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EMOTIONAL DISORDERS IN PATIENTS WITH MOTOR NEURON DISEASES IN THE REPUBLIC SAKHA (YAKUTIA)

The article describes the study of patients with motor neuron disease and their families according to the Hospital Anxiety and Depression Scale (HADS). Motor neuron diseases (MND) are a group of neurodegenerative diseases of unknown etiology and pathogenesis, accompanied by the death of central and / or peripheral motor neurons , steady progression and inevitable death. Objective: To investigate the incidence and severity of anxiety and depression in patients with MND and their families.

Keywords: motor neuron diseases, amyotrophic lateral sclerosis, anxiety, depression, hospital anxiety and depression scale, HADS

Introduction. Motor neuron diseases (MND) are a group of neurodegenerative diseases of unknown etiology and pathogenesis, accompanied by the death of central and / or peripheral motor neurons, steady progression and inevitable death. MND in adults includes: sporadic and familial forms of amyotrophic lateral sclerosis (ALS), progressive muscle atrophy (PMA), progressive bulbar palsy (PBP), primary lateral sclerosis (PBS). Among the scientists of the world scientific community, there are different points of view on the form of diseases from the MND group: is it worth separating them or should it be considered phenotypic variants of ALS? [14,12,16]. The incidence of ALS in the world is 1.89 per 100 thousand of the population, and the prevalence is 5.2 cases per 100 thousand of the population [17]. Among ALS patients, 7% have been ill for more than 5 years. Their average life expectancy is 2.5 years with bulbar and 3.5 years with spinal ALS onset. In recent years, there has been an increase in the incidence of MND in the world. For example, the direct age-standardized incidence in 2016 in Scotland, which maintains a national registry, was 2.89 per 100 thousand population (95% CI 2.50-3.34), which was higher than in previous years ... However, researchers attribute this to improved diagnostics [10]. In Yakutia, the incidence as of 2018. was 0.5 cases per 100,000 population.

The clinical picture of the disease is manifested by the development of paresis and paralysis, atrophy of the muscles of the trunk and limbs, involuntary contractions of muscle fibers. At the onset of the disease or as it progresses, symptoms of pseudobulbar and bulbar syndromes join.

A characteristic feature of the clinical picture of ALS, in contrast to other neurodegenerative diseases, is the absence of oculomotor disorders, dementia (with the exception of some subgroups: the familial form and with the complex "parkinsonism-ALS-dementia'on the island of Guam and ALS-front-temporal dementia syndrome) [1,9], dysfunctions of the pelvic organs and the absence of bedsores, despite the fact that patients are bedridden for a long time.

The main cause of death in ALS is restrictive or restrictive obstructive respiratory failure, which develops due to paresis of the diaphragm muscles, respiratory muscles and aspiration of food and saliva in bulbar disorders. According to Hong Kong researchers, pneumonia (54.8%) and respiratory failure (40.5%) were the main causes of death in patients with MND [5].

Anxiety-depressive disorders can be attributed to the non-motor manifestations of MND. Given the steady progression of the disease and the fatal outcome, a high prevalence of depressive and anxiety disorders can be expected in patients with MND, as well as in their family members or their close associates. Published studies have described the presence of subclinical and clinical manifestations of anxiety and depressive disorders in patients with ALS. Different methods for detecting depressive disorders, together with different representativeness of patient samples used in previous studies, may partially explain the different incidence of anxiety-depressive disorders in this pathology [6].

The aim is to investigate the incidence and severity of anxiety-depressive disorders in patients with motor neuron disease and their relationship with clinical forms and the rate of progression of the disease.

Materials and methods. In our study, we used data from the personalized register of patients with MND of the Center for Neurodegenerative Diseases of the Yakutsk Scientific Center for Complex Medical Problems of the Republic of Sakha (Yakutia). Patients from 1986 were retrospectively included in the register. until now. The register has been maintained since 01.01.2006. As of 01.01.2019. the

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personalized register consisted of 165 patients. The register includes patients with significant ALS according to El Escorial criteria [2], as well as patients with PBS, PBS, and PMA. In the current study, 55 patients with an established diagnosis of ALS, PBS, PBS and PMA were selected from this MND register for the period from 2006 to 2018. In addition, we included in the study a group of 55 people, which consisted of members of their families and close associates, to assess their emocional state. All study participants gave written informed consent to participate in the study.

Study inclusion criteria:

1.patients with clinically significant ALS using El Escorial criteria;

2.patients with progressive bulbar paralysis,

3. Patients with progressive muscular atrophy;

4. patients with primary lateral sclerosis;

5. relatives or close people who take part in caring for patients with MND.

Exclusion criteria for patients from the study:

1.patients with ALS-mimicking syndromes;

2. patients with MND with severe cognitive impairment;

3. patients in the terminal stage of the disease who are on a ventilator;

5. relatives of patients who do not take part in caring for patients with MND.

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Research methods

1. Psychometric - using the HADS (Hospital Anxiety and Depression Scale) to identify states of depression, anxiety and emotional distress among patients and their families or loved ones.

2. Clinical research method (assessment of somatic and neurological status).

3. Using the ALS Functional Rating Scale (ALSFRS) to determine the rate of disease progression, functional deficit was assessed using a 4-point ALSFRS scale. The rate of progression was defined as: fast, if the patient lost more than 10 points per year; average - with a loss of 5 to 9 points per year; slow - with a loss of up to 5 points per year.

4. Statistical analysis of the research results was carried out using the Statistica v.12 software (StatSoft, USA) using descriptive statistics, analysis of variance and the Kruskal – Wallis method to compare mean values. The critical level of significance (p) was taken equal to 0.05.

Results and discussion. Of the 55 patients included in the sample, 35 patients are patients with significant ALS, 5 with PBP, 5 with PBS, 10 with PMA. Distribution of patients by ethnicity: 12 (21.8%) representatives of the Russian ethnic group; 43 (78.2%) the Yakut ethnic group. The distribution of patients by sex: men - 31 (56.3%) people, women - 24 (43.7%) people. The age ranged from 30 to 72 years. The average age was 53 ± 11.8 years. At the same time, the age group 30-50 years old was 15 people. (27.2%), 51-60 years old - 14 people. (25.4%), 61 years and older - 26 people. (47.7%). According to the ALSFRS scale, a fast rate of disease progression was revealed in 50.9% of patients, an average rate - in 21.8%, a slow rate - in 27.3%. The onset of the disease was established in 12 (21.8%) cases.

Drug treatment of depression was carried out with a drug from the group of tricyclic antidepressants - amitriptyline 50-75 mg orally at night in 10 patients, of which 6 patients had severe sialorrhea. The use of anxiolytics for anxiety in patients and relatives was irregular and rare.

Anxiety and depression in patients with MND on the HADS scale

We found that in patients with established ALS the level of anxiety averaged 17.74 ± 0.48 points, depression - 13.60 ± 0.68, with PBP the level of anxiety was 21.20 ± 1.27 points, depression 16, 60 ± 1.8 points. With PBS, the level of anxiety averaged 14.60 ± 1.27 points, depression - 10.50 ± 1.27 points. In the group with PMA, an average level of anxiety was revealed - 13.40 ± 0.9 points, and depression - 10.50 ± 1.27 points. Figure 1. As can be seen from the figure, the level of clinically expressed anxiety was significantly higher in the group of patients with ALS. and PBP than in the group of patients with PBS and PMA (F = 6.014; p = 0.0002).

Figure 2. Figure 2 shows that the level of depression was also significantly higher in patients with ALS and PBS than in patients with PBS and PMA (F = 3.51; p = 0.042).

Anxiety and depression in relatives and close people from the patient's environment according to the HADS scale

Since the indicators of anxiety and depression in this group do not correspond to the law of normal distribution, the median with quartiles was calculated. In relatives of patients with ALS, the median anxiety was 14 points, with PBS - 15 points, and PBS and PMA - 12 points. The median of depression in family members in all groups was 6 points.

There were no statistically significant results of the dependence of the level of anxiety and depression on age in both patients and their relatives (p = 0.08). In the general group, anxiety and depression did not depend on the rate of progression of MND (p = 0.09 and p = 0.9, respectively). Separate analysis, depending on the form of MND, also revealed no differences (p> 0.05). The HADS survey showed that all patients experience clinically significant anxiety and depression, which they associated with their illness. At the same time, the level of anxiety and depression was statistically significantly higher in patients with ALS and PBS than in patients with PBS and PMA. However, a HADS examination of family members and close people of patients in the entire MND group revealed clinical manifestations of anxiety disorders without depressive disorders.

Thus, our study shows that all patients had pronounced anxiety-depressive disorders, which can be attributed to non-motor manifestations of MND. These data correlate with the data of researchers from Brazil (2017), in whose studies the symptoms of anxiety and depression were correlated and often met in patients with ALS [8]. Motataianu Anca et al. (2020, Romania) published data from a small sample of ALS patients (n = 50). The prevalence of depression in the sample after excluding ALS patients with cognitive impairment was 42.8%, which indicates a high prevalence of depression in ALS patients. In addition, they showed a relationship between sociodemographic factors and the development of depression: a low level of education, lack of psychological support from relatives, severe physical weakness of patients, as well as custody of sick children or parents were associated with the development of depression. In contrast, a high level of education, psychological support, high ALSFRS scores, and spousal custody of the patient were associated with the absence of depression in ALS patients [13]. Researchers from the University of Normandy (France, 2019) cite the conclusion of Rabkin et al. (2009) and Burke et al. (2015) that it is cognitive and behavioral disorders, and not the physical disability of patients, that increase the burden on caregivers and increase their anxiety [4]. A Chinese study (2015) found a very strong correlation between depression and anxiety between patients and their caregivers.

However, the severity of depression and anxiety in caregivers of ALS patients correlated with their age. [7] Scientists from Sweden and Norway (2016) concluded that ALS patients are at higher risk of developing depressive disorders and a consequence of taking antidepressants both immediately before and after the diagnosis. In their studies, they showed that within 1 year after the diagnosis of depression, the risk of ALS increased 3.6 times. There was also a higher risk of ALS in the second and third years after the diagnosis of depressive disorder. Patients with ALS are more likely to use antidepressants than in the control group, especially during the year before diagnosis [15].

In addition, depression can become an obstacle to treating a patient. Thus, researchers from Poland published a protocol for the complex treatment of a 71-year-old patient with ALS, which included the method of electroencephalography with biofeedback (EEG-BFB). The method is based on the use of the interaction between the patient's mental state and brain activity, allowing the patient to actively and consciously participate in the management of their neurophysiological processes. The inclusion of this method in the aggravation of depressive disorders and the refusal of the patient with ALS to continue physiotherapy sessions made it possible to complete the planned course of complex treatment, since after the first three sessions of EEG-BFB there was a clear improvement in the patient's mood and interest in continuing the physiotherapy sessions [3]. A group of researchers from Korea also published research results (2019) that suggest that biofeedback may be an effective method as an additional treatment not only for comorbid depressive disorders, but also for functional recovery in patients with drug-resistant depression [11].

Conclusion. Thus, despite the small sample of patients with MND, our data are consistent with the data of foreign researchers. In the surveyed sample, all patients (n = 55) suffered from anxiety-depressive disorders, which are non-motor manifestations of MND. At the same time, the relatives were worried about isolated anxiety without symptoms of depression. Patients with MND may have anxiety and depressive disorders, both at the onset of the disease and at subsequent stages of its development. The high incidence of comorbidity of anxiety-depressive disorders in ALS patients requires the development of an integrated approach to the treatment of MND, including medication, psychotherapeutic, physiotherapy, and other methods. Also, taking into account the previously published data on the development of depression in ALS, which can be both a non-motor symptom in ALS + frontotemporal degeneration, and the beginning of the development of damage to the upper motor neurons in classical ALS, it can be assumed that the clinical picture of ALS consists of non-motor symptoms at the beginning disease and the subsequent attachment of movement disorders in the advanced stage of the disease. Biomarkers, taking into account behavioral and mood disorders, as well as the search and investigation of other probable non-motor manifestations of MND, as well as screening of the population using questionnaires adapted to MND, would help diagnose the disease in the early stages.

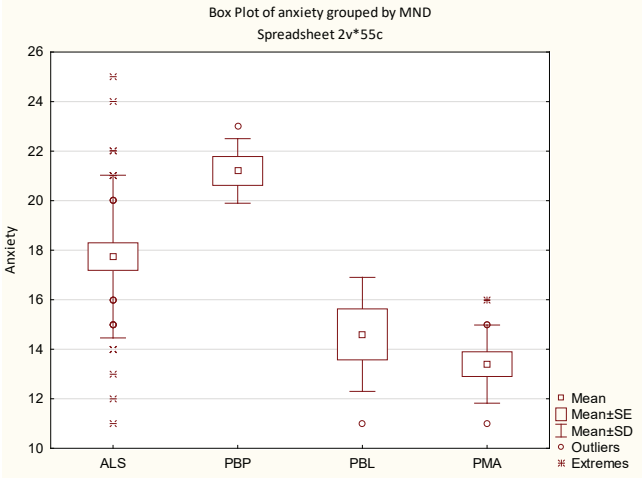

Fig. 1. Anxiety levels in patients with ALS, PBP, PLS, PMA

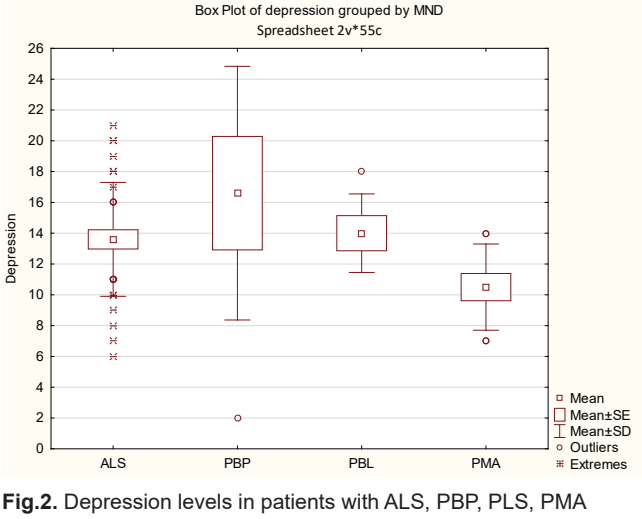

Fig.2. Depression levels in patients with ALS, PBP, PLS, PMA

Conflict of interest

The authors report no conflicts of interest regarding the concepts discussed in this article.

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Respect for the rights of patients and the rules of bioethics

All patients and family members signed informed consent to participate in the study.

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STUDY OF THE PARAMETERS OF ESTERIFIED FATTY ACIDS IN BLOOD PLASMA IN PERSONS WITH VIBRATION PATHOLOGY

Objective: to study the spectrum of esterified polyunsaturated fatty acids in the blood of persons with vibration pathology.

Materials and methods. 97 people were examined, of which 2 groups were formed: the main group I included 52 workers with an established diagnosis of vibration disease (average age 49.0 ± 0.8 years), group II (comparison group) consisted of 45 conditionally healthy men (average age - 52.0 ± 0.8 years), who had no contact with vibration. The determination of esterified fatty acids was carried out by gas chromatography-mass spectrometry on a gas chromatograph Agilent 7890A with a mass-selective detector Agilent 5975C. The data were processed in the program Statistica 6.1.

Results. The distribution of parameters of polyunsaturated fatty acids (PUFA) ω-3 and ω-6 in the examined groups was studied. In the group of persons with vibration disease, a statistically significant increase in the level of ω-3 docosahexaenoic acid was noted. The ω-3 index was calculated, according to which the representatives of the cohorts were divided into 4 subgroups (less than 2.5%, 2.5 - 5%, 5 - 7.5%, more than 7.5%). The main group was dominated by persons with an ω-3 index in the intervals of 2.5-5% and 5-7.5%, while in the comparison group there was a uniform distribution of persons between 4 subgroups ($\chi 2 = 11.2$, $p = 0.011$). Comparison of the sums of the main representatives of ω-3 PUFAs (eicosapentaenoic and docosahexaenoic acids) and ω-6 (arachidonic and linoleic acids) showed that the sum of the main ω-6 PUFAs was statistically significantly higher than the sum of the main ω-3 PUFAs in both groups.

Conclusion. The conducted study of esterified fatty acids parameters in blood plasma in persons with vibration disease revealed a higher content of C22:6ω3. It was found that the ω-3 index in both groups and varied in the range: 2.0–9.2% in persons with vibration disease and 1.3–12.7% in the comparison group.

Keywords: polyunsaturated fatty acids, omega-3 index, chromatography-mass spectrometry, vibration disease.

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Introduction. In the structure of occupational morbidity, vibration disease (VD) occupies one of the leading places [3, 13]. The factors that aggravate the harmful effects of vibration on the body include unfavorable climatic conditions of carrying out production activities and living, especially low temperature of environment. It is known that cold enhance the negative exposure of vibration on the organism and increases the risk of developing vibration disease due to increased vascular reactions [1]. It should be borne in mind that one of the key roles in its pathogenesis is played by endothelial dysfunction, which, along with changes in the nervous system, leads to the formation of systemic microangiopathies [6]. It is believed that these disorders are caused both by the direct exposure of vibration on the vascular endothelium, and by an imbalance of redox processes, neurohumoral, neuroimmune mechanisms, metabolic disorders [2]. As the latter, changes in lipid metabolism of a proatherogenic orientation are noted. At the same time, the study of lipid profile indicators does not always answer the question of the possible mechanisms of the development of these disorders.

One of the approaches to solving this problem is study blood lipids in terms of their primary components, namely fatty acids, assess the balance of their various fractions for the diagnosis, prognosis and treatment of dyslipidemia, cardiovascular pathology and other diseases [5, 8, 12]. One of the fractions of blood fatty acids are esterified polyunsaturated fatty acids (PUFAs), the ratio between the components of which can play an important role in the development of vascular disorders caused, among other things, by exposure to vibration.

In this regard, the aim of the work was to study the spectrum of esterified polyunsaturated fatty acids in the blood of persons with vibration pathology.

Materials and methods. The present study involved 97 people who were examined at the clinic of our institute, of which 2 groups were formed: the main