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A Critical Review on Motor Neuron Disease (Amyotrophic Lateral Sclerosis- ALS) and their Management through Ayurvedic Aspect

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ABSTRACT

Motor neuron disease is a neurodegenerative condition caused by loss of upper and lower motor neurons in the spinal cord, cranial nerve, nuclei and motor cortex. MND is a rare condition that affects the nervous system. Annual incidence is about 2/1,00,000 with a prevalence of about 7/1,00,000. The average age of onset 65, with 10% presenting before 45 years. The most common form of MND is amyotrophic lateral sclerosis (ALS). ALS is characterised by combination of upper and lower motor neuron sign; there are rarer, pure lower (Progressive muscular atrophy) or upper (progressive lateral sclerosis) motor neuron variants of MND. In motor neuron disease, sensory system, cerebellum and other areas of brain are not affected. There is no precise equivalent correlate for MND in Ayurveda. In the Samprapti of MND, all the three Doshas are involved. The Vyadhi Swarupa of MND shows predominant involvement of both Vata and Kaphain Samprapti. If the Avarana caused by aggravated Kapha with the Kaphakara Nidana may lead aggravation of Vata and produce the disease. If there is Anubandh of the Pitta the degeneration may be faster. The Tikshna, UshnaGunas of Pitta together with Shoshna Svabhava of Vata leads to Ashukari degeneration seen evident of bulbar onset from the disease in which there is Shosha of the bulbar muscle leading to dysphasia, dysarthria. So the treatment in Ayurveda mainly focuses on the pacification of Vata and Kapha& bringing back the equilibriums between all three Doshas.

Key Words: *MND, ALS, Ayurvadic Treatment*

INTRODUCTION

Motor neuron diseases are a group of degenerative disorders selectively affecting upper or lower motor neurons, or both. The condition is progressive has a fatal outcome. Symptoms vary in severity and include muscle weakness and atrophy, fasciculation's, emotional liability and respiratory muscle weakness[1]. Annual incidence is about 2/1,00.000 with a prevalence of about 7/1,**00**,000[2]. Out of every 10 people with MND 6 are men and 4 women[3]. ALS is the commonest type of MND affecting the anterior horn cells (responsible for LMN signs) and the corticospinal tract (responsible for UMN signs). Other motor neuron diseases involve only particular subsets of motor neurons[1]. Normally message from the nerve cells in the brain (called upper motor neurons) are transmitted to nerve cells in the brain stem and spinal cord (called lower motor neurons) and from them to particular muscles. Upper motor neurons

direct the lower motor neurons to produce movements such as walking or chewing. Lower motor neurons control movement in the arms, legs, chest face, throat and tongue. Spinal motor neurons are also called anterior horn cells. Upper motor neurons are also called carticospinal neurons. When there are disruption in the signals between the lower motor neurons and the muscles, the muscles do not work properly, the muscles gradually weaken and may begin wasting away and develop uncontrollable twitching (called fasciculations). When there are disruption in the signals between the upper motor neurons and lower motor neurons, the limb muscles develop stiffness (called spasticity) movement become slow and effortful, and tendon reflexes such as knee and ankle jerks become over reactive. Over the time, the ability to control voluntary movement can be lost[4]. In *Ayurveda* MND can be considered as *Vata* predominant disease. *Vata* is considered a chief factor for physiological maintenance of the body[5]. Most of the sign and symptoms of MND like fasciculation, cramps, wasting, weakness, spasticity bulbar etc. match that of the classical signs and symptoms of *Vata* derangement described in *Ayurveda*[6]. In the *Samprapti* of MND, all the three doshas are involved. If the *Avarana* is caused by aggravated *Kapha*, with the *Kaphakaranidana.* It may lead aggravation of *Vata* and produce the disease. If there is *Anubandha* of pitta, the degeneration may be faster. The *Tikshna, Ushna Gunas* of *Pitta* together with *Shoshana Svabhava* of *Vata* leads to *Ashukari* degeneration and form of the disease in which there is *Shosha* of bulbar muscles leading to dysphagia, dysarthria[7]. In modern medicine there is no effective treatment for MND. The first line of MND treatment is avoid all causative factors[6]. In *Ayurveda* the line of treatment of MND mainly focuses on to remove *Avarana* of *Kapha* and pacification of *Vata.*

The difference between upper motor neuron and lower motor neuron shown below in table 1.

Table 1 Differences between upper motor neuron and lower motor neuron[8]

	Upper motor neuron	**Lower motor neuron**
Affection	Muscle groups	Individual muscle
Tone	Clasp knife rigidity	Flaccidity
Nutrition	Slight wasting due to disuse	Marked wasting
Involuntary movements	Flexor spasms sometimes	Fasciculation sometimes
Reflexes	Deep jerk brisk plantars extensor	Deep jerks absent, plantars flexor
Electrical reaction	Normal	Degeneration

Causes[9]:

Scientists are not sure why motor neurons start to lose function. Several inter related factors are responsible that causes MND such as-

Excess glutamate – Glutamate is neurotransmitter that transmits data from cell to cell. Abnormally high levels of glutamate may be toxic and could lead to a disturbance in the chemical communication required for proper nerve function.

Cell metabolism- Transport systems exist in all cells that bring nutrients and chemical component

into the cell while at the same time moving waste products out. These transport systems are disturbed in the motor neurons during the initial stage of MND.

Aggregates – Unusual clumps of protein molecules have been found to accumulate in the motor neurons of MND which undermines the hormonal functioning of motor neurons.

Lack of antioxidant production – Researches indicates that motor neurons of patients with MND do not produce enough antioxidants to neutralize the free radicals that emerge as a natural by product of cell activity.

Mitochondria of motor neurons – The mitochondria of motor neuron cells of people with MND appear to be abnormal, which alter the allergy production.

Neurotrophic factors- These are molecules, usually proteins which facilitate the growth or repair of nerve cells it has been found that neurotrophic factors are not produced property in patients with MND

Glia cells- These cells surround neurons and provide support for them and isolation between them. They also provide motor neurons with nutrients and relay data from one cell to another. In some cases problems with glia cells can effects the motor neurons.

Prions and ALS link: Recent researchers have discovered a vital link between prions and ALS.

Clinical features:

MND typically presents focally, either with limb onset (e.g. foot drop or loss of manual dexterity) or with bulbar symptoms (dysarthria, swallowing difficulty); respiratory onset is rare but type 2 respiratory failure is a common terminal event. Sensory, autonomic and visual symptoms do not occur, although cramp is common. Examination reveals a combination of lower and upper motor neuron signs without sensory involvement. Cognitive impairment is under-recognised in MND[10]. There is no bladder involvement[11].

Sign &symptoms[12]:

Wasting & fasciculation of muscles.

Weakness of muscles of limbs, tongue, face and palate.

Pyramidal tract involvement, causing spasticity, exaggerated tendon reflexes, extensor plantar responses

External ocular muscles and sphincters usually remain intact

No objective sensory deficit

Evidence of cognitive impairment with frontotemporal dominance

Course: Symptoms often begin focally in one part and spread gradually but relentlessly to become widespread[12].

Types[13]: The types of MND shown below in table 2.

Table 2 Types of MND

Type of MND	Type of degeneration
ALS	Both UMN and LMN
PLS (Primary lateral sclerosis)	UMN
PMA (Progressive muscular atrophy)	LMN in Spinal cord

Progressive Balbar palsy	LMN – Bulbar Region
Pseudobulbar Palsy	UMN – Balbar Region

Amyotrophic lateral sclerosis (ALS)

ALS is also called Lou Gehrig's disease. It is a progressive, ultimately fatal disorder that eventually disrupts signals to all voluntary muscles. Approximately, 75% of the people with classic ALS will also develop weakness and wasting of the bulbar muscles[14].

Etiology

Most of the ALS cases are sporadic[1], only 5% to 10% of cases are familial ALS having autosomal dominant (AD), Autosomal recessive (AR) or X-linked pattern of inheritance. Following are risk factors for the development of ALS[15].

Genetic factors

Smoking

Old age

Toxins: lead, tin and mercury

Electric shock

Radiation exposure

Excess glutamate activity[1]

Pathology:

The main pathology is death of anterior horn cells of the spinal cord and cranial motor nuclei of the lower brainstem (except those that innervate ocular muscles). The pyramidal tracts show degenerative changes and there may be secondary demyelination[1].

The cause of sporadic ALS is not well defined. Several mechanisms that impair motor neuron viability have been elucidated in mice and rats induced to develop motor neuron disease by SOD1 transgenes with ALS-associated mutations. It is evident that excito-toxic neurotransmitters such as glutamate participate in the death of motor neurons in ALS. This may be a consequence of diminished uptake of synaptic glutamate by an astroglial glutamate transporter,EAAT2. It is striking that one cellular defence against such excitotxicity is the enzyme SOD1, which detoxifies the free radical superoxide anion. Because SOD1 is mutated in some familial cases of ALS, it may be that glutamate excitotoxicity and ALS result from free radical accumulations in motor neurons. The mutant protein is conformationally unstable and prone to aberrant catalytic reaction. In turn these features lead to aggregation of SOD1 protien, impairment of axonal transport, reduced production of ATP other perturbation of mitochondrial function, activation of cyclo-oxygenase within the ALS spinal cord, ultimately induction of cell death via pathways that are at least partially dependent on casepases. Reduce VEGF (vascular endothelial growth factor gene) expression increase the risk of ALS[16].

Clinical features:

Initial symptom is usually insidious onset of weakness and clumsiness of one hard for skilled activity which progresses and gross activity also becomes difficult.

Overtime the opposite hand is involved and whole of both upper limbs may be affected.

LMN signs such as wasting, flaccidity, loss of tendon reflexes and fasciculations are seen along

with UMN sign such as spasticity and exaggerates reflexes.

Lower limb involvement may precede or follow upper limb involvement. There is difficulty in walking with spastic gait and pyramidal signs. The knee and ankle jerks are exaggerated. Planter response is extensor bilaterally.

Involvement of cranial nerve nuclei causes difficulty in swallowing, nasal regurgitation and slurred speech. Tongue shows atrophy and fasciculations. UMN involvement results in pseudobulbar palsy with exaggerated jaw jerk.

There is no sensory loss but subjective sensation like numbness, cramps, neuralgic pain may be complained of. Impotence occurs early in the disease. There is no loss of sphincter control[17].

In addition to motor symptoms, patients with ALS often have non-motor associated symptoms including sleep disturbance, subtle cognitive dysfunction and mood changes[18].

Complications[19]:

Breathing in food or fluid (aspiration)

Loss of ability to care for self

Emotional lability

Lung failure

Pneumonia

Pressure sores

Weight loss LM

Usual duration of survival in balbar palsy is about 2 years, ALS 4-5 years and PMA 8-10 years. Final state consist of anarthria, aphagia and widespread limb weakness in a person with full consciousness. Death occurs from pneumonia or respiratory failure[20].

***Ayurvedic* aspect:**

There is no precise equivalent correlate for MND in *Ayurveda*. Though all three *Doshas* are involved in the *Samprapti* of MND, The *Vyadhi Swarupa* of MND shows predominant involvement both *Vata* and *Kapha* in *Samprapti*. If may lead aggravation of *Vata* and produce the disease.

If there is *Anubandha* of *Pitta,* the degeneration may be faster. The *Tikshna, Ushna Gunas* of *Pitta* together with *Shoshana Svabhava* of *Vata* leads to *Ashukari* degeneration, seen evident in the bulbar onset from of the disease in which there is *Shosha* of bulbar muscles leading to dysphagia, dysarthia. The *Vyana Kopa* also means lack of sufficient nutrition to the *Dhatus*, causing *Kshaya* of *Dhatus* especially that of *Mamsa Dhatus*. The *Dhatukshaya l*eads to further aggravation of *Vata* that may lead to *Anyonya Avarana* of *Vata.*

When *Udana* is obstructed by *Avarana* of *PranaRodha* to *Nishvasa*, *Ucchvas* and *MukhaShosha* is seen.

Avarana to*Prana* by *Udana* causes loss of *Bala*, *Ojas*, and *Varna*

Avarana of *Prana*and *Udana* are considered to most *Gurutara* among all types of *Avarana* by *Susuruta. Pidana*of them leads to loss of *Bala* and life. *Samarodha*to *Nishvasa* and *Uchvasa* due to *Pranakopa*. Ultimately leads to *Pranahani* and death[7].

SamptiGhataka*[21]*:

Dosha : All three *Doshas* are involved but in ALS is a *VataKapha* predominant disease and bulbar palsy shows *Pittanubandha*.

Dushya: Mamsa, Medas, Asthi, Majja, Sira, and Snayu

Srotasa: Masavaha, Medovaha, Majjavaha, Asthivaha

Rupa*[22]*:

Balashaya

Sphurana

MamsaShosha

Vakvikriti

Minminatva

Stambha

Lalashrava

Bhaktarodha

Investigation:

Blood tests: Usually normal, other than a mildly raised creatine kinase.

Sensory and Motor nerve conduction studies: Normal but there may be reduction in amplitude of motor action potentials due to axonal loss.

EMG: Usually confirm the typical features of widespread denervation and re-innervation.

Spinal fluid analysis: not usually necessary

Genetic testing: testing is increasing in importance, with mutations found in SOD1, FUS, TARDBP and C9orf72 that may help predict risk and phenotype of disease in those with a family history of MND[12].

Cervical spine CT or MRI to be sure there is no disease or injury to the neck which can mimic ALS[19].

TMS (Transcranial magnetic stimulation): To measure activity of upper motor neurons[5].

Muscle biopsy: To recognized Denervation progresses, muscle atrophy[23].

Treatment: In modern medicine

There is no effective drug for the treatment of MND[17].

Patients should be managed within a multidisciplinary service, including physiotherapists, speech and occupational therapists, dietitians, ventilatory and feeding support, and palliative care teams, with neurological and respiratory input.

The drug Riluzole has been approved for ALS because it produces a modest lengthening of survival. Riluzole blocks release of glutamic acid and may slow the progression of disease by disrupting glutamate- mediated neurotoxicity[12].

The absence of specific therapy for MND, rehabilition measures helpful. Foot drop splints facilitate walking and finger extension splints can potentiate grip. If there is difficulty in chewing and swallowing, gastrostomy is helpful for restoring nutrition and hydration[17].

Treatment principle: In *Ayurveda*

To remove *Avarana* of *Kapha.*

*F*ollowed by *Kevala Vata Chikitsa.*

Maintained the *Agni* in equilibrium.

In initial stage *Katu Rasa, Ushna Virya Ausadhas* are given. Then *Madhura Rasa Ausadhas* are given to treat *Kevala Vata Avastha*[24].

Following therapeutic regimens are advocated for its management[6]:

Avoid causative factors: The first line of MND treatment is to avoid all possible causative factors.

Vaspa Sweda: This is performed after an oil massage viz- *Mahamasa Taila, Narayana Taila, Lakshad iTaila* etc to control vitiated *Vata Dosha*.

Shashtika Shali Pinda Sweda: It is performed over the affected body parts. It strengthens the muscles improve the blood circulation and provide nourishment to the affected body parts.

Panchkarma therapy: Treatment like *pichu, Sirovasti, Sirodhara,* and *MatraVasti*are helpful

Nourishing and Rejuvinative treatment: Drugs like *Ashvagandha, Medhya Rasayanas, Amalakirasayana, Pippalirasayana, Triphala*and*Swarna preparation.*

Medicated paste bandage over affected part to tone the muscle nerve and conserve the power of muscles.

Compound formulation: Drug like *Tryodashangguggulu, Panchamritalauhaguggulu, dashangaguggulu, dashmulaghanavati, mahayograjguggulu, mahavatavidhvashi rasa, Rasaraj rasa, Dashamulakashaya, MaharashnadiKshaya, Ashvagandharishta, Draksharista, Balarishta*etc are helpful to MND patients.

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