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Approval Process

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Motor Neuron Disease-Amyotrophic lateral sclerosis (ALS) Diagnostic and Therapeutic Guidelines

1. Introduction

Motor neuron diseases or amyotrophic lateral sclerosis is a fatal multisystem neurodegenerative disease characterized by progressive loss of the upper and lower motor neurons throughout the central nervous system leading to progressive weakness of the bulbar, limb, thoracic and abdominal muscles. It is important to recognize the spectrum and heterogeneity of motor neuron diseases presentations so as not to miss early cases, since the median survival in ALS cases does not exceed 48 months, from the time of symptoms onset. Considering the seriousness of the disease and the limited options for treatment, it is important to reassure MND patients that treatments are available to improve survival, quality of life, and physical functioning, as there are no curative therapies for this fatal disease.

2. Scope

These guidelines apply to all healthcare workers dealing with MND/ ALS adult patients.

3. Purpose

To provide a standardized approach to the management of adult patients with MND/ALS.

4. Definitions

Motor neuron diseases (MNDs): are a group of rare neurodegenerative disorders that selectively affect motor neurons, the cells which control voluntary muscles of the body. They include amyotrophic lateral sclerosis (ALS), progressive bulbar palsy (PBP), pseudobulbar palsy, progressive muscular atrophy (PMA), primary lateral sclerosis (PLS), and monomelic amyotrophy (MMA), as well as some rarer variants resembling ALS.

Amyotrophic lateral sclerosis (**ALS**): also known as **motor neuron disease** (**MND**) or **Lou Gehrig's disease**, is a specific disease characterized by progressive degeneration of the motor nerve cells in the brain and spinal cord that control the voluntary muscles.

B. A useful nerve conduction study support for ALS is identification of a split-hand pattern of involvement, in which the compound muscle action potential (CMAP) amplitudes recorded from thenar and first dorsal interosseus muscles are reduced to a greater extent than that of the hypothenar muscles.

C. EMG should include cervical, thoracic, and lumbar segments, starting in the most clinically affected region. If ongoing motor axon loss is not detected in three segments, cranial muscles should be sampled. EMG findings include:

i. Enlarged polyphasic motor unit action potentials activating in a reduced recruitment pattern (chronic motor axon loss pattern).

ii. Moment-to-moment amplitude variation, if seen, indicates ongoing denervation and reinnervation and suggests a progressive process.

iii. At rest, muscles show abnormal spontaneous activity, including fibrillation potentials and fasciculation potentials.

D. Distal muscles are more likely to be abnormal when compared to proximal muscles.

5.3.2. Neuroimaging

A. Conventional Neuroimaging plays a crucial role in diagnosis and exclusion of MND/ALS.

B. Conventional magnetic resonance imaging (MRI) is most useful in excluding MND/ALS mimics in addition to other spectra of diseases, such as multiple sclerosis or other inflammatory conditions, which can appear radiographically.

C. Most commonly, Cervical MRI is done to exclude UMN lesion such as cervical myloradiculopathy and others MND mimics.

D. When suspecting ALS, conventional MRI sequences demonstrate bilateral symmetric T2 and FLAIR hyperintensities anywhere along the corticospinal tract, superiorly from the cortices extending caudally to the brainstem. This to be done during working hours to be supervised by neurologists to locate the area of MRS.

E. MR spectroscopy (MRS) also has potential value where it demonstrates increased choline and myoinositol metabolic substrates localized to the precentral gyrus.

B-The diagnosis of ALS requires the **absence of (diagnosis by exclusion)**:

i. Sensory signs
ii. Sphincter disturbances
iii. Visual disturbances
iv. Autonomic features
v. Basal ganglion dysfunction
vi. Alzheimer-type dementia
vii. Others ALS mimics syndromes

C. The diagnosis of ALS is supported by:

i. Fasciculation's in one or more regions
ii. Neurogenic changes in EMG test results
iii. Absence of conduction block on nerve conduction study.

5.4.2. The revised El Escorial diagnostic criteria for ALS with the Awaji Electro diagnostic algorithm included.

These criteria provide consensus guidelines for the diagnosis of ALS **(Table 2).**

5.5. Amyotrophic Lateral Sclerosis Mimics

Up to 10% of patients initially diagnosed as ALS can have an alternative diagnosis many of which are treatable. No patient should be stamped as having MND without having a proper work-up of all its differentials as there might be a treatable condition masquerading as MND.

5.5.1. Conditions with both upper motor neuron (UMN) and lower motor neuron (LMN) signs and symptoms, which can be mistaken for MND/ALS:

A. Cervical Spondylotic myeloradiculopathy
B. Intramedullary spinal cord tumours
C. Syringomyelia
D. Non compressive myeloradiculopathy
E. Radiation-induced radiculomyelopathy
F. Chronic organophosphrous poisoning
G. Thyrotoxicosis
H. Hyperparathyroidism
I. Human immunodeficiency virus (HIV) infection

F. Effective channels of communication and coordination are essential between the hospital-based multidisciplinary clinic team, the primary healthcare sector, the palliative care team (if available) and community services.

5.6.1 Physical Therapy:

Physical Therapy is an integral component of the ALS multidisciplinary team and is well grounded in rehabilitation and active living concepts despite the lack of a cure and rapidly progressive nature of the disease.

A. According to the nature and significance of the activity limitations impairments and patient's restrictions , decision- making to provide plan of treatment to help patient be independent in activity of daily living as possible throughout the course of the disease.

B. Gentle, low impact aerobic exercise such as walking, swimming and stationary bicycling can strengthen unaffected muscles, improve cardiovascular health and aid patient fight fatigue, depression and contracture of muscles.

C. Appropriate physical therapy interventions:

i. Fatigue through energy conservative

ii. Muscle shortening and cramps through stretching exercises

iii. Pain (intervention dependent on the source of pain)

D. Exercise should focus on improving posture, prevent joint immobility and slowing the progressive muscle weakening and atrophy

E. Stretching and strengthening exercises may help reduce spasticity, increase range of motion and improve circulation.

5.6.2. Medications:

A. **Riluzole** (local Purchase):

i. A. Patients with ALS should be offered treatment with Riluzole **50 mg twice daily**.

B. Treatment should be initiated as early as possible after diagnosis and realistic expectations for treatment effects and potential side effects should be discussed with the patient and caregivers.

B. Patients should be referred to a dietitian as soon as dysphagia appears. A speech and language therapist can give valuable advice on swallowing techniques.
C. The timing of PEG is based on an individual approach taking into account bulbar symptoms, malnutrition (weight loss of over 10%), respiratory function and the patient's general condition. Early insertion of a feeding tube is recommended.
D. Tubes with relatively large diameter are recommended to prevent tube obstruction.
E. Prophylactic medication with antibiotics on the day of the operation may reduce the risk of infection.
F. NGT feeding may be used in the short-term and when PEG is not suitable.
G. Home parenteral nutrition may be used in patients with advanced ALS.

5.6.5. Speech and Communication in patients with MND/ALS

A. Regular assessment (i.e. every 3–6 months) of speech and language function by a trained speech and language therapist is recommended.
B. Those with evidence of early language deficits should undergo full neuropsychological testing.
C. The use of appropriate communication support systems with eye-gaze technology (ranging from pointing boards with figures or words, to computerized speech synthesizers) should be individualized and appropriate training and support provided as required.

5.6.6. Symptomatic Treatment

The following conditions and symptoms: Sialorrhea, Bronchial secretions, Pseudo bulbar Emotional Liability, Cramps, Spasticity, Depression and anxiety, Insomnia and fatigue and Venous thrombosis, should be evaluated and assessed regularly through clinical visit and should be addressed to the caregiver. For the management of each condition please refer to **(table 3)**.

5.6.7. Unproven Therapies (Stem cell transplant and/or Gene therapy)

A. Clinical trials testing cellular therapies have yet been incomplete, not well-designed, carried out in an insufficient number of patients, lacking safety and clinical efficacy as well as not supported by pathological evidence.

5.9. Palliative and end-of-life care

5.9.1. Should follow local hospital rules and regulations in regard to end-of-life care, palliative and DNR status. See **Do-Not- Resuscitate Guideline**

5.9.2. As ALS remain incurable, end-of-life counselling is an important component of patient care and is an American Academy of Neurology quality measure.

5.9.3. End of life care is best held early in the disease course before a respiratory or nutritional crisis.

5.9.4. Quality-of-life discussions include defining what interventions are consistent with the patient's wishes. Palliative and hospice care may have a role. Caregiver fatigue and burden should be assessed on an ongoing basis and addressed.

5.9.5. Discussions regarding quality of life should be framed in the context of disease progression to best understand end-of-life decisions.

6. Responsibilities

6.1.Head of Neurology:

6.1.1. Ensure all doctors are aware about these guidelines.

6.1.2. Ensure all staff is adhering to these guidelines.

6.2.Director of Radiology:

6.2.1. Ensure all staff is aware about these guidelines.

6.2.2. Ensure all radiographer are aware bout the sequences.

6.3. Director of laboratory:

6.3.1. Ensure all staff is aware about these guidelines.

6.3.2. Ensure all laboratory staff are aware about the laboratory test related MND.

6.4. Director of Pharmaceutical Care & Medical Supplies:

6.4.1. Ensure all staff is adhering to these guidelines.

6.4.2. Ensure all staff is Checking prescription before dispensing.

6.5. Director of Rehabilitation and Physiotherapy:

6.5.1. Ensure all staff are adhering to these guidelines.

6.5.2. Ensure all staff includes speech, dietitian, physiotherapist and occupation

6.5.3. Therapists are aware about their rules in regard to MND management

10. References:

Title of book/ journal/ articles/ Website	Author	Year of publication	Page
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Appendix 2

Table 2: The revised El Escorial diagnostic criteria for ALS with the Awaji electrodiagnostic algorithm included.

Clinically definite ALS UMN and LMN clinical signs or electrophysiological evidence in three regions
Clinically definite ALS – laboratory supported UMN and/or LMN clinical signs in one region *and* the patient is a carrier of a pathogenic SOD1-gene mutation
Clinically probable ALS UMN and LMN clinical or electrophysiological evidence by LMN and UMN signs in two regions with some UMN signs rostral to the LMN signs
Clinically possible ALS UMN and LMN clinical or electrophysiological signs in one region only, or UMN signs in at least two regions, or UMN and LMN signs in two regions with no UMN signs rostral to LMN signs. Neuroimaging and laboratory studies (Table 2) have excluded other diagnoses.

ALS, amyotrophic lateral sclerosis; EMG, electromyography; LMN, lower motor neuron; UMN, upper motor neuron.

Appendix 4

Table 3: Overview of symptomatic treatment strategies in ALS

Symptom	Treatments and Interventions[a]
Sialorrhea	Anticholinergics (amitriptyline, atropine ophthalmic drops, glycopyrrolate, scopolamine patch); botulinum toxin injections; external radiation; suction device
Bronchial secretions	Mechanical insufflator-exsufflator; suction device; hydration; guaifenesin; nebulization (saline); beta receptor antagonist; humidifier
Pseudobulbar affect	Inform patients and caregivers that it is a symptom of amyotrophic lateral sclerosis; tricyclic antidepressants; selective serotonin reuptake inhibitors (SSRIs); dextromethorphan-quinidine
Cramps	Stretching, massage, hydrotherapy; magnesium; tonic water; mexiletine; levetiracetam
Spasticity	Physical therapy including stretching and range of motion; antispasticity medications (baclofen, tizanidine); benzodiazepines; dantrolene; botulinum toxin injections; intrathecal baclofen pumps
Depression and anxiety	Tricyclic antidepressants; SSRIs; serotonin norepinephrine reuptake inhibitors (SNRIs); psychotherapy; counseling
Insomnia	Treat causative symptoms (depression, cramps, pain, respiratory distress); tricyclic antidepressant or hypnotic; sleep hygiene
Fatigue	Treat causative symptoms (depression, cramps, pain, respiratory distress); energy conservation; stimulant
Dyspnea	Elevation of head of bed; noninvasive ventilation; in palliative approaches: benzodiazepine, opioid
Constipation	Fluid and fiber intake; osmotic laxative; stimulant laxative; enteral nutrition adjustments
Pain	Physical therapy, especially to limit joint contractures; repositioning, pressure relief, mechanical support for weak limbs; analgesics (acetaminophen, nonsteroidal anti-inflammatory drugs, opioids)
Dysarthria	Speech-language pathology evaluation; assistive communication (writing, electronic devices); mouth care
Dysphagia	Speech-language pathology evaluation; enteral nutrition
Nutrition	Nutritionist evaluation; appetite stimulants; snacks, more frequent meals
Weakness	Physical therapy; occupational therapy; adaptive equipment (build-up handles, zipper pulls, button aids); use of orthotics (ankle-foot orthoses); splints; falls assessment; home safety evaluation; driving assessment; transfer training, sliding boards, use of Hoyer patient lift; wheelchair assessment
End-of-life decision making	Early conversations with patients, family members, and caregivers regarding treatment choices
Cognitive dysfunction	Family and caregiver education; respite care

[a] These therapies, in most cases, represent good clinical practice as very few clinical trials or trials involving patients with amyotrophic lateral sclerosis exist to support these interventions.