Review Modern Treatment of Patients with Myasthenia Gravis

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ABSTRACT

The review presents current data on the methods of treatment of myasthenia gravis. The features of the course of myasthenia gravis, their influence on approaches to treatment are highlighted. The features of medical tactics aimed at preventing crises are considered. The issues of the effectiveness of thymectomy and rehabilitation of patients after surgery are highlighted. According to modern concepts, the correct management of patients during and after thymectomy is essential to improve the outcomes of the operation.

Keywords: myasthenia gravis, drug therapy, thymectomy , efficiency, rehabilitation

Introduction. To select an adequate treatment for patients with myasthenia gravis, it is necessary to take into account the characteristics of the course of the disease. In half of the cases, the disease manifests with eye symptoms, and in 80% of patients these symptoms appear during the first month of the disease. In 10% of patients with myasthenia, the disease begins with weakness of the bulbar muscles, in 10% - with weakness in the limbs, in 10% - with general weakness, in 1% - with weakness of the respiratory muscles. In 40% , symptoms become generalized , with generalization of symptoms in 90% of this group of patients occurring within the first year of the disease. The isolated ocular form throughout the disease is observed in 15-20% of patients. More often the disease proceeds with periods of exacerbation and remission. Weakness reaches its maximum in the first 3 years after the onset of the disease [11,25]. This indicates the need for careful dynamic monitoring and individually selected treatment by neurologists in identifying a reliable diagnosis of myasthenia gravis. The patient should be informed about the course of his disease, including possible options and unpredictable moments, about all methods of treatment, the possibilities of its effectiveness and complications.

Main part . In patients with severe forms of myasthenia, exacerbation can occur within a few hours. If breathing problems develop, the patient should be immediately hospitalized in the intensive care unit. Hospitalization during periods of exacerbation is required for patients with severe dysphagia, weight loss, and rapidly progressive or severe muscle weakness. In a hospital setting, it is possible to continuously monitor the patient's condition, provide emergency assistance for respiratory disorders and select the optimal treatment. The course of myasthenia can be aggravated by concomitant diseases, primarily thyroid diseases (hypothyroidism or hyperthyroidism), therefore, in order to achieve positive treatment results, their correction should be carried out by the appropriate specialists.

Conservative treatment. Drug therapy for myasthenia gravis is largely aimed at normalizing neuromuscular transmission. Anticholinesterase drugs (ACEPs) are prescribed: pyridostigmine bromide orally at a

maximum daily dose of 240-360 mg (30-120 mg per dose). The secretion of acetylcholine improves ipidacrine at a dose of 120-160 mg / day orally, 45 mg / day parenterally. AHEP can be combined with potassium preparations (for example, potassium chloride at a dose of up to 2.5 g per day with intravenous drip in 500 ml of isotonic sodium chloride solution), potassium-sparing diuretics (spironolactone orally at a dose of 0.025-0.05 g 3-4 times per day), prolonging the effect of AHEP [17].

Many authors are of the opinion that if ACE is ineffective and it is impossible to perform thymectomy , treatment with glucocorticoids is prescribed [8,12,17]. Currently, the most optimal is the use of glucocorticoids according to the scheme every other day. The dose of prednisolone is selected individually, focusing on the severity of the patient's condition. On average, it is 1 mg / kg per day), but not less than 50 mg. The drug is taken once a day in the morning. Treatment is desirable to begin in a hospital setting. The effect is evaluated after 6-8 receptions. In the first few days, some patients may experience episodes of deterioration in the form of increasing muscle weakness and fatigue. Perhaps these episodes are associated with the direct action of glucocorticoids on the release of the synaptic mediator and desensitization of receptors. This circumstance necessitates a temporary reduction in the dose of anticholinesterase drugs. As the effect is achieved and the condition of patients improves, the dose of prednisolone is gradually reduced to maintenance. With prolonged use of glucocorticoids , a number of patients may develop side effects, among which the most common are weight gain, hirsutism, cataracts, impaired glucose tolerance, arterial hypertension, osteopenia . With the development of side effects, it is necessary to reduce the dose of the drug until it is completely canceled. It is inappropriate to use glucocorticoids during periods of surgical interventions, primarily thymectomy . These drugs adversely affect the regenerative processes in tissues, aggravating both the operation itself and the course of the postoperative period [17,22,24].

With insufficient effectiveness of glucocorticoids or the development of pronounced side effects, cytostatic drugs are used. Among the most preferred cytostatics are azathioprine , mycophenolate mofetil , cyclosporine , cyclophosphamide . To correct possible side effects of glucocorticoid and immunosuppressive therapy , immunomodulators derived from the thymus gland (thymus extract, thymalin , etc.) can be used. Plasmapheresis indicated for rapidly progressive deterioration, the threat of developing a myasthenic crisis or directly with a myasthenic crisis, as well as when surgical treatment is necessary.

When managing patients with myasthenia gravis, it should be taken into account that some groups of drugs are contraindicated in this disease. First of all, these are drugs that can slow down neuromuscular transmission. It is not recommended to prescribe the following groups of drugs: beta-blockers, muscle relaxants , magnesium salts, antipsychotics, tranquilizers (except grandaxin), fluorine-containing hormones, quinine derivatives, diuretics (except spironolactones), antibiotics (except for cephalosporins).

Surgery. One of the leading places in the complex treatment of patients is surgical treatment of myasthenia gravis [1,11]. With belated diagnosis, patients die within one to two years from progressive weakness and involvement in the pathological process of the muscles that perform vital functions - breathing and swallowing, without receiving effective medical care [11] Postoperative mortality in thymoma reaches 20-36%, and good long-term the results after thymectomy are 2-3 times worse than with thymic hyperplasia [11,24,27]. Indications for thymectomy , according to different authors, are contradictory, while this issue is extremely important. However, despite a rather lively discussion in the specialized literature, complex issues of indications and contraindications for surgical treatment, the optimal time and technique for performing the operation, methods of preoperative preparation and postoperative management are still far from being finally resolved, and the

recommendations of the authors are often contradictory [6,8,26]. Criteria such as the age and sex of the patient, the duration and severity of the disease, which correlate with the effect of the operation, have been identified [6,10,12]. A number of authors obtained significant correlations with the histological structure of the thymus [6,25]. Optimal surgical treatment of myasthenia gravis prevents the development of severe neurological disorders and creates favorable conditions for stable clinical remission of the disease and restoration of the patients' ability to work [18-23].

Efficiency of thymectomy. To evaluate the results of the operation, the scheme of G. Keynes (1949) is used in the modification: A - excellent effect, B - good, C - satisfactory, D - no effect, E - lethality. For an excellent effect, they take a complete restoration of motor functions, performance without medical support; for a good effect - a significant improvement in the condition, almost complete restoration of motor function and performance with a decrease in the daily dose of kalimin compared to the preoperative 2 times or more and no need for immunosuppressive therapy; for a satisfactory effect - a slight improvement in motor function with constant intake of kalimin and sometimes prednisolone, the absence of disease progression [18,19]. The effectiveness of thymectomy in myasthenia is now generally recognized , however, in the literature there are differences in approaches and interpretation of the degree of improvement in the condition of patients: excellent and good results (A and B , according to the Keynes scheme) vary from 58.7% [7] to 88% [25] . Most authors note the dependence of the improvement in the condition after thymectomy on the age of the patient and the duration of the operation after the manifestation of the disease: the younger the patient and the shorter the duration of the disease, the higher the effectiveness of surgical treatment [7,11,13]. Some emphasize that the effect of surgery is much better in patients with thymic hyperplasia than in patients with thymoma [27].

Management of patients in the postoperative period. Correction of the patient's condition in the early postoperative period is the selection of the dose of ACEP, if necessary; in many patients, immediately after surgery, the introduction of AHEP is not required to restore breathing due to sufficient independent respiratory activity, most of this group do not need to take AHEP in the future. In the first 3-5 days, according to the indications, combined treatment is carried out - pathogenetic in combination with restorative treatment - correction of protein metabolism disorders, acid-base state (albumin solutions, plasma, electrolyte mixtures, vitamins). All patients within 3-5 days after surgery, in order to prevent purulent complications, receive antibiotic therapy - it is preferable to use cephalosporin antibiotics , which are not contraindicated in myasthenia gravis) [18-23]. Rehabilitation is necessary for many diseases of the nervous system, including vascular, neuromuscular, traumatic lesions. From the timely started rehabilitation, the course and prognosis of the disease [2-5,9,14-16]. Rehabilitation in the late postoperative period of thymectomy consists of the selection of an individual maintenance dose of ACEP, long-term use of spironolactone and potassium chloride. Perhaps the use of antioxidants, immunomodulators.

Of the physiotherapy methods used: electrophoresis with prozerin on the shoulder area, electrophoresis with thiamine endonasally , electrophoresis with heparin for the prevention of thrombotic complications, with intestinal atony - electrical stimulation. To improve the drainage function of the bronchi after surgery, along with breathing exercises, inhaled bronchodilators are applicable . In the late postoperative period, the chest and limbs are massaged [11].

Conclusion. Thus, in the treatment of myasthenia gravis, it is necessary to develop an individual treatment program, taking into account the form of myasthenia gravis, concomitant somatic pathology and possible side effects of the drugs used.

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