tearing), *vilayana* (dissolving), and *sodhana* (cleaning).

It has also indicated for as excision, incision, extraction and scarifications in various conditions such as *nashaarsha* (nasal polypi) and *Arbuda* (malignant tumors) [9].

Ayurveda has also mentioned the contraindication of *kshara-karma* (chemotherapy) in phobic, weak, emaciated and *vata* and *pitta* vitiated patients. It is also contraindicated in the patients of facial paralysis, Hyperpyrexia, diarrhoea, anaemia, *shiroroga* (disease of head) and heart disease, *prameha* (diabetes), *Akshi paka* (inflammation of eyes), cataract and anorexia. It cannot be given also the patients who under gone emesis and purgation during menstruation, pregnancy and having inflamed ovary, vagina and alcoholic patients [10].

Table 2: Comparison between Chronic Toxicity of *Kshara-dravya* and Chemotherapeutic Agents

Sr.	Chronic Toxicity of <i>Kshara-dravya</i>	Chronic Toxicity of Chemotherapeutic Drug
1.	Impotency (<i>Shandaya</i> ⁹¹ [10] & <i>Punshatva-Nashak</i> ^[11]), Male Infertility (<i>Shukraghana</i> ^[12] & <i>Shukravahini dusti</i> ^[13])	Infertility
2.	Blindness (<i>Aandhya</i> ^[14] , <i>Drastighana</i> ^[16])	Cataracts
3.	Alopecia (<i>Khalitya</i> ^[15])	-
4.	Premature greying of Hair (<i>Palitya</i> ^[17])	-
5.	Cardiac pain (<i>hridayapakartina</i> ^[18])	Cardiomyopathy
6.	Burning in the body (<i>dahana</i> ^[19])	-
7.	Tearing (<i>avadharana</i> ^[20]) and scarifications (<i>lekhana</i> ^[21]) of cells	-

Table 3: Preventive measure in chemotherapy w. s. r to *Rasayana*:

Sr. No.	<i>Rasayana</i>	CS	SS	AH	AS	BR
1.	<i>Nagabala Rasayana</i> ^[22, 23, 24, 25]	+	+	+	+	-
2.	<i>Baladi Rasayana</i> ^[26, 27, 28]	+	+	-	+	-
3.	<i>Vijayaradi Rasayana</i> ^[29]	-	+	-	-	-
4.	<i>Trifala Rasayana</i> ^[30, 31, 32, 33]	+	-	+	+	+
5.	<i>Shankhpushpi ghrita</i> ^[34]	-	-	-	+	-
6.	<i>Aindra Rasayana</i> ^[35]	+	-	-	-	-
7.	<i>Medhya Rasayana</i> ^[36, 37, 38]	+	-	+	-	+
8.	<i>Neelkanth Rasayana</i> ^[39]	-	-	-	-	+
9.	<i>Chyawanprash</i> ^[40, 41]	+	-	+	-	-
10.	<i>Punarnava rasayana</i> ^[42]	-	-	+	-	-
11.	<i>Gokshuraka rasayana</i> ^[43]	-	-	+	-	-
12.	<i>Guduchiyadi Rasayan</i> ^[44]	-	-	-	-	+
13.	<i>Shishukalpdrum ghrita</i> ^[45]	-	-	-	-	+
14.	<i>Lauhabhasmadi rasayan</i> ^[46]	-	-	+	-	-

CS = *Chrak Samhita*, SS=*Sushrut Samhita*, AH=*Astang - Hridya*, AS= *Astang Sangraha*, BR=*Bhaisajya Ratnavali*,

Ayurvedic Management of chronic toxicity of Chemotherapy

Management of *Asthi - Vaha Srotas Vikriti*

6 gm *Asthisanharadi* churna twice a day along with ghee should be given ^[47].

Procedure ^[48]- *Pancha tikta Ksheer Basti* containing *Ksheer*, *Ghrिता* and *Tiktatmaka Rasa dravya* (*Guduchi*, *Nimba*, *Vasa*, *Kantakari* and *Patol*) should be given at morning after breakfast for 30 days per rectally in the treatment of *asthikshaya*.

Management of *Indriya - Vaha Srotas Vikriti* -

External application of *Sukhavati varti* ^[49] should be use on eye twice a day with 10-20 ml oral medicaments including *Mahatriphala Ghrita* ^[50]

Management of *Mano- Vaha Srotas Vikriti* -

10-20ml *Kalyanaka Ghrita* twice a day should be given in *Mano- Vaha Srotas Vikriti* ^[51].

Management of *Vata- Vaha Srotas Vikriti* -

10-20 ml *Amritaghya tailam* twice a day should be given in *Vata- Vaha Srotas Vikriti* ^[52].

Management of *Prana-Vaha Srotas Vikriti* -

3-6 gm *Soma Churna* twice a day should be given with warm water in *Prana- Vaha Srotas Vikriti* ^[53]

Management of *Mutra-vaha srotas Vikriti* -

Niruha basti of *Punarnavadi kvatha* should be given per rectally for 30 days with 20-40 ml oral medicaments including *Punarnavadi kvatha* ^[54, 55].

Management of *Anna-Vaha Srotas Vikriti* -

500mg-1000mg *Rohitakadi Vati* should be given orally twice a day with *Karela Swaras* (*Bitter Gourd juice*) ^[56].

Management of *Sukra-Vaha Srotas Vikriti* -

Male Infertility

3-6 gm *Kapikachhuadi* churna should be given twice a day with cow's milk ^[57]

Female Infertility

6-12 gm *Phala Ghrita* should be given twice a day *with* warm milk or warm water ^[58]

Management of *Rasa-Vaha Srotas Vikriti* -

5-10 gram *Kharjuradi leha* should be given twice a day *with madhu* and *ghrita* ^[59, 60].

Discussion

Chemotherapy is a type of treatment that includes a drug or combination of drugs for the treatment of cancer. The number of blood cell like white blood cell which protects body from infection, red blood cell which carries oxygen through the body will be damage rapidly along with cancer cells and other normal living cells during Chemotherapy which causes acute

and chronic toxicity during the whole procedure of Chemotherapy. As per Ayurveda the Chemotherapy is one form of *kshara-karma* which is indicated for various diseases along with *arbuda* (Cancer). Most of the important chemotherapeutic drugs include alkylating agents like *kshara-dravya* used for *kshara-karma*. Both the chemotherapeutic drugs and *kshara-dravya* will be showed near about similar therapeutic effect as well as toxic effect on living body. Osteoporosis, avascular necrosis, Cataracts, Neuropsychiatric deficits, Cognitive decline, Neuropathy, Hearings loss, Cardiomyopathy, Pulmonary fibrosis, Pulmonary hypersensitivity, Decreased function of kidney, hypomagnesaemia, Altered function of liver, Infertility, premature menopause, Aplasia, myelodysplasia and Secondary leukemia, these are the common chronic toxic effect of various chemotherapeutic agents used in modern science. Clinically Glucocorticoids affects *Ashthi -Vaha Srotas* (Skeletal-system) and *Indriya- Vaha Srotas* (Sensory organ), Methotrexate & cytarabine affects *Mano- Vaha Srotas* (Psychological System), Vincristine affects *Vata-Vaha Srotas* (Nervous-System), Anthracycline, Trastuzumb & Bleomycin affects *Prana- Vaha Srotas* (Respiratory and cardiovascular system), Platinum affects *Mutra- Vaha Srotas* (Excretory System), Alkylating agents affects *Sukra-Vaha Srotas* (Reproductive System) while miscellaneous drugs affects *Anna- Vaha Srotas* (Digestive System) and *Rasa- Vaha Srotas* (Lymphatic-System). According to Ayurveda there are two type of *kshara-karma*, *Bahya parimarjana* (External application) and *Abhyantara parimarjana* (Internal application). The *Kshara-dravya* possesses the predominance of *katu* (pungent) *rasa*, *lavana* (salt) *rasa*, *tikshna* (penetrating) and *ushna* (hot) in potency and causes *dahana* (burning), *panchaka* (digesting), *avadharana* (tearing), *Vellayani* (dissolving), and *sodhana* (cleaning). Hence excessive use of these drugs may produce the acute and chronic toxicity in the body. Ayurveda has also mentioned some chronic toxicity like Impotency (*Shandaya & Punshatva-Nashak*), male infertility (*Shukraghana & Shukravahini dusti*), blindness (*Aandhya, Drastighana*), Alopecia (*khalitya*), Premature greying of Hair (*Palitya*), Cardiac pain (*hridayapakartina*), Burning in the body (*dahana*), Tearing (*avadharana*) and scarifications (Iekhana) of cells due to prolong and excessive therapeutic use of these *Kshara-dravya*. Out of which infertility, Blindness and cardiac pain are also found as a chronic toxicity of chemotherapy. Except this chronic effect, Osteoporosis, avascular necrosis, Neuropsychiatric deficits, Cognitive decline, Neuropathy, hearing loss, pulmonary fibrosis, pulmonary hypersensitivity, decreased function of kidney, hypomagnesaemia, altered function of liver, premature menopause, Aplasia, myelodysplasia and Secondary Leukemia has also found as a toxic effect of chemotherapy. It is due to use of potent toxic chemical agent in Chemotherapy. As it is already proved that the chemotherapeutic agents will be produced the chronic toxicity so it may be need to prevent by adding such a drugs or therapy which will be counter the toxic effect of chemotherapy. In Ayurveda, *Rasayan* therapy for the purpose of an enhancement of the health and pacifying sleep disorder, drowsiness, tiredness, laziness and weakness. It also help to pacify & settle down to *vata* dosha. It also help to enhance the digestion (*jathragni*) along with colour and complexion of the body. The person taking *rasayan* therapy regularly may become capable to tolerate the physical and mental distress ^[61]

as most of the drug and formulations of *rasayan* therapy have *ojovardhaka* properties which are opposite to *visha* (poison). As the chemotherapeutic agents are a potent toxic in nature, its toxicity can be counteracting by giving *rasayan* therapy. Hence *Rasayan* therapy may be useful to prevent the toxicity caused due to induction of chemotherapy. As per Acharya chraka, Ghee and milk is the best drug in *rasayan* therapy ^[62]. Acharya chraka has been also suggested to give a plenty of ghee during the *Kshara-Karma* in *kafaja Gulma* ^[63]. The chemotherapeutic agents like glucocorticoids causes *asthivaha srotas vikarti* which is one of the place of *vata*, *Nagbala rasayan* or *Baladi rasayan* should be use to prevent osteoporosis and avascular necrosis as this *rasayan* have *vatashakmak* property. *Vijaysaradi Rasayan* or *Trifala rasayan* ^[64] should be use to prevent the cataract due to glucocorticoids as it is *chakshukshya* property (wholesome for eyes). *Shankhpushpi* ghritha should be use to prevent hearing loss caused due to Vincristine, platinum & taxanes. *Aindra Rasayana* or *Medhya rasayan* should be use to prevent the *vikrati* in *mano-vaha srotas* caused due to chemotherapeutic agents Methotrexate, Cytarabine as it is indicated in mental illness. *Neelkanth rasa* is a *rasayana* which is indicated for heart disease should be use in cardiomyopathy caused by chronic toxicity of Anthracycline & Trastuzumb. *Prana- Vaha Srotas vikrati* like pulmonary fibrosis and pulmonary hypersensitivity has the chronic toxicity due to induction of Bleomycin and Methotrexate which will be prevented by giving *Chyawanprash rasayana*. *Punarnava rasayana* or *Gokshuraka rasayana* should be used in renal failure caused by chronic toxicity of chemotherapeutic agents like Platinum. Some chemotherapeutic agents cause chronic toxicity in the form of hepatic dysfunctions and jaundice which can be prevented by given *Guduchiyadi rasayan* along with that chemotherapeutic agent. The infertility will be found in male while premature menopause along with infertility will be found in females due to chronic toxic effect of chemotherapeutic agent like Alkylating agents which can be prevented by using *Shishukalpdrum Ghritha Rasayan*. *Rasa-Vaha Srotas vikrati* in the form of anaemia due to bone marrow failure caused by induction of chemotherapeutic agents which can be prevented by giving *Lauhabhasmadi rasayan* along with chemotherapy. Thus, the *rasayan* therapy mentioned in Ayurveda may play a major role to prevent chronic toxicity of chemotherapeutic agents, if it is given along with chemotherapy.

As the various chemotherapeutic agents causes various toxic effect, hence it should be need to treat the chronic toxicity by using basic principles of management of *srotas vikriti*.

The *asthivaha srotas vikrati* found in chronic toxicity of chemotherapeutic agents due to vitiation of *vata*. In this condition the *Panchatikta ksheer basti* should be given to pacify the vitiation of *vata* in the *asthivaha srotas* which one of the places of *vata* and *Asthisanharadi* churna will be useful to fulfill the damage due to the chronic toxicity of chemotherapeutic agents in the form of osteoporosis and osteonecrosis. *Mahatriphala Ghritha* and *Sukhavati varti* will be helpful to cure immature cataract (*kanch*) caused by chronic toxicity of chemotherapy while patient should be refered to surgery in case of mature cataract. As *Somalata* have *swashar* and *hridya* property by doing bronchodilation and cardiac stimulant respectively pacifying increase *vata*, *kafa* with in the *Pranavaha srotas*. It can be given to cure *Pranavaha srotas*

vikrati in the form of pulmonary fibrosis, pulmonary hypersensitivity and cardiomyopathy.

Punarnavadi kvatha is proved drugs in the management of renal failure (*mutraghata*) which is given orally as well as in the form of *Basti*. Chemotherapeutic agents like Platinum causes renal toxicity, the *Punarnavadi kvatha* should be given to cure the renal failure. *Rohitakadi vati* is the reference drug for *yakrit vikara* (liver deformity), hence it can be useful to cure the alter function of liver.

As Alkylating agents causes chronic toxicity of gonads (testis & ovaries) which produce *Sukravaha srotas vikriti* in the form of infertility, hence *Kapikachhuadi churn* and *phal ghrita* should be given to male and female to cure infertility respectively. *Kalyanaka Grita* is especially indicated for mental illness (*unmada*), hence it should be given in *manovaha srotas vikrati* in the form of psychiatric disorders due to chronic toxic effect of chemotherapeutic agents like Methotrexate & cystarabine.

As *Amritaghya tailam* is the best medicine to cure *vata vyadhi* if it is use orally and externally for massage, hence it should be given to cure *vata vaha srotas vikrati* produce by chronic toxic effect of chemotherapeutic agents like Vincristine, platinum & taxanes.

Kharjura is one of the chief ingredient in *Kharjuradi leha* which have property of *rasa tarpana* (satiating), some chemotherapeutic agent causes *rasavaha srotas vikrati* in the form of anaemia, hence *Kharjuradi leha* to fulfil the *rasa kshya* (exhaustion of rasa).

By using specific *Rasayan* therapy and therapeutic drug (*Vyadhi pratyatmak* and *dosha pratyatmak chikitsa*) chronic toxicity of chemotherapy can be prevented and cured respectively. Thus Ayurveda may play a major role to prevent and cure the chronic toxicity of Chemotherapy during the management of cancer.

Conclusion

The *Kshara-Karma* mentioned in Ayurveda and Chemotherapy given in cancer mentioned in the modern science has similarity as the properties, indication, contra-indication, and complications has same somewhat. The chemotherapy causes toxicity by producing *srotas vikrati* like *Ashthi -Vaha Srotas* (Skeletal-System), *Indriya-Vaha Srotas* (Sensory organ), *Mano- Vaha Srotas* (Psychological System), *Vata- Vaha Srotas* (Nervous- System), *Prana- Vaha Srotas* (Respiratory and cardiovascular system), *Mutra- Vaha Srotas* (Excretory- System), *Anna- Vaha Srotas* (Digestive System), *Sukra-Vaha Srotas* (Reproductive System) and *Rasa- Vaha Srotas* (Lymphatic-System). From the above discussion it can be concluded that *Ayurvedic Rasayana* Therapy and *Ayurvedic* formulations has a better preventive and curative role in the management of toxicity caused by chemotherapy. Thus we can prevent and cure the toxicity of Chemotherapy during the management of cancer.

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