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Improvement of Diagnostic and Therapeutic Approaches to Motor Neuron Disease

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Abstract: To date, motor neuron disease (MND) is one of the incurable diseases. All therapeutic agents are aimed at slowing down the progression of the pathological process and improving the patient's quality of life. The disease is characterized by degeneration of motor neurons in the cerebral cortex, brainstem, corticospinal tracts, and spinal cord. The result is progressive muscle paralysis.

Keywords: motor neuron disease, amyotrophic lateral sclerosis, lesions of the central and peripheral motor neurons, ALS-FRS-R, edaravone.

Introduction: Motor neuron disease (MND) combines a group of neurodegenerative diseases with similar clinical manifestations in the form of progressive muscle weakness of the skeletal and/or bulbar muscles, developing muscle atrophies. Among the different forms of MND, the proportion of amyotrophic lateral sclerosis (ALS) reaches 80%, so the term MND is often used as a synonym for ALS. Classical ALS is a form with relatively uniform damage to the central and peripheral motor neurons, a steadily progressive course, increasing muscle weakness, bulbar dysfunction, and respiratory disorders.

- progressive muscular atrophy (PMA) (Aran-Duchenne disease), in which predominantly motor neurons of the spinal cord are involved and flaccid paresis and paralysis are formed without involvement of pathways and central motor neurons throughout the course of the disease, the proportion is 8%;
- primary lateral sclerosis (PLS) is a rare form (up to 2%) with a predominant lesion of the motor neurons of the brain and the development of cognitive and pseudobulbar disorders, pyramidal spastic paresis;
- Progressive bulbar palsy (PBP) (10%) - are affected mainly in the nucleus of the caudal group of cranial nerves, progressive bulbar disorders are observed.

According to the international classification of diseases ICD-10, motor neuron disease is coded in subparagraph G12.2 of paragraph G12 - Spinal muscular atrophy and related syndromes and is considered in block G10-G13 - Systemic atrophies affecting mainly the central nervous system.

ALS is the 3rd most common neurodegenerative disease after Alzheimer's and Parkinson's. According to epidemiological studies, the prevalence of ALS ranges from 0.8 to 7.3 per 100,000 cases per year. The incidence among patients over 18 years of age is 2.1–2.7 per 100,000 of the population; among men, the rate is slightly higher than among women, 3.0 versus 2.4. The ratio of sick men and women is 1.3, and at the age of 65 it levels off.

The disease was first described by the Frenchman Jean-Martin Charcot in 1869. This is the most common form of the disease (about 80-85% of all cases of MND), when the motor neurons of both the brain and spinal cord are involved in the pathological process.

The disease is characterized by steadily progressive muscle weakness and muscle atrophy. Depending on the level of localization of the primary lesion of motor neurons, the bulbar form of

the disease is distinguished, when motor neurons in the brainstem are primarily damaged, the cervicothoracic form - when the primary lesion is localized at the level of the cervical thickening, and the lumbosacral form of the disease. The most favorable course is considered to be the lumbosacral form of ALS. The average life expectancy of such patients can reach 7-8 years. In some cases, the duration of the disease reaches 10 or even 15 years. The disease develops, as a rule, in the 5-6th decade of life and is 2 times more common in men.

Symptoms

Progressive muscular atrophy is caused by dystrophic processes in motor neurons. Clinical manifestations will depend on which group of cells the disorder has occurred. If motor neuron disease with amyotrophic lateral sclerosis results from damage to neurons in the precentral gyrus and spinal cord then spastic paraplegia develops. Progressive bulbar palsy occurs against the background of changes in the work of the bulbar group of caudal nerves with damage to their nuclei and roots.

The disease has the following characteristic symptoms:

- The work of the hands, fine motor skills are deteriorating. It is difficult for the patient to perform the simplest tasks: open the door handle or faucet, take an object, press a button;
- weakness in the legs increases, which leads to difficulties in movement;
- the muscles of the neck weaken, as a result of which it becomes difficult for the patient to breathe, swallow food and water;
- the disease often affects the muscles that are involved in the breathing process;
- With damage to the areas of the brain responsible for emotions, the patient may not control his behavior, periodically laughing or crying for no reason.

Diagnostics

There are several neuroimaging methods such as MRI of the brain and spinal cord and ENMG indicating the suffering of motor neurons and muscles, functional diagnostic scales for the study of somatic and neurological status include the ALS-FRS-R scale (ALS Functional Rating Scale Revised (ALS-FRS-R). Version: May 2015.)

Purpose of the study: To study the efficacy of edaravone and the change in the ALSFRS-R score in ALS.

Results: The patients were divided into 2 groups: 1) the main group: 31 (70%) patients who received the new drug "Edaravone"; 2) control group: 21 (30%) patients who received standard ALS treatment. ALSFRS-R (Amyotrophic Lateral Sclerosis Functional Rating Scale Revised) 12 weeks. All patients included in the study maintained self-care, mobility, and also received riluzole. Thirty-one study participants received edaravone plus riluzole, while 21 received placebo. Patients treated with edaravone 60 mg intravenously for 3 months had slower disease progression during the study period on the ALSFRS-R score (-4.01 vs -6.50 in the placebo group); the difference between the groups was 1.49 ($p = 0.0007$)). So, when taken together with riluzole, the positive effect of edaravone was achieved in the group of patients with an initially slow rate of disease progression (slows down the progression of the disease by 20%).

Discussion: Research is ongoing to determine the effectiveness of this drug. It is recommended to administer edaravone at a dose of 60 mg intravenously slowly (over 1 hour), dissolved in saline, daily for 14 days followed by a 14-day break. Each subsequent course includes 10 injections, 14 days. There are 5 courses in total with 14-day breaks. The total duration of treatment is 24 weeks.

Conclusions: ALS has a short survival rate and a poor prognosis for most patients. New biochemical, neurophysiological and morphological biomarkers are important as early diagnostic and prognostic factors. It is important to create ALS registries with voluntary enrollment of patients with ALS for a better understanding of this disease, including specific care and treatments. ALS patients should be referred to a multidisciplinary team that will help them, their families and caregivers.

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