Section: Research Paper

CLINICAL AND NEUROLOGICAL FEATURES OF MYASTHENIA GRAVIS, ASSESSMENT OF COGNITIVE FUNCTION AND OPTIMIZATION OF TREATMENT METHODS

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Annotation.Worldwide and in Uzbekistan, myasthenia gravis is a rare neurological disease, and women have a higher risk of developing myasthenia gravis than men (3: 2). The prevalence of myasthenia gravis is 17.5-20.3 per 100 thousand population, the indicator increases by 5-10% annually. The first signs of myasthenia gravis are manifested in the form of lethargy and weakness of skeletal muscles compared to a high load during the day, in addition, in a calm state there is a tendency to decrease. In 2/3 of patients, the ocular muscles are initially damaged, and later skeletal and bulbar muscles are connected to the process. Generalized weakness is observed in 85% of patients. The disease develops very quickly and spontaneous remission is rare

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In adults, an anomaly of the thymus gland is observed in 90% of patients with myasthenia gravis, of which about 70% is hyperplasia of the thymus gland, 10-20% is thymoma. Currently, the main drugs used for the treatment of myasthenia gravis are anticholinesterase drugs, immunopharmacological agents (prednisolone, azathioprine, cyclosporine, mycophenolate mofilet, cyclophosphamide, tacrolimus, rituximab), plasmophoresis, intravenous immunoglobulins and thymectomy surgery. [1]The researchers note that with myasthenia gravis, subjective memory disorders and other cognitive disorders, changes in the electroencephalogram are most common, and some authors indicate the absence of neuropsychological disorders, and also associate these changes with side effects of drugs used to treat myasthenia gravis. The contradiction of opinions indicates the need for in-depth study of this problem. [5]

The fact that patients experience untimely medication intake due to a decrease in cognitive functions indicates the need for early detection and correction

of this defect. In Uzbekistan, insufficient attention is paid to these aspects of myasthenia gravis, and due to the peculiarities of the course of the disease, slowing down diagnostic and rehabilitation measures, patients have problems in cognitive activity, which leads to a decrease in the quality of life. Therefore, modern approaches to the early diagnosis and treatment of post-myasthenic cognitive disorders, improvement of the correct diagnostic and therapeutic approach are urgent requirements of our time. [3]

Cognitive impairment in myasthenia gravis is a high percentage and, therefore, has been studied by many world researchers . The translation was made by Eisagirre M. B. et al., who found that in 24 of 2017 patients suffering from myasthenia gravis, 37.5% had attention disorders, 33.3% had verbal memory disorders and 29.2% had violations of daily activity. In Brazil, David Melamed found that in 2020, 59% of patients had short-term and 56.4% had long-term memory impairments. The results of the study showed that 66.7% of respondents indicated significant cognitive problems. According to the Elworth scale, 23.1% of patients had daytime sleepiness, 41% had signs of depression on the Beck scale. [7] The Beck scale showed the presence of mild depression in 20.5% of cases and severe depression in 7.7% of cases. In Egypt in 2014 , Sheriff A. Hamed and co-authors used the MMCE scale, the Stanford-Bean Intelligence Assessment Scale from the 4th Review (VLSI) and the definition of the Wexler Memory Test (WMS C-P) in patients with myasthenia gravis. Proposals have been put forward regarding several mechanisms for the formation of cognitive impairments in myasthenia gravis, the most reliable of which is the central one in this work and the central cholinergic deficiency through the central cholinergic pathways. It has been suggested that myasthenia gravis has cognitive impairments that do not depend on the presence of depression. [8] In a study conducted in Russia, patients with myasthenia gravis underwent a comprehensive neuropsychological examination, and in 36.6% of cases, the presence of intellectual and mnestic disorders (memory impairment, decreased short-term memory, difficulty concentrating) was revealed (Nalkin S.A. 2022). Changes in memory and attention were more noticeable in patients with thymoma before thymectomy surgery and in patients who underwent it for more than 10 years.

The role of laser therapy in the complex treatment of myasthenia gravis has been studied in Uzbekistan. To date, no work has been carried out in Uzbekistan on the observed changes in the cognitive system in myasthenia gravis. The need for early assessment of cognitive changes in patients with myasthenia gravis, improvement of the quality of life of patients and the level of medical care for

patients, development of a unified principle of patient management formed the basis for our choice of the topic of this study.

Bulbar and masticatory muscles (80%), neck muscles (65%) and deltoid muscles (75% of cases) are significantly more often affected in patients with myasthenia gravis in combination with thymoma and in patients with late onset of the disease without The role of laser therapy in the complex treatment of myasthenia gravis has been studied in Uzbekistan (R.S.Seydametova, 1997). To date, no work has been carried out in Uzbekistan on the observed changes in the cognitive system in myasthenia gravis. The need for an early assessment of cognitive changes in patients with myasthenia gravis, improving the quality of life of patients and the level of medical care for patients, developing a unified principle of patient management formed the basis for our choice of the topic of this study.

Bulbar and masticatory muscles (80%), neck muscles (65%) and deltoid muscles (75% of cases) are significantly more often affected in patients with myasthenia gravis in combination with thymoma and in patients with late onset of the disease without thymoma. Seronegative myasthenia gravis is characterized by relatively rare lesions of extraocular (10%) and trunk (35%) muscles, as well as more frequent lesions of bulbar (90%) and respiratory (65% of cases) muscles. Sudden violations of vital functions, called crises, are observed in 10-15% of patients. Crises with myasthenia gravis are myasthenic, cholinergic and mixed. Myasthenic crises occur with insufficient treatment of AHEP. Myasthenic crisis is characterized by the rapid development (within a few hours or minutes) of mydriasis, dry skin, increased blood pressure and tachycardia, urinary retention, intestinal paresis, absence of bundle twitching in the muscles, respiratory disorders. With an overdose of ACEP, a cholinergic crisis develops. It is characterized by slow development (a day or more), myosis, hyperhidrosis, decreased blood pressure and bradycardia, frequent urination, increased intestinal peristalsis and diarrhea, fascicular twitching is observed in the muscles, the patient suffers from respiratory disorders. Respiratory disorders are manifested by rhythm lability, cyanosis, inclusion of auxiliary muscles in the breathing process, arousal and changes in consciousness [6,9]. The diagnosis is "Severe myasthenia gravis". When collecting anamnesis of the disease, attention is drawn to the presence in the past of short-term episodes of weakness and fatigue, which completely or partially regressed spontaneously or against the background of nonspecific treatment. In 90% of cases, extraocular muscles are involved in the process, which is manifested by diplopia and ptosis. Episodes of bulbar disorders or weakness of the muscles of the trunk are much less common. Family history is also important (whether relatives have neuromuscular, autoimmune or oncological diseases). Muscle

weakness in myasthenia gravis is characterized by selective lesion of individual muscle groups, inconsistency of localization of weakness in the innervation zone of individual nerves, lability of clinical manifestations of weakness and a decrease in weakness after taking anticholinesterase drugs [9]. Scales for assessing the clinical manifestations of myasthenia gravis To assess the severity of motor disorders, the limb muscle strength scale proposed by A. Shobor (1976) is used, while muscle strength can vary from 0 (pronounced paresis) to 5 points (norm). To objectively evaluate severity of clinical manifestations of myastheniagravis, the quantitative myasthenia gravis score (score QMGS), proposed by R. J. Barohn, is used etal. [18]. It provides an assessment of the severity (0, 1, 2, 3) of involvement in the pathological process of various muscles (oculomotor, bulbar, mimic,respiratory, proximal and distal muscles of the extremities, as well as neck muscles). To perform the study, you need a stopwatch, dynamometer, spirometer, and a glass of water. The study is performed after preliminary cancellation of anticholinesterase drugs. The total quantitative index of myasthenia gravis can range from 0 (absence of any oculomotor and bulbar disorders, as well as muscle weakness-complete remission) to 39 points (the greatest severity of oculomotor and bulbar disorders, as well as muscle weakness). To assess the form and severity of myasthenia gravis, as well as summarize data on the scope of therapy and treatment outcomes, we use the classification proposed by a group of leading researchers of the Myasthenia Gravis Foundation of America (America MGFA) for conducting all studies on generalized myasthenia gravis [20]. Pharmacological test The most significant criterion for the diagnosis of myasthenia gravis is a pharmacological test with the introduction of anticholinesterase drugs. Neostigmine methyl sulfate is used (with a patient's body weight of 50-60 kg – 1.5 ml; 60-80 kg-2 ml; 80-100 kg-2.5 ml of a 0.05% solution) or pyridostig mine bromide (with a patient's body weight of 50-60 kg-10 mg; 60-80 kg-20 mg; 80-100 kg-30 mg). In children, the dose of these drugs is 1.0 ml or 5 mg, respectively. If возникновении muscarinic effects of anticholinesterase drugs occur, atropine (0.2-0.5 ml of 0.1% solution) is administered after evaluating the effectiveness of the test. Evaluation of the test results is carried out in the interval from 40 minutes to 1.5 hours after administration of the drug. Full compensation of motor disorders is detected in 15% of patients with myasthenia gravis (full compensation involves restoring muscle strength to normal values, that is, 5 points, regardless of the degree of its initial decrease). Most patients with myasthenia gravis (75%) have an incomplete reaction to the administration of drugs, that is, an increase in muscle strength by 2-3 points, but not to the norm. In case of complete and incomplete compensation of motor disorders, the test is considered positive, in case of partial –

doubtful, in case of no reaction – negative [9]. Laboratory tests An important criterion for the diagnosis of myasthenia gravis is the study of blood serum for the level of autoantibodies. The study of the level of autoantibodies to titinprotein is most often found in patients with myasthenia gravis combined with thymoma (an increase in this indicator was noted in 78% of cases), as well as in patients with late-onset myasthenia gravis without thymoma (84%). In myasthenia gravis combined with thymoma, an important indicator is an increase in the level of antibodies to the ryanodine receptors of the sarcoplasmic reticulum (detected in 35% of cases), indicating a severe course of the disease. Autoantibodies to muscle-specific tyrosine kinase are found in 40-50% of patients with seronegative myasthenia gravis [9]. Instrumental studies To date, the generally accepted diagnostic criteria are electromyography (EMG) data, which can be used to detect a violation of neuromuscular transmission. Electromyographic verification of the diagnosis is performed using the method of indirect rhythmic supramaximal muscle stimulation with recording of the M-response with surface electrodes (decrement test). EMG study shows a decrease (decrement) M-response amplitudes increased by more than 10% [10-13].

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