Rehabilitation of the Patients with Myasthenia Gravis as an Integral Part of the Patient's Treatment Algorithm in the Postoperative Period

Rehabilitacja pacjentów z miastenią jako integralna część algorytmu leczenia pacjenta w okresie pooperacyjnym

DOI: 10.36740/ABAL202103104

Olena L. Tovazhnyanska[1], Olena M. Klimova[2], Hanna P. Samoilova[1], Dmytro V. Minukhin[2], Kateryna V. Ponomarova[1], Denys O. Yevtushenko[1], Vasiliy G. Hroma[1]

[1]Kharkiv National Medical University, Kharkiv, Ukraine
[2]State Institution „V. T. Zaycev Institute of General and Urgent Surgery National Academy of Medical Sciences of Ukraine", Kharkiv, Ukraine

SUMMARY

Aim: The purpose of this article is to determine the role of rehabilitation in the structure of the treatment algorithm for patients with myasthenia gravis.

Materials and Methods: All patients admitted to the SI «Zaycev V.T. Institute of General and Urgent surgery of National Academy of Medical Sciences of Ukraine», Kharkiv, Ukraine for surgical treatment for thymoma or carcinoma of the thymus gland. 102 people aged 18 to 69 with myasthenia have been comprehensively surveyed and their data have been analyzed and studied. Diagnosis of myasthenia was established according to the tenth edition of the International Classification of Diseases ICD-10 (WHO, 1992).

Results: The severity of the patients' condition corresponded to grade IIIA in 5 patients (16.7%), IIIB grade – 14 patients (46.7%), IVA grade – 7 patients (23.3%), IVB grade – in 4 patients (13.3%). According to the clinical classification of MGFA, the severity of the condition in most patients in this group corresponded to Class IIB (32.4%) and IIIA class (35.2%).

Conclusions: The results of our study suggest that clinical and anamnestic features of myasthenia in absence of structural thymus disorders are debut before the age of 40 years, predominant affection of skeletal muscles, mild course (severity of the disease corresponds to 12.7 ± 1.76 points on the QMGS scale) and characterized by a debut after 40 years regardless of sex, manifestation of generalized muscle weakness and severe course (in 68.4% of cases severity of the disease was 31.68 ± 3.76 points on the QMGS scale).

Key words: rehabilitation, myasthenia gravis, thymic hyperplasia, thymoma, MGFA

Słowa kluczowe: rehabilitacja, miastenia, rozrost grasicy, grasiczak, MGFA

Acta Balneol, TOM LXIII, Nr 3(164);2021:155-159

INTRODUCTION

Myasthenia gravis remains an urgent medical and social problem due to the predominant lesion of the motor system and rapid disability of the patient. Despite current achievements in practical medicine and science in the study of etiopathogenesis, clinical features and approaches to myasthenia treatment, many issues remain unresolved [1, 2]. Even constant expansion of the arsenal of medicines aimed at inhibition of pathological autoimmune processes in myasthenia often does not allow to achieve the appropriate therapeutic control over this severe, life-threatening illness [3-5].

According to various authors, the number of myasthenia cases increases annually and reaches at present 14.2-20.3 cases per 100,000 populations. The disease is observed predominantly in women (3:1), and the start of it is at a young age (90% - up to 40 years) [6, 7]. In women, the debut of the disease occurs earlier and its course is more severe than that of men [8-10].

Development of myasthenia is traditionally associated with thymus pathology. According to the American National Institute of Neurological Disorders and Stroke, 10% of patients with myasthenia are thymoma and 70% have thymic hyperplasia. In this case, thymectomy, as one of the most common methods of treating myasthenia, does not always lead to sustained remission [11-13].

AIM

The purpose of this article is to determine the role of rehabilitation in the structure of the treatment algorithm for patients with myasthenia gravis.

MATERIALS AND METHODS

All patients admitted to the SI «Zaycev V.T. Institute of General and Urgent surgery of National Academy of Medical Sciences of Ukraine», Kharkiv, Ukraine. for surgical treatment for thymoma or carcinoma of the thymus gland underwent standard clinical and laboratory tests. 102 people aged 18 to 69 with myasthenia have been comprehensively surveyed and their data have been analyzed and studied. Diagnosis of myasthenia was established according to the tenth edition of the International Classification of Diseases ICD-10 (WHO, 1992) – G 70.2 (Congenital and acquired myasthenia). All patients independently signed an informed consent to participate in a scientific clinical research.

The exclusion criteria were the age of patients younger than 18; refusal of the patient to participate in the scientific clinical research at any stage and reluctance to sign an informed consent to participate in it; available decompensated cardiovascular pathology and respiratory diseases that were not a result of muscle weakness in myasthenia; Lambert-Eaton syndrome and other myasthenic syndromes against the background of somatic and endocrine pathology.

For diagnostic purposes, a classical pharmacological test with subcutaneous administration of 2 ml 0,05% solution of proserine was conducted. 30 minutes later muscular strength of the patient was evaluated, limited to the gradual assessment of the test.

Structural condition of thymus in patients with myasthenia was evaluated using the apparatus of the spiral computer tomography (SCT) SeleCT SP (Marconi). Neuromuscular transmission was assessed, applying stimulation electromyography, using 4-channel neuromyograph Neuro-MSP of Neurosoft Company based on the amplitude of M-response negative phase analysis and the decrement-test index.

The statistical analysis of the results was carried out by methods of variation statistics, using standard software packages Exel (version 7), Biostat and Statistica (StatSoft Inc., USA). The type of sign distribution in the sample was carried out using the Shapiro-Wilk criterion and the dispersion equality of features distribution in groups – by using the Leuven criterion. The two groups with normal distribution were compared using the parametric classical Student t-criterion for independent samples and the Student t-criterion with separate dispersion estimates. The data are presented in the form of an average arithmetic and standard error average.

A correlation analysis using the Pearson coefficient (r) was used to determine presence and determination of the strength and direction of the probable link between the indices. Differences were considered statistically significant at ($p < 0.05$).

RESULTS

Taking into account the purpose of the study and the data of MSCT of chest organs, patients with myasthenia were divided into three groups. The first group consisted of 35 patients with myasthenia without structural thymus disorders (group M), the second group consisted of 37 patients with myasthenia against the background of thymic hyperplasia (group MH), the third group included 30 patients with myasthenia against the background of thymomas (MT group).

Analysis of clinical and anamnestic data has shown that in patients with myasthenia without structural thymus disorders the average age of the debut disease was in women – 31.7 ± 8.3 years, in men – 32.1 ± 9.4 and manifested by ocular disorders in 20% patients, in those with bulbar disorders – 11.4%, generalized muscle weakness of 68.6%.

In patients with myasthenia against the background of thymic hyperplasia the disease manifested earlier in women than in men (24.4 ± 7.2 and 33.4 ± 12.1 years, respectively) and was characterized by the appearance of local forms: ocular - 37.8%, pharyngeal -facial - 46%; and only in 16.2% of patients the disease debut manifested as a generalized muscle weakness. In patients with myasthenia against the background of thymomas, there was a late disease debut regardless of sex (men – 48,7 ± 8,3, women 52,9 ± 9,7). In 70% of patients in this group myasthenia manifested by generalized muscle weakness. The bulbar form was diagnosed at the beginning of the disease in 20% of the patients, the ocular form – in 10%. Subsequently, the disease was slightly unstable and difficult. This was confirmed by the fact that only in this group 17% of patients had urgent states in the form of myasthenic crisis according to anamnesis of the disease given in the medical documentation provided by the patients under study.

Generalized neurological status data showed that oculomotor disorders were found in M group most often in the form of nystagmus – 40.0% of patients, ptosis was observed in 11.4% of cases, and diplopia and obliquity – in 14.3% of patients. In MH group, oculomotor disorder manifested with the following frequency: ptosis in 18 (9.0%) patients, diplopia, nystagmus, and strabismus in 45 (9.0%). In MT group, only 10% of patients had ptosis, but the highest frequency of nystagmus (83.3%), diplopia and strabismus (50.0%) was noted.

In MH and MT groups, respiratory failure was recorded in (5.6% and 36.6% of patients respectively) but was not found in M group. Unlike patients in MH group, 13.3 % of patients in group MT prior to being included into the study, needed artificial ventilation to compensate for respiratory distress (after that they were included in the study). This phenomenon was not observed in other groups.

In all patients we observed a reduced muscle tone and decreased muscle strength in the limbs. Thus, in patients from M and MT groups upper limb muscle lesions (54.3% and 53.4%of patients, respectively) predominated, unlike in MH group patients, where lower extremities were more often affected (54.0% of cases). However, maximum reduction in muscle strength in general was observed in MT group patients. Thus, in 16.6% of patients in this group muscle strength was 1.0-1.5 points, 50.0% - 2.0-2.5 points and 33.4% – it corresponded to 3.0-3.5 points. In MH group, 16.2% of the patients experienced a decrease in muscle strength to 2.0-2.5 points, in 70.2%-3.0-3.5

points and in 13.6% of patients to – 4.0-4.5 points. The slightest changes in muscle strength were observed in M patients group, whose indicators were not less than 3.0 points (3.0-3.5 points – 71.4% of the cases, 4.0-4.5 points – 28.6 % of cases).

The fact that 87.0% of patients in these three groups had hyperreflexia may be explained by theories of autoimmune myasthenia gravis and similar pathophysiological mechanisms of other diseases of the nervous system with the autoimmune mechanism's development. According to the data obtained by MGFA classification, the severity of the patients with myasthenia status without structural thymus disorders was in line with grade IIA in 21 patients (60.0%), IIB grade – 9 patients (25.7%), grade IIIB – in 5 patients (14.3 %)

In patients with myasthenia against the background of thymic hyperplasia, the severity of the patients' status corresponded to grade IIA in 5 patients (13.5%), grade IIB – 12 patients (32.4%), grade IIIA – 13 patients (35.2%) IIIB grade – in 5 patients (13.5%), in IVA grade – in 2 patients (5.4%). The most severe course of the disease according to MGFA classification was observed in patients with myasthenia against the background of thymomas.

The severity of the patients' condition corresponded to grade IIIA in 5 patients (16.7%), IIIB grade – 14 patients (46.7%), IVA grade – 7 patients (23.3%), IVB grade – in 4 patients (13.3%)

A quantitative scale of myasthenia clinical manifestations (QMGS) was performed to objectivize the severity of the patients' condition with different forms of myasthenia. The average severity of the disease in patients with myasthenia without structural thymus disorders was 15.4 ± 4.5 points, in patients with myasthenia against the background of thymic hyperplasia 19.4 ± 4.5 points, and in patients with myasthenia against the background of thymomas, maximum index was 29.8 ± 4.36 points, which is 1.9 times higher than that of M group and 1.5 times higher than that of MH group. The data obtained quantitatively confirm the most severe course of myasthenic symptoms in patients with myasthenia against the background of thymomas, and the lighest – in patients with myasthenia without structural thymus disorders.

When comparing clinical and electromyographic data, it has been found out that myasthenia without structural changes in the thymus is characterized by a predominant lesion of skeletal muscles, mild course of myasthenia (according to QMGS scale), and less pronounced changes in EMG rates compared with patients in other groups. In the vast majority of patients in this group (60%), the severity of the condition corresponded to grade IIA according to MGFA classification, which indicates a mild course of the disease. Certain clinical-neurophysiological dissociation was observed, too. Skeletal muscle lesion was more prevalent than oropharyngeal in the clinical picture but changes in EMG-values in skeletal muscles were less pronounced compared to those in oropharyngeal muscles.

Myasthenia in combination with thymus hyperplasia is characterized by a direct correlation between the severity of clinical manifestations, severity of patients' condition and deterioration of neurophysiological parameters. Lesions prevalence of bulbar and ocular group of muscles over skeletal muscles is accompanied by a more pronounced decrease in the amplitude of M-response negative phase in the corresponding muscles. More severe course of the disease according to the QMGS scale score is combined with higher rates of the decrement test. According to the clinical classification of MGFA, the severity of the condition in most patients in this group corresponded to Class IIB (32.4%) and IIIA class (35.2%).

Patients with myasthenia against the background of thymomas differed from the patients of other groups by the most severe course of the disease (severity of the majority of patients' conditions corresponded to IIIB class (46.7%) and IVA class (23.3%), the greatest violations of the parameters of neuromuscular transmission in all subjects, as well as a relatively lower effectiveness of anticholinesterase drugs.

CASE REPORT №1

Patient R., 58 years old, applied to the SI «Zaycev V.T. Institute of General and Urgent surgery of National Academy of Medical Sciences of Ukraine», for surgical treatment. He considers himself ill since February 2016, when he first drew attention to the violation of chewing, dynamic drooping of the left eyelid, double vision, then weakness of the muscles of the neck, proximal extremities, bulbar disorders. Generalized myasthenia gravis was diagnosed at the place of residence. The diagnosis was made: Myasthenia gravis, generalized form, III A class . According to the MSCT data: in the anterior mediastinum, a neoplasm of 7.0x5.0x2.0 cm is determined (Figure 1). The patient was referred to the thorax department, where in March 2016 was performed videothoracoscopic removal of the thymus tumor. In the pathomorphological study of the drug: type B1 thymoma with signs of capsule invasion. The postoperative period was uneventful. For decreasing inflammation, symptoms of swelling, lower of production of sputum and improving lung ventilation we prescribe Pulmicort by 1 inhalation 2 times per day. For movement activity the patients needs put on the stilts for 2 days after the thymthymomectomy.

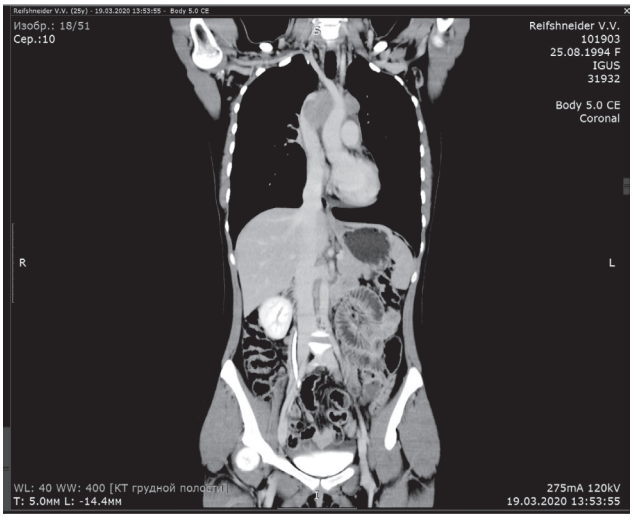

Figure 1. MSCT of the chest organs: in the region of the anterior-superior mediastinum, a tumor of a heterogeneous structure with dimensions of 3.0x2.7x2.5 mm is determined

DISCUSSION

Currently, there are clinical guidelines for the treatment of myasthenia gravis. However, the rehabilitation of patients in the postoperative period, after exacerbations during the period of remission, still remains a big problem [14,15].

Rehabilitation alone or in combination with medical treatment can improve symptoms in MG. A multidisciplinary rehabilitation approach is important to optimize functional abilities. This approach also has the goal of preventing further disease-associated illness (e.g. recurrent pneumonias). Such an approach includes therapy (physical therapy, occupational therapy, speech therapy, respiratory therapy) as well as evaluation for and training with assistive device, other durable medical equipment (DME), and/or orthotics [16].

Physical therapy evaluation includes assessment of strength, flexibility, mobility, balance, safety/fall prevention, gait, endurance/activity tolerance, and transfers. Speech therapy evaluation includes assessment of dysphonia, dysarthria, and dysphagia. Occupational therapy evaluation includes evaluation of ADLs including endurance/activity tolerance and areas of improvement for energy conservation and assistive device use in ADLs (e.g. bathing and grooming, dressing, eating, household management), physical environment modification. The benefit of a rehabilitation program has also been seen pre- and post-thymectomy, with not only significant reduction in operative risk and postoperative morbidity but also significantly faster recovery [17].

Pulmonary function is often improved with treatment. Routine PFTs should be monitored in the setting of acute exacerbation. Chest physical therapy involves respiratory and upper limb rehabilitation, diaphragmatic breathing, postural drainage, chest percussion and vibration, turning, deep breathing exercises, and coughing. In more severe cases, nocturnal non-invasive ventilation may be required.

Though muscle weakness from MG worsens with repeated muscle use, this should not preclude patients from being or staying active in some way. In fact, patients with stable MG should find an optimal balance between physical activity and rest to gain as much function as possible. Maintaining activity limits significant muscle atrophy and physical deconditioning and addresses skeletal as well as respiratory strengthening / cardiovascular health [18].

During an exacerbation, energy conservation is the goal rather than exercise. Mobility should be safe and supervised, utilizing assistive devices if necessary. Use of electric appliances can help with energy conservation. Safety precautions should also be used at home including home modification for fall prevention (e.g. adding grab bars, removing throw rugs).

Patients with stable MG should undergo an aerobic and resistance exercise program as discussed below .

The recommended intensity of physical activity/training is of low to medium intensity, avoiding exercise-related fatigue (including but not limited to worsening of MG symptoms e.g. ptosis or diplopia during exercise). Not only is physical activity tolerated in MG; clear benefit has been seen in these patients from strength training. General exercise programs for patients with MG should focus on strengthening large muscle groups, particularly of the shoulder and hip girdle. Timing of exercise is also key and should be targeted to the time of day when the patients are not feeling tired (often the morning). If a patient takes pyridostigmine, exercise should be timed with the peak dose effect (1.5-2 hours after taking a dose). In addition to strength testing, aerobic exercise and balance strategy training may be effective and should be supervised [19].

If swimming is part of the exercise program, supervision is important, and patients should only swim in water where they can touch the bottom. Swimming in deeper water may lead to over-exertion which can be dangerous. Care should be taken to control other factors that can worsen MG symptoms e.g. heat. Aerobic exercise may improve respiratory function as well as stamina [20].

Depending on the level of weakness, an assistive device and/or orthotic may be necessary for gait support. Assistive devices range from a cane to a walker to powered mobility. Orthotics such as an ankle foot orthosis (AFO) may be helpful as well to assist with ankle dorsiflexion [21].

Rehabilitation with speech language pathologists is indicated for those with bulbar deficits. Exercises may work on breath control, voice quality, swallowing, and articulation. Postural exercises also assist with breathing, speaking, and swallowing. A formal neuroophthalmological exam is recommended. Corrective surgeries for ptosis often provide relief, however, may lead to dry eyes. Adaptive glasses with ptosis crutch or support can also be used. Ocular may require surgical intervention [22, 23].

CONCLUSIONS

1. Although, rehabilitation of patients with myasthenia gravis is not the main, but a very important part of the patient's treatment algorithm.
2. Clinical and anamnestic features of myasthenia in absence of structural thymus disorders are debut before the age of 40 years, predominant affection of skeletal muscles, mild course (severity of the disease corresponds to 12.7 ± 1.76 points on the QMGS scale) and presence of clinical neurophysiological dissociation (prevalence of skeletal muscles lesions in clinical picture, but-EMG changes are more pronounced in oropharyngeal muscles).
3. Neurophysiological disorders in patients with myasthenia, regardless of structural changes in the thymus, are manifested by a decrease in the amplitude of the negative phase of M-response in m. orbicularis oculi and m. abductor digiti minimis and an increase in the decrement test.

This study containes the results of the treatment and rehabilitation patients with myasthenia gravis after surgical operation. Since using our methods we improve results in the postoperative period and realize the full effect of treatment and rehabilitation in these patients.

Since the usage new ways of surgical treatment, conservative treatment and rehabilitation in patients with myasthenia gravis can notice improving of results. We plan to develop an algorithm that will reduce the number of postoperative complications.

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The topic of GDR surgery of the thoracic cavity of the State Institution "Zaycev V.T. Institute of General and Urgent Surgery of the National Academy of Medical Sciences of Ukraine", P.01.14, Development of surgical tactics with thymomas complicated by the superior vena cava syndrome, № UA 0119U002466. This research became a fragment of this research work.

Conflict of interest:
The Authors declare no conflict of interest

Received: 22.06.2021
Accepted: 23.08.2021

ADDRESS FOR CORRESPONDENCE:
Kateryna V. Ponomarova
Kharkiv National Medical University
4 Nauky Avenue, 61000 Kharkiv, Ukraine
phone: +38(066) 224-96-79
e-mail: eponkat@gmail.com

ORCID ID and AUTHORS CONTRIBUTION
0000-0002-7551-3818 – Olena L. Tovazhnyanska(A)
0000-0002-4007-6806 – Olena M. Klimova(C)
0000-0003-3119-5480 – Hanna Petrivna Samoilova(B)
0000-0003-3371-1178 – Dmytro V. Minukhin(E)
0000-0001-7327-0632 – Kateryna V. Ponomarova(D)
0000-0003-1941-7183 – Denys O. Yevtushenko(F)
0000-0003-1886-3181 – Vasiliy G. Hroma(C)

A – Research concept and design, B – Collection and/or assembly of data, C – Data analysis and interpretation, D – Writing the article, E – Critical revision of the article, F – Final approval of article