Role of Pakshaghata Chikitsasutra in the Management of Ischemic Heart Disease (IHD) w.s.r to Herbal Antithrombotic Drugs

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Publication Date: 24 January 2017

Article Link: http://medical.cloud-journals.com/index.php/UAAYUSH/article/view/Med-332

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Abstract Myocardial infarction results when a blood clot interrupts or blocks blood flow to the heart, which starves the heart muscle of oxygen and causes heart muscle cells to die; the same process in the brain causes a stroke. Hemiplegia is included under Pakshaghata described in the chapter of Vatavyadhi chikitsa. Antithrombotic is any medication that decreases clots in the body. The concept of Antithrombotic is not as such mentioned in Ayurvedic classics. The paper critically analyses the concept of antithrombotic drugs in Ayurvedic classics and the role of Pakshaghata chikitsasutra in the management of ischemic heart disease. Some of the ayurvedic herbal drugs scientifically validated for antithrombotic activity are also presented.

Keywords Pakshaghata chikitsasutra; Ischemic Heart Diseases; Antithrombotic drugs

1. Introduction

Charakasamhita enumerates Hridroga under Trimarmiya chikitsa [1], while the management of Pakshaghata is described in the chapter of Vatavyadhichikitsa [2]. Reason for non-inclusion of Pakshaghata (hemiplegia) under shriomarmagatavyadhis is not known. Hemiplegia is usually included under pakshaghata and the main causative factor i.e., hypertension was not directly referred in ayurvedic classics. Cerebral ischemia may result due to thrombin or hemorrhage in cerebral vascular structures. During the progress of this condition initially patient may suffer from transient ischemic attacks and it may lead to stroke or death. Same chain of events takes place even in coronary artery leading to either angina or myocardial infarction. Ischemic heart disease is the generic designation for a spectrum of disorders resulting from imbalance between the myocardial need for oxygen and the adequacy of blood supply [3]. Coronary vasospasm alone or superimposed atherosclerotic narrowing may contribute to the reduction in the flow. Blood vessels injured by smoking, cholesterol, or high blood pressure develop cholesterol-rich build-ups (plaques) that line the blood vessel; these plaques can rupture and cause the platelets to form a clot. A heart attack (myocardial infarction) results when a blood clot interrupts or blocks blood flow to the heart, which starves the heart muscle of oxygen and causes heart muscle cells to die; the same process in the brain causes a stroke. Antithrombotic is any medication that decreases clots in the body (by dissolving already formed clots or preventing clot formation [4]. This includes the drug classes like
anticoagulants, antiplatelets, and thrombolytics. Antithrombotics can be used therapeutically for prevention (primary and secondary prevention) or treatment of dangerous blood clots (acute thrombus).

Ayurvedic classics, compendia, research journals and internet publications were referred to compile the relevant information.

2. Observation and Discussion

2.1. Concept of Antithrombotic Drugs in Ayurveda

Anatomical and physiological aspects of antiplatelet/anticoagulant/thrombolytic drugs are not as such mentioned in Ayurvedic classics. Due to defective metabolism (impaired function of agni) morbid accumulation of kapha and medas (sanghata) occurs in the Rasaraktavaha srotas. Due to this flow gets obstructed. "Shonitasanghatabhedana" is the term used to describe the drugs which remove the sanghata (obstruction) and facilitates free movement in the raktavahasrotas [5]. Katu rasa is ascribed with the property of "shonitasanghatabhedana". Katu rasa with its ushna, tikshna and laghu gunas acts as agnideepana (corrects the digestive and metabolic functions) lekhana (scrapes/dries up the kapha and medas) and chedana (disunites/separates the adhered kaphadidoshas from the srotas).

The drugs of Katu rasa skanda [6] including Pippalyadi, Salasaradi and Surasadi gana dravyas and that of lekhaniya dashemani [7] and chedaniya dravyas [8] can be judiciously used in dissolving the clots. Dalhana interprets lekhana as medonashana [9]. Acharya Sushruta in Sonitavarnaniya adhyaya describes a group of drugs which facilitates the free flow of blood [10]. The drugs included are Ela (Elettaria cardamomum), Karpoora (Cinnamomum camphora), Kushta (Saussurea lappa), Tagara (Valeriana wallichii), Patha (Cissampelos pariera), Bhadradaru (Cedrus deodara), Vidanga (Embella ribes), Chitraka (Plumbago zeylanica), Trikatu (Piper longum, Piper nigrum, Zingiber officinale), Agaradhuma, Haridra (Curcuma longa), Arkankura (Calotropis procera) and Naktamalaphala (Pongamia pinnata). The drugs are prescribed for avagharshana with lavana and thaila externally. The internal use of these drugs may be useful in dissolving the obstruction (clot) and facilitating the free flow of blood. Kshara dravyas (alkalis derived from herbs) described also helps in removing the obstruction in the srotas. Charaka advises the use of ksharas of Utpalanala (Nymphaea stellata), Ambhoja (Nelumbo nucifera), Palasha (Butea monosperma), Asana (Pterocarpus marsupium), Priyangu (Callicarpa macrophylla), Madhuka (Glycyrrhiza glabra) with honey and ghee in dissolving the blood clots (kaphanubhanda grathita rakta) [11]. According to Chakrapani sonitasthapana drugs remove the vitiation of rakta and help to bring back the normalcy of rakta dhatu [12]. Similarly drugs like sariva, manjishta which are raktaprasadana also purify the vitiated rakta. Even though anticoagulant/antiplatelet activity is not mentioned as such, acharyas of ayurveda explained various procedures and drugs which help to remove the obstruction in the raktavaha srotas and help in the normal functioning of Raktadhatus.

2.2. Pakshaghata Chikitsasutra and Thrombolytic Activity

The chikitsasutra for pakshaghata consists of snehana, swedana followed by virechana (purgation) [13]. Any obstruction in the Rasaraktavahasrotas (srotosangha) causes interruption to interchange of nutrient material and waste material between capillaries and cells. The nutritive material passes through the semi permeable capillary walls in to the tissue fluid by the net outward pressure that is the difference between the arterial blood pressure and osmotic pressure inside the capillary. Extraction of waste (water and waste products from cell) fluid from the tissue fluid in to the venous
blood vessels occurs due to net pressure. If any interruption occur in this process it causes accumulation of waste material (vitiated dosas or metabolites in the tissue). *Sweda karma* hastens this process by increasing the permeability of capillary and bringing the morbidities into extra cellular fluid by dilating and clearing the channels of the body. *Charaka envisages* the concept about pharmacokinetics of *vamana and virechana* drugs in kalpasthana [14]. *Virechana dravyas* that are *ushna, tikshna, sukshma vyavayi* and *vikashi* reaching the heart by virtue of their potency (virya) circulating through the large and small blood vessels pervade the whole body. One can easily conceive that *virechana dravyas* plays a pivotal role in removing the block in the *srotas* (thrombolytic activity) [15]. *Rechana* is also indicated in *urdhwagata raktapitta* [16] and cerebral hemorrhage may be categorized under it. This may be the reason for *virechana* being the prime treatment of *Pakshaghata* which is a *vataja nanatmajavikara*. Treatment modalities like *snehana, swedana* and *rechana* may exert thrombolytic effect and facilitates to improve collateral circulation and blood supply to the affected area. So the chikitsasutra suggested for the management of *pakshaghata* may hold good to treat ischemic heart diseases.

### 2.3. Some Scientifically Validated Herbal Antithrombotics

**Haridra (Curcuma longa Linn)**

Haridra is a common house hold condiment and a domestic remedy for cuts and wounds. Haridra possess *katu, tikta rasa* and *ushna virya* [17]. It is included in *lekhaniya dashemani* by Charaka. *Vaghbhata* mentions *Haridra* as the *agyoushadha* for *prameha* along with *Dhatri* [18]. *Curcuma longa* is experimentally proven for its hypolipidaemic, antiatherosclerotic, antioxidant and anti-diabetic activities [19]. *Curcumin* inhibit platelet aggregation and enhance fibrinolytic activity. *Curcuma longa* preparations have shown antithrombotic activity in experimental rats. In rabbits with experimental atherosclerosis turmeric extract as well as curcumin have shown antiatherosclerotic activity. An in vitro thrombolytic model was used to check the clot lysis effect of aqueous herbal extracts of *C. longa*, along with *Streptokinase* as a positive control and water as a negative control. The percentage (%) clot lysis was statistically significant (p<0.0001) when compared with vehicle control. *C. longa* showed moderate clot lysis activity 32.94 ± 3.663% whereas standard streptokinase showed 86.2 ± 10.7 % clot lysis [20].

**Bhunimba (Andrographis paniculata Nees)**

*Andrographis paniculata* known as *Bhunimba* in traditional system of medicine is highly used for the treatment of jaundice and other liver disorders. *Bhunimba* possess *tikta rasa* and *kushta guna* and *katuvipaka* [21]. It is *deepana* and *kaphapitta vaha*. Several in vivo studies in rats and mice have proved the hypoglycemic, hepatoprotective, anti-inflammatory and antioxidant activities of *Andrographis paniculata* [22]. Considerable work has been carried out on the effect of extracts of this plant as well as that of its constituents on cardiovascular system. *Andrographolides* of the plant has shown antihypertensive activity in rats. The crude extract as well as andrographolide inhibited PAF-induced human platelet aggregation. Animal experiments have shown *A. paniculata* has anti-atherosclerotic activity and it has been suggested that this plant preparation may help in preventing re-stenosis of arteries after coronary angioplasty. Crude ethanol extract and soluble fraction of ethanol extract have shown in vitro thrombolytic properties [23].

**Madhuka (Glycyrrhiza glabra Linn)**

*Glycyrrhiza glabra* has been recognized as a highly valuable medicinal herb from the times of *Caraka* and *Susruta*. *Madhuka* is included in *Jivaniya, Sandhaniya, Varnya, Kandughna* and
Angamardaprasamana dashemani by Caraka [24]. Glycyrrhiza glabra has received significant attention from modern scientific researchers, chiefly because it is an important herbal medicine in Europe, and is official in several pharmacopoeias. Flavonoids from the root have significant antioxidant activity [25]. Glycyrrhiza glabra has shown clot lysis activity in invitro thrombolytic model [26]. The chemical constituents Glycyrrhizin and Glycyrrhetic acid have shown corticoid like activity. Crude drug because of its mineralocorticoid activity of its main constituent glycyrrhizin, if ingested orally in large doses (>50g crude drug per day) over an extended period of time leads to hypokalaemia, hypernatreamia, oedema, hypertension and cardiac disorders. These problems disappear in the course of a few days after stopping the drug. Preparations of liquorice should not be taken for longer than 6 weeks [27].

**Sariva (Hemidesmus indicus R. Br.)**

Sariva commonly known as Indian sarsaparilla is a perennial climbing plant and native of India. The plant is well known for its anti-oxidant and anti-inflammatory activity [28]. Methanolic extract of roots on intravenous administration in rabbits (5mg/kg) delayed plasma recalcification time and enhanced the release of lipoprotein lipase enzyme, thus indicating significant antithrombotic activity. The extract also inhibited ADP induced platelets aggregation (in vitro) and the effect was comparable to that of heparin [29].

**Ananta (Fagonia arabica Linn.)**

*Fagonia arabica* is an ethno-pharmacologically important Ayurvedic herb known to have many medicinal properties like anti-inflammatory, analgesic, antipyretic and antioxidant effects [30]. An in vitro thrombolytic model was used to check the clot lysis effect of *Fagonia Arabica*. *Fagonia arabica* showed significant clot lysis (75.6%) with reference to Streptokinase (86.2%) [31].

**Tulasi (Ocimum sanctum Linn)**

Tulasi is highly valued in ayurveda for normal health maintenance and possess katu tikta rasa and is considered hridya [32]. It is deepana, mitigates the deranged kapha vata and useful in diseases of blood. *O.sanctum* leaves have been demonstrated to exhibit hypoglycaemic, hypolipidaemic and antioxidant activities [33]. Alcohol extract of the leaves of *O. sanctum* (different doses upto 400mg/kg,p.o) showed cardioprotective effect against isoproterenol (200mg/kg subcutaneously) induced myocardial infarction in rats. Aqueous herbal extracts of *O. sanctum* has shown in vitro thrombolytic activity, along with Streptokinase as a positive control and water as a negative control. The percentage (%) clot lysis was statistically significant (p<0.0001) when compared with vehicle control. *O. sanctum* showed moderate clot lysis activity 32.94 ± 3.663%) whereas standard streptokinase showed 86.2 ± 10.7 % clot lysis [34].

**Pippali (Piper longum Linn)**

Pippali is one of the ingredients of trikatu and is employed in very large large number of Ayurvedic formulations meant for therapeutic end uses. Pippali is deepana vrichya laghu and anushna. It mitigates the deranged Kapha vata. Bhavamisra mentions that Pippali when used with honey acts as kapha medohara [35]. *Piper longum* has been experimentally proven for hypoglycemic and coronary vasodilatory activities [36].

The anticoagulant activities of Piperlongumine (PL) were examined by monitoring activated partial-thromboplastin-time (aPTT), prothrombin-time (PT), and the activities of thrombin and activated factor
X (FXa). The effects of PL on the expressions of plasminogen activator inhibitor type 1 (PAI-1) and tissue-type plasminogen activator (t-PA) were also tested in tumor necrosis factor-α (TNF-α) activated HUVECs. The results showed that PL prolonged aPTT and PT significantly and inhibited the activities of thrombin and FXa. PL inhibited the generation of thrombin and FXa in HUVECs. In accordance with these anticoagulant activities, PL prolonged in vivo bleeding time and inhibited TNF-α induced PAI-1 production. Furthermore, PAI-1/t-PA ratio was significantly decreased by Piperlongumine [37].

**Sunthi (Zingiber officinale Roscoe)**

Ginger is valued as a spice and has been used through ages in almost all systems of medicine against many maladies. Sunthi is kaphavatahara, pachana and vibandhabhedana [38] (breaks down the obstruction). Different extracts of ginger is reported to have, antibacterial, antioxidant, antiulcer, anti-inflammatory, cardioprotective and hypocholesterolaemic activities [39].

In a study some of the isolates from *Z. officinale* were subjected into the evaluation of their antiplatelet aggregation and vasorelaxing bioactivities. Among the tested compounds, [6]-gingerol and [6]-shogaol exhibited potent anti-platelet aggregation bioactivity. In addition, [10]-gingerol inhibited the Ca²⁺-dependent contractions in high K⁺ medium [40].

**Lashuna (Allium sativum Linn)**

Garlic (*Allium sativum*) is among the oldest of all cultivated plants. Most recent data published convincingly point out that garlic and its various forms reduce cardiovascular risk, including abnormal plasma lipids, oxidized low density lipoproteins (LDL), abnormal platelet aggregation and a high blood pressure [41]. Stimulation of nitric oxide generation in endothelial cells seems to be the critical preventive mechanism. Garlic may promote an anti-inflammatory environment by cytokine modulation in human blood. Cardioprotective effects of dietary garlic are mediated in large part via the generation of hydrogen sulfide (H2S). Garlic-derived organic polysulfides are converted by erythrocytes into hydrogen sulfide which relaxes vascular smooth muscle, induces vasodilation of blood vessels, and significantly reduces blood pressure. There are data on potential ability of garlic to inhibit the rate of progression of coronary calcification [42].

**Dronapushpi (Leucas aspera Willd)**

*Leucas aspera* (Willd.) Linn. known as Dronapushpi is distributed throughout India from the Himalayas down to Ceylon. Dronapushpi is hot in potency (ushna) and mitigates kapha and ama. It is tikshna and bhedana [43]. *Leucas aspera* has shown antioxidant, hypoglycemic, diuretic and antimicrobial activities in different experimental models. An invitro thrombolytic model was used to check the clot lysis effect of organic extract of Leucas Aspera using streptokinase as a positive control and water as a negative control. Venous blood drawn from twenty healthy volunteers was allowed to form clots which were weighed and treated with the test plant materials to disrupt the clots. Leucas aspera showed very significant (p < 0.0001) percentage of clot lysis compared to reference drug streptokinase (75.00 ± 3.04%) [44].

**Ikshvaku (Lagenaria siceraria) (Molina) Standl.)**

Ikshavaku has been recognized as a drug for therapeutic emesis from the period of Caraka and is particularly indicated in Prameha [45]. Ikshvaku possess tikta rasa, laghu ruksha guna and katuvipaka. It is kaphapitahara and hridya [46]. Antiatherosclerotic potential of L.siceraria has been proved experimentally. The flavonol and kaempferol present in L. siceraria were shown to exhibit...
fibrinolytic activity comparable to streptokinase activity [47]. An ethanolic extract of L. siceraria fruit had a membrane-stabilising role in isoproterenol-induced myocardial infarction in rats [48].

**Haritaki (Terminalia chebula Retz)**

Haritaki (Terminalia chebula Retz) is held in high esteem in Ayurveda for its properties to prevent and cure diseases. According to Acharya Susruta Haritaki is the best drug to be used in santarpanotha vikaras [49]. Haritaki is hridya, medhya and kaphavahara. Haritaki is laghu, ruksha ushna and possesses deepana, pachana, vibhandhahara properties [50]. The crude methanolic extracts of Terminalia chebula exhibited potent platelet aggregation inhibition activity (in vitro) in a dose-dependent manner at concentration range (1 to 10 mg/ml) [51].

**Brahmi (Bacopa monnieri (Linn) Pennell)**

Bacopa monnieri, a plant commonly used in Ayurvedic medicine, has an age-old reputation for being an effective and powerful herb helpful for memory and combating stress. Brahmi is rasayana, Hridya, swarya and medhya [52]. Bacopa monnieri has been proven for its Antioxidant, Hypotensive, Vasodilator and Antidiabetic activities [53]. Chloroform extract of Bacopa monnieri showed significant clot lytic properties in human blood samples. The mean percent clot lytic activity of chloroform plant extract of Bacopa monniera was found to be 48.39% [54].

### 3. Conclusion

Atherothrombotic diseases such as myocardial or cerebral infarction are serious consequences of the thrombus formed in blood vessels. Antithrombotics can be used therapeutically for prevention and treatment of blood clots. Treatment modalities of Pakshaghata like snehana, swedana and rechana may exert thrombolytic effect and facilitates to improve collateral circulation and blood supply to the affected area. The drugs described by virtue of their katu rasa (pungent taste), ushna virya (hot potency), tikshna guna (sharp nature), deepana, vibhandhahara (removes obstructions) and lekhana (scrapes/ dries up the kapha and medas) karmas remove the obstruction in the strotas and may act like antithrombotic drugs. So the chikitsasutra suggested for the management of pakshaghata and the judicial use of the above mentioned ayurvedic herbs may hold good to treat ischemic heart diseases.

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