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Review Article

CONCEPTUAL ASPECT OF DUCHENNE MUSCULAR DYSTROPHY

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ABSTRACT

The muscular dystrophies (MD) are a group of genetic diseases characterized by progressive weakness and degeneration of the skeletal muscles that control movement. DMD is one among the most common muscular disorders. The incidence is 1:3500 live male birth. It is X-linked recessive disease caused by a deficiency of a normal muscle protein called dystrophin, which maintains the integrity of the muscle cell wall. Degeneration of the skeletal muscles, which control movement leading to lose the ability to stand, walk and loss of ambulation before 10 years, with progression of the disease most patients succumb to death in their early 20s.Disease is having bad prognosis if the treatment start in early stages of the disease, it may slow or stop the progressive degeneration of muscles. As there is no specific treatment in any system of medicine for DMD, in modern therapeutic approach of muscular dystrophy is represents on corticosteroids, physical therapy, respiration assistance and gene therapy. All major neuromuscular disorders are identified with *Vata dosha.* In Ayurveda this pathogenesis can be clearly understood by the concept of *Adi bala pravritta vyadhi.* Here the pathogenesis occurs due to the *Beejabhagavayava Dushti* which leads to *Mamsa Vata Dushti.* The Ayurvedic treatments relevant to *Rasayana* group of herbo-mineral medicines and specified *Panchakarma* therapies have definite protective influence and long survival on *Dhatu Kshaya.* Keep upon this view in present study the therapies and medicines is useful for DMD is taken with their logical understanding.

KEYWORDS: Duchenne muscular dystrophy, Dystrophin, *Beeja Dushti, Mamsa-Vata Kshaya, Agni, Srotoshodhan.*

INTRODUCTION

The word dystrophy comes from Latin and Greek roots meaning of faulty nutrition. The disease was first described by Neapolitan physician Giovanni Semmola in 1834 and Gaetano Conte in 1836.However DMD was named by French neurologist Guillaume-Benjamin-Amend Duchene in 1806-1875[1]. Dystrophinopathies are a group of disorders resulting from mutations in the dystrophin gene located on the short arm of X chromosome in the Xp21 region. Duchenne muscular dystrophy is the most common dystrophinopathy. Duchene muscular dystrophy is known as x-linked recessive disorder. It affects muscles and lead weakness of muscular strength and function of muscles. This syndrome is marked by either generalized or localized. In DMD involve mutations in the dystrophin gene [2] Dystrophin is cytoskeletal protein localized in the inner surface of the muscle membrane and it forms dystroglycal-glycoprotein complex.[2]. This complex helps to maintain the integrity of muscle cells. So absence of dystrophin results in the destabilization of the entire dystroglycan-glycoprotein complex. So muscle mass is not growth well and cause to weakness of muscles. This condition is most apparent or symptomatic in skeletal muscle only heart and diaphragm muscle often involved. Most patients die because of heart failure or respiratory problems. An incidence of 1 in 3500 live male births. Each child of a carrier mother has a 50% chance of DMD. Though girls can be carrier, more than 80% shows no DMD related syndrome. Diagnosis of these disorders is based on clinical presentation, genetic testing, Muscle biopsy and muscle imaging. No any treatment is at present in DMD definitely in any medical field. Therapeutic approach of muscular dystrophy is represents on corticosteroids, physical therapy, respiration assistance and gene therapy.

Genetic Appraisal

Over 4700 mutatios have been reported in the leiden Duchenne muscular dystrophy mutation database. Deletion of >1 exons is the most common mutation seen. In dystrophinopathies, 65%of the pathogenic changes are large partial deletions. Mutations in the dystrophin gene can cause Duchenne muscular dystrophy or Becker muscular dystrophy. This is explained by the reading frame hypothesis, which states that mutations that disrupt the reading frame eventually leads to dystrophin deficiency and usually cause Duchenne muscular dystrophy.[3]

Pathogenesis

Dystrophy is a genetic defect and is caused by lack of a single muscle protein Dystrophin. DMD and BMD are due to different changes in the dystrophin gene, which contains information for a protein that is important for muscle cells to work properly. This gene is located on the X chromosome. Dystrophin is localized to the sarcolemma in normal skeletal muscle, but is completely absent in muscle from DMD patients.[4] At present a hypothesis postulates a defect in the sarcolemma membrane which allows a

substance as yet unknown but which could possibly be calcium, to enter the muscle fiber too freely, and there to activate neutral proteases which in turn maintain an excessive degree of muscle catabolism and lead to muscle fiber necrosis.[5, 6, 7, 8]

Clinical Features

Children with Duchenne muscular dystrophy usually become symptomatic before age of 5 yr and may even have history of delayed walking. Gait disturbances often become apparent at 3-4 yr of age. Waddling gait, Gower sign, and calf muscle pseudo hypertrophy are classical findings at this stage. Neck flexor muscle weakness is early. The progression of weakness may plateau between 3 and 6 yr of age. Subsequently there is increasing gait difficulty, development of contractures and increased lumber lordosis. Natural history studies have shown the age at loss of independent ambulation in untreated Duchenne muscular dystrophy to be between 8.8 and 10.5 yr. After loss of ambulation, there is worsening kyphoscoliosis, increasing upper limb weakness and bulbar dysfunction.

Weakness of intercostals and diaphragmatic muscles with spinal deformity affects the respiratory function. Dropping of vital capacity <20% of normal leads to nocturnal hypoventilation. Cardiomyopathy and arrhythmias are the major cardiac manifestations in Duchenne muscular dystrophy. Children with deletions of exons 48 to 53 are especially prone for cardiac complications. The cause of death in Duchenne muscular dystrophy patients is usually a combination of respiratory insufficiency and cardiomyopathy. Other clinical features of Duchenne muscular dystrophy include variable degree of intellectual disability and impaired gastric motility.

Around 10% of female carriers may show variable, degree of weakness with elevated creatine kinase levels, calf hypertrophy, cramps and increased risk of dilated cardiomyopathy. Full Duchenne muscular dystrophy phenotype may be present in case of complete inactivation of normal X chromosome.

Muscles Feature

Hypertrophy of calf muscles is striking feature, Calf, Glutei, deltoid, brachio-radialis and tongue muscles may appear large, Sternal head of pectoralis major and supraspinatous are atrophied

Laboratory Findings

The Serum creatine kinase levels are generally elevated. It has no correlation with severity of the disease or response to treatment. Multiplex PCR and the more sensitive multiplex ligation-dependent probe amplification are commonly employed genetic techniques for detection of mutations. Muscle biopsy may be required in mutation negative cases and also to differentiate between these two dystrophinopathies. The muscle biopsy shows features of muscular dystrophy which include necrosis and attempted regeneration of individual muscle fibers, increased variability of muscle fiber diameter with both hypertrophic and small fibers, and central nuclei. In end stage biopsy, almost the entire muscle is replaced by fibro fatty tissue. To confirm the clinical diagnosis immune histo chemical analysis of the muscle biopsy is usually performed. Absence of dystrophin stating is seen in Duchenne muscular dystrophy.

Diagnosis

Damaged muscles release enzymes such as Creatine Kinase (CK) into the blood. High blood levels of CK suggest a muscle dystrophy.

Electromyography: Changes in the pattern of electrical activity can confirm a muscle disease.

Muscles Biopsy

The analysis distinguishes muscular dystrophies from other muscle diseases. Special tests can identify Dystrophin and other markers associated with specific forms of muscular dystrophy.

Complications

- Respiratory muscle involvement and respiratory failure
- Pharyngeal weakness
- Contractures
- Scoliosis and thoracic deformities
- Cardiomyopathy leading to CCF
- Intellectual impairment
- Learning disabilities

Table 1: Differences from Becker Dystrophy

	Duchenne Dystrophy	Becker Dystrophy
Agetill ambulatory	10-12 years	Late adolescence or early adult life
Learning disabilities	common	less frequent
Onset of weakness	Earlier	Later
Death	By 18 years	25-40 years[9]

MANAGEMENT

There is currently no cure for any form of muscular dystrophy in modern medical science

Treatment is only helps in prevention or reduction in deformities.

monitoring

Pulmonary function tests-every 6 months if non – ambulatory, annually in ambulatory patients

Echocardiography: once in 2yr for<10 yr of age, annually if>10 yr

Serum calcium, phosphate annually

Physical therapy

Effective stretching and appropriate positioning at various joints, assistive devices to prevent contractures, avoid high resistance strength training, surgery for fixed contractures and spinal deformities

Other components

Respiratory and cardiac care

Management of gastrointestinal problems

Psychosocial management

Family education and genetic counselling

Newer therapies

Exon skipping, gene therapy, cell therapy

Management of a child with Duchenne muscular dystrophy requires a multidisciplinary team. The mainstays of management are maintenance of strength and joint range of motion by exercise, physiotherapy and avoidance of prolonged immobility. Corticosteroids are the only therapies proven to improve strength and prolong ambulation in children with DMD. Other supportive management includes pulmonary and cardiac care, nutrition, calcium homeostasis, appropriate immunization and orthopaedic care.

Ayurvedic Parlance

Body is originally composed of *Doshas, Dhatus and Malas*.[10] in normal status of *Doshas* etc. They should be preserved in all ways by the method as prescribed in the code of healthy living. [11].Pathogenic factors in the body are *Vayu, Pitta and Kapha*, while those in the mind are *Rajas* and *Tamas*. *Vata* occupies the most prominent place among the pathogenic factors in the body. Its prominence is due to the acuteness, varieties and seriousness of disease caused by it. [12] The *Vata* in its normal state of functions sustains all the organs of the body. It prompts all types of actions. It brings about compactness in all the tissue elements of the body.[13] *Vata* when aggravated afflicts the body with various types of disease and affects the strength, complexion, happiness and the span of life.[14] Aggravation of *Vayu* gives rise of contraction, stiffness of joints and pain in the bones as well as joints, atrophy of limbs and insomnia.[15] The function of *Sleshma* is to build fresh tissues (*Brimhana*), to increase its strength (*Balakrita*) and to give firmness to the limbs (*Sthairya krita*). [16] *Rasa* provides contentment and saturation and nourishes blood, blood generates clarity in complexion, nourishes muscles and sustains life, Muscle strengthens the body and nourishes *Medas*. *Mamsa Dhatu* is responsible for movements like extension, flexion, upward and downward movement (Su.Ni.1/17-18), make *Sharira Pushti* - Strengthen the body (S.Su.15), *Medas Pushti* - *Uttardhatu Poshana* an also Ojokar – promote immunity and resistance. In decrease of muscles, wasting of buttocks, cheeks, lips, pubic region, thigh, chest, axilla, calf abdomen and neck, roughness, piercing pain, malaise and looseness of arteries.[17] These all are the normal and abnormal function of the *Doshas and Dhatus.*

Factors Responsible for Abnormality in Foetus

Because of the defects in seeds (Sperm, Ovum), actions associated with the Soul, uterus, time and food as well as regimen of the mother, *Doshas* get variously vitiated and this results in the impairment of the shape, colour and sensory as well as motor organs of the offspring. *So* the foetus in the uterus of the mother gets afflicted with the vitiated *Doshas* [18]

Factors for Hereditary Defects

As a matter of fact, the sense organs of all living beings are born out of the soul and their existence or otherwise is determined by the fate i.e. the result of the past action. So the offspring of the dull parents do not invariably resemble their parents. [19]

DMD cannot be directly co-related with any single disease in *Ayurveda*. All most all major neuromuscular disorders are identified with *Vata Dosha.* This disorder can be considered under *Vata vikar* due to *Beeja Dushti* because of *Adibalapravritta*. [20] The important causative factors can be brought under *Aatma Karmaja* and *Beeja Dosha*.[21] These factors bring *Khavaigunya* at *Mamsa Dhatu* levels leading to *vitiation* of *Vata* which causes *Bhutagni* impairment. [22] Thus these causes attribute to DMD may be analysed as *Beeja Dusti* and *Atma Karma* are responsible for the X-linked recessive disease as well as gene mutations.

Samprapti Ghataka

The principal factors involved

Dosha: *Vata and Kapha*

Dushya: *Mamsa*

Srotasa: *Mamsavaha*

Srotodushti: *Sang*

Agni: *Mamsa-Dhatvagni*

Samprapti

Samprapti may take place under *Srotorodha, Beej Dushti* and *Agni*. *Ayurvedic Acharyas* carefully consider this condition as *Adibala-Pravrit Mamsa Vata Kshaya* due to *Srotorodha.* There is depletion of *Mamsagni* paving the way of *Ama* formation. It is followed by *Vitiation* of *Kapha Dosha*. [23, 24, 25] while *Srotorodha* produces hypertrophy in particular region, it also manifests as first *Prakopa* then depletion of *Vata* aliment. This complex pathogenesis is responsible for progressive wasting and necrosis of the affected muscle fibers.

Also *Samprapti* can be sort out as it is result of *Mamsa-Vata Kshaya* due to *Beeja Dosha* which leads to *Vata Vaishamya* of *Mamsa Dhatu.* This *Vitiated Vayu* causes improper formation of *Mamsa Dhatu* by its influence on the *Dhatvagni* of *Mamsa*.[26] So depletion of *Mamsagni* causes formation of *Ama* which leads to faulty nutrition and causes progressive relentless degeneration of muscle tissue.[27][65]

Dhatus are those substances which are retained by the body and always rejuvenated or replenished *Ras-Raktadi* seven *Dhatus* which develops in human body in a fixed sequential manner one from the other. Each succeeding *Dhatu* is a metabolic refinement of the previous *Dhatu* and get nourished by it. The first *Dhatu, Rasa* is the metabolic end product of the digestion that takes place within gastro-intestinal tract. *Rasa Dhatu* has to metabolized in to *Rakta Dhatu.* The *Mamsa Dhatu* comes from *Rakta Dhatu* and in turn give rise to *Meda Dhatu*. The *Asthi Dhatu* is the product of *Meda Dhatu Paka* that contains *Majja Dhatu* which is the prime seat of *Vata* element.[23,25] If the circulating *Rasa* of Mother is undernourished or defective, the development of *Mamsa Dhatu* is affected. *Agnis* are responsible for the process of metabolism. Each of seven *Dhatus* has individual *Dhatvagnis*. The increase or decrease of a particular *Dhatus* depends upon the increase or decrease of respective *Dhatvagnis*. According to *Charak, Mamsa Kshaya* may be present when there is prolonged *Majjagata Kupit Vata*. This is always followed by depletion of *Vata* element. It is genetic predisposition(*Beejadosha*) that convert physiological *Vata* element in to pathological morbidity. The *Srotodushti* is responsible for the *Mamsa Dhatu Kshaya*.

Management

Acharyas while explaining the *Dhatupaka Avastha* clearly signifies the importance of *Agni* which is whole and sole responsible for the formation of next *Dhatus*. Thus correction of *Agni* should be done by administration of *Deepan* and *Pachan Dravyas* in order to strengthen the process, *Doshas* must be balanced and metabolic toxins must be eliminated from *Dhatus* through *Panchakarma*.[28].The pre operative process quoted by *Acharyas* has the concept of "*Bruhmanyastu Mrudu Langyet*" that signifies the usage of *Rukshana* for better *Brimhana* treatment modalities.[29] For example *Udvatrana* with *Kola-Kulattha* which helps in the removal of *Srotorodha* and does *Sthiri Karan* of *Angas*. *Pachana* medicines are also explained as a mode of *Rukshana Chikitsa* and it is also must in the treatment of DMD initially with *Deepana* like *Parisheka* with *Dhanyamla*.[30, 31]

There is no any other excellent treatment for *Vata Dushti* such as *Basti Therapy*[32] *Niruha Basti* is the superlative therapy in *Pancha karma* field and it has a pivotal ability to re-construct of damaged muscles or nerves.[33] *RajYapan Basti* does priority which are supplying proper tone to the muscles and promoting the blood circulation with both *Shodhana* and *Brumhana* properties of its own as well as very much beneficial which pacifies the provoked *Vata Dosha*, increased strength of the person, maintains health and longevity.[34] *Rajyapan Basti* is having *Sadhyo Balajanana* and *Rasayan* properties means, it increase the power of the body and promotes strength of the body quickly.[35] By this *Sadhyo Balajanana* and *Vatashamak* properties of *Rajayapan Basti*, normalize and enhance the action of *Udan Vata* even enriched the *Rasa Dhatu. Deepana, Pachana* properties of *Basti* help to kindling of *Agni*[36]. *Agni* is very essentials for the formation of *Dhatus* and process of metabolic transformation[37]. *Rajyapan Basti* can be given for a long time period. Colonic mucosa transport irons, small molecules and water through the colonic membrane back and forth between lumen and plasma as a systemic effect. So it can get absorbed *Rasayana* effects without involving of drugs metabolism which occurs in *stomach*. So directly and quickly body get effect of whole drugs. So body nourished quickly and longer time duration without any complication.[38] Besides colon is enriched mucosal immune system. So immune system is even enhancing by the cleansing of colon. *Drug* can properly reach up to cell level due to removal of *Srotorodha* and helps to correction of *Mamsagata Dushti*. According to *Sushruta* there is better absorption occurs in *Rasayana* drugs after the elimination process. So body will quickly get *Brimhana*.[39]

Enteric nervous system is immensely complex of neurons and present in the wall of gastrointestinal tract. This system mediates directly to regulate the intestinal blood supply and mucosal epithelial water and electrolytes transport[40]. Due to *Sadhyo Balajanan* and *Rasayan* effect of *Basti,* the immensely number of nerves which located in ENS can get nourished directly. So can be supposed in DMD muscle weakness is getting decreased and muscles gets proper nourishment daily by given *Rajyapan Basti*.

Due to *Madhura, Guru* and *Jeevaneeya* properties of milk gives *Rasayana*, *Vrishya, Balya, Medhya* and *Brimhana* benefits[41]. Due to *Yogvahi, Rasayana* and *Tridoshahara* properties of Honey helps to nourished the muscles and scraps adhered *Doshas* from *Srotas*. Paste help to increase the functions of *Brimhana* and *Balya* upon the properties which they have and also give required thickness to the *Basti* material. So *Basti* may be retained in *Pakvashaya* for appropriate time. Due to *Sukshma* property of rock salt it reaches up to the micro channel of the body. Due to its *Tikshna* property it helps to break down the morbid materials and *Dosha Sanghatan*[42]. Sodium iron fulfils essential action during absorption process by *Basti*. By the adding of Ghee enhances *Varna, Bala, Rasa, Shukra* and *Ojas* in DMD due to the properties of *Madhura Rasa, Sheeta Veerya* and *Vatapittahara* properties[43] *Rajyapan Basti* drugs also enriched with *Tikta Rasa* dominance such as *Daruharidra* (*Berberis aristata* DC), *Guduchi* (*Tinospora cordifolia* (thumb) etc. In one study on spinal cord injury had been proved stem cells implantation due to Curcumin (Diferuloylmethane) which is the active ingredient of Turmeric (*Curcuma longa* L)[44].Turmeric is a *Tikta Rasa* (Bitter test) dominant plant. There by it may have positive impact on cell implantation by *Tikta Rasa* dominance and *Tikta Ras* helps to reduce the degeneration of *Asthi* and *Majja*. It resultant to decrease of muscle wasting.[44, 45] By all these impacts which are adding to the *Rajyapan Basti* given logical and beneficial effect in the DMD to enrich their weakened muscles.[67]

Research has shown that *Virechana* does the detoxification which lead to better absorption of *Rasyana Drugs*, other *Brihmana Dravyas* and correction of *Agni*.[46] *Matra Basti* is another variety of the Karma. It also rejuvenates the body and further helps in improving from the *Dhatukshaya* caused due to *Vata Dosha* that is why both *Virechana* and *Basti* are explained in the principle of *Medomamsa Dushti*.[47]

Not only these invasive therapies like *Virechana, Basti* etc. but *Upkarma* i.e., *Para Panchakarma* procedures are very much essential for the same. It is very well understood in the treatment principle of *Vata Roga* by *Charaka* and *Yogaratnakar* that *Upakarmas* like *Swedana* is having prime treatment modalities.[48] *Abhyantra Snehana* helps to pacifies the *Vata Dosha.* [49] Whereas *Swedana* like *Shastika Shaali Pinda Swedana* also improves the tone of the body.[50] *Swedana Karma* increases the metabolic activity which in turn increases the oxygen demand and blood flow. This vasodilatation stimulates the superficial nerve ending causing a reflex dilatation of the arterioles. Due to the effect of heat on the sensory nerve ending there will be a reflex stimulation of sweat glands in the areas exposed to heat. This rise in temperature induces muscle relaxation and increases the efficacy of muscle action as the increased blood supply ensures the optimum condition for the muscle contraction.[51] *Swedana* also acts by the mechanism of thermoregulation regulated by skin and coordinated with the functions of the other excretory organs. It is supplied with many groups of nerves, which conduct various stimuli. The secretion of sweat is under nervous system control, especially autonomous. The hair of the skin is tactile sense organs and their secretion produces some nervous changes. Thus, *Swedana* can bring about changes indirectly on the autonomic nervous system

and the heat can bring about changes in conduction of nerve stimuli, by changing sodium-ion concentration.[52] Thus these modalities are of prime importance as no treatment acts on prime pathogenesis and present approach is taken to improve quality of life over muscular dystrophy.[66]

Vata and *Rakta Dhatu* are two major life sustaining elements in the body. The *Vata* has been attributed like genetic material that carriers life information essential for different activities. The *Rakta Dhatu* is the basis of biological force that provides nutrition at cellular level and paves the way of excretion of metabolic toxins. The driving force beyond *Rakta Dhatu* is *Vata* element which circulates itself to cellular level along with *Rakta*. The conjoint circulation of both *Rakta* and *Vata* is manifestation of life (*Prana*). This *Prana* is responsible for the contraction and relaxation of muscle fibers or muscular activity. It means we have to focus our attention on the *Dhatvagnis Paka* of *Rasa-Rakta-Mamsa-Medo Dhatus*. In this context *Ayurvedic Rasayana* Therapy has significant role to play[53,54] Ancient *Ayurvedic* physicians had developed certain dietary and therapeutic measures to delay degeneration process and rejuvenating whole functional dynamics of the body system. This revitalization and rejuvenation is known as the *Rasayan Chikitsa. Rasayana* are special *Ayurvedic* resources that increase enzymatic essence of each *Dhatu* starting from *Rasa Dhatu. Ayurveda* uses herbal mineral and metallic source for this purpose. The pure gold *Bhasma* in law dose has been used successfully in the management of degenerative disease of *Mamsa* and *Majja Dhatu.*[55,56,57] Certain *Ayurvedic* herbs known for their *Rasayana* effects are being scientifically verified for their possible effect in the Management of Muscular Dystrophy. The well known herb Curcuma longa has been widely investigated for the immune-localized and activation of nuclear factor-{Kappa}B in polymyosities, dermatomyositis and DMD. *Withania somnifera* is used for stamina and brain functions. It contains Withanolide which is anti –inflammatory, induces significant regeneration of axons, pre-synapses and post –synapses in the neurons. It suppress free radical generation, It also ameliorates neuronal dysfunction.[58,59,60] The cardiac problems associated with some forms of muscular dystrophy sometimes need treatment. *Terminalia Arjuna* has remarkable cardio protective, heart muscle strengthening properties. Regular use of *Arjuna* improves pumping activity of heart, improves cardiac muscle strength. *Tinospora cordifolia* have been used in general debility. It is also an effective immunostimulant. It is used in *Ayurvedic Rasayana* to improve the immune system and the body's resistance to infections.[61]

Usually *Rasayana* molecule does not work without purificatory procedures. After the purification *Rasyana* therapy can be adopted. The *Deepana, Pachana* process must be strengthened the *Dosha* must be balanced and metabolic toxins must be eliminated from *Dhatu* through *Panch karma* procedures in order for *Rasayana* molecule to work.[62,63] *Yogic* support is always found useful in the management of Muscular Dystrophy. *Pavanmuktasana* series of *Yoga Asanas* and *Bhastrica Pranayama* are important, especially when the dystrophy has progressed for several years. Deep breathing and laughing is often recommended to optimize respiratory care.[55, 56]

Ayurvedic management did not claim for the genetic effect of restoring dystrophin production, it did reduce serum CK levels. This could be a sign of decreased muscle damage. Since there was definite improvement in functional ability, it is possible that complementary *Ayurvedic* treatment allow longer survival with minimum disability.

CONCLUSION

Beej Dushti, Agni, Srotorodh are responsible for the disease. *Ama Pahan, Agnidipan* Drugs, *Anti Visha* Dugs, Psychotropic Drugs *Brimhana* Drugs *Rasayan* Drugs, *Sroto Shodhak* Drugs are beneficial for the treatment. *Shodhan* purpose *Udvartana* with *Kola-Kulattha Churna*, *Shashtik Shali Pinda Sweda* and *Yapan Basti* are beneficial. Treatment is only helps in prevention or reduction in deformities. "By the Ayurvedic treatment We cannot add year into the life but we can add quality in life".

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