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Myasthenia gravis complicated by the development of COVID-19: an analysis of case series

Myasthenia gravis (MG) is an autoimmune disease characterized by increased dynamic muscleweakness. Patients with myasthenia gravis are united by the phenomenon of deterioration of the clinicalcondition after infection, refusal of treatment or taking certain medications, surgical intervention, exposureto heat and stress. In the context of the COVID-19 (Coronavirus disease 2019) pandemic, the study ofpatients with myasthenia gravis and a new infectious disease may reveal new pathogenetic patterns andchange the therapeutic strategy.

Objective — to identify clinical and paraclinical, therapeutic regularities in patients with MG and COVID-19.

Methods and subjects. From April 2021 to November 2021, the course of MG against the background ofCOVID-19 in 11 patients was analyzed. The control group consisted of 7 patients with COVID-19, butwithout MG. General clinical, neurological, instrumental, laboratory and statistical examination methods,scales Myasthenia Gravis Foundation of America (MGFA), The Quantitative Myasthenia Gravis Score (QMGS), Myasthenia Gravis Activities of Daily Living (MG-ADL), The National Early Warning Score 2 (NEWS2) and questionnaires were used.

Results. In the experimental and control groups, the level of SpO_2 when breathing atmospheric air wascorrelated with the presence of bronchial asthma (BA) (r = –0.791), diabetes mellitus (DM) (r = –0.553),hypertension (r = –0.301). A positive correlation (r = 0.271) was found between the presence of MG and the level of SpO_2 when breathing atmospheric air, which may be associated with the intake of pyridostigmine anda decrease in muscle mass in patients with MG. Presence of a relationship between the NEWS2 indicatorwith DM (r = 0.501), BA (r = 0.483), obesity (r = 0.376), hypertension (r = 0.352), multinodular goiter (r = 0.204), hydrothorax (r = 0.204) and MG (r = 0.120). In the myasthenia group, a relationship was established between the duration of treatment for COVID-19 and body mass index (BMI) (r = 0.523), age (r = 0.504), pyridostigmine intake (r = –0.243) and weight (r = 0.228). NEWS2 in the experimental group was correlated with pyridostigmine intake (r = –0.386), weight (r = 0.355) and BMI (r = 0.256). Duration of treatment for COVID-19 was associated with duration of MG (r = 0.570), obesity (r = 0.572), and BMI (r = 0.526). NEWS2 is related to the level of SpO_2 when breathing atmospheric air (r = — 0.907), hemoglobin (r = –0.847) and vital capacity of the lungs (VC) (r = –0.699). Obesity (r = 0.787), anemia (r = 0.684) and BA were correlated with NEWS2. The finding of an inverse correlation between NEWS2 and pyridostigmine intake (r = –0.684) was promising. Soft palate paresis (r = –0.614), dysphagia (r = –0.614) and nasality (r = –0.545) were correlated with a decrease in VC. A correlation was found between VC and the NEWS2 (r = –0.699). The duration of COVID-19 (r = –0.646) and patient age (r = –0.626) were correlated with VC.

Conclusions. MG with the addition of COVID-19 tends to worsen the course, progress of muscle weakness,development of respiratory failure and hypoxia. Aggravating factors are age, duration of MG, duration ofCOVID-19, BMI, concomitant pathology (DM, hypertension, BA, obesity, anemia). Constitutional features(lower BMI and weight) may contribute to shortening the duration of treatment. Taking pyridostigmineallows to reduce not only the duration of treatment, but also the risk of worsening of the condition, whichmay be associated with the suppression of the inflammatory process when taking an anticholinesteraseagent.

Keywords: myasthenia, myasthenia gravis, myasthenic crisis, antibodies to acetylcholine receptors, AChR, muscle-specific tyrosine kinase, MuSK, COVID-19, SARS-CoV-2, MGFA, NEWS2, pyridostigmine.

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Myasthenia gravis is an autoimmune disease characterized by increased muscle weakness and skeletal muscle fatigue during exercise and re-exercise (a symptom of dynamic muscle weakness), as well as at least partial recovery after a period of rest.

The distribution of the disease and the severity of MG are classified according to the Myasthenia Gravis Foundation of America (MGFA) Clinical Classification of Myasthenia gravis (ophthalmic), or generalized mild (class IIA and IIB), moderate (class IIIA and IIIB), severe (class IVA, IVB and V) MG. Ocular MG (10—20 % of patients) is manifested by ptosis and diplopia, which may be temporary, variable, or progressive during the day. In turn, generalized myasthenia gravis involves in the pathological process mainly the muscles of the torso (subtype A on the MGFA scale) or oropharyngeal muscles (subtype B on the MGFA scale) [6]. As a rule, all cases of ocular MG tend to generalize within 1—2 years.

The disease is mediated by antibodies targeting proteins of the neuromuscular junction. In most patients (~85 %) antibodies against muscle acetylcholine receptor (AChR) are detected, and in 6 % — against muscle-specific tyrosine kinase (MuSK). In ~10 % of patients with MG autoantibodies cannot be detected by classical diagnosis of antibodies to AChR and MuSK, in such cases seronegative MG may be the correct diagnosis. In recent years, using advanced high-sensitivity assays, it has become possible to detect other autoantibodies in patients with myasthenia gravis: antibodies to low-density lipoprotein receptor-related protein 4 (RP4), titin, ryanodine receptor (RyR), agrin, collagen Q (ColQ), voltage-gated potassium channel (Kv1,4) and cortactin [10].

The clinical picture of patients with myasthenia gravis also includes an increase muscle strength after administration of a cholinesterase inhibitor, a positive response to immunosuppressive therapy, a significant improvement after plasma exchange or intravenous administration of immunoglobulin (IVIg).

Auxiliary diagnostic methods reveal a decrement of the muscle response during re-stimulation of peripheral nerves: in myasthenia gravis re-stimulation at a rate of 2—3 Hz per second reveals a characteristic decrement (> 10 %), which decreases after cholinesterase inhibitor. Examination of a single muscle fiber reveals jitter.

Almost all patients with myasthenia gravis are united by the phenomenon of deterioration of the clinical condition after joining the infectious process, refusal of treatment or taking certain illicit drugs, surgery, and exposure to heat and stress.

Limb and respiratory muscle weakness [12], respiratory failure [11] are known to be common symptoms of COVID-19. In this context, it is interesting to study the impact of COVID-19 on the degree of progression of muscle weakness, involvement in the pathological process the muscles of the upper and lower respiratory system in patients with myasthenia gravis, since these targets of infectious aggression are the most victimized in patients with neuromuscular pathology. That is why the clinical study of patients with acute infection, especially COVID-19, is an urgent task in the new epidemiological conditions.

Objective — to identify clinical, paraclinical and therapeutic patterns in patients with myasthenia gravis during the accession of acute intercurrent disease — COVID-19.

Methods and subjects

The course of MG was analyzed against the background of the addition of an acute intercurrent disease (COVID-19) in 11 patients in period from April 2021 to November 2021. The control group consisted of 7 patients with COVID-19 but without MG, who were selected by age, sex, list of comorbidities and severity of COVID-19 according to the study group.

All participants signed a written informed consent to participate in the study, with the subsequent use of the information received for analysis and publication. Research materials, including the form of written informed consent, approved by the Commission on Bioethical Expertise and Ethics of Scientific Research Bogomolets National Medical University dated 21.12.2020 (protocol # 140).

The research methods included:

1. General clinical (collection of complaints, anamnesis, examination of the patient) and neurological (specific neurological examination).

2. Specific clinical using scales:

- subjective assessment of the severity of muscle weakness on a 4-point scale (minor, mild, moderate and severe);
- MGFA (Myasthenia Gravis Foundation of America — clinical classification of myasthenia);
- QMGS (Quantitative Myasthenia Gravis Score);
- MG-ADL (Myasthenia Gravis Activities of Daily Living — scale of daily activity in myasthenia gravis);
- NEWS2 (The National Early Warning Score 2 — a scale that takes into account respiratory rate, saturation, need for oxygen therapy, body temperature, systolic blood pressure, heart rate, level of consciousness and allows to identify patients at high risk of clinical deterioration with COVID-19 [1]. Interpretation of the obtained score on the NEWS2 scale is presented in Table 1 [8].

3. Questionnaires MG-QOL15 (15-item Myasthenia Gravis Quality of Life scale), PHQ-9 (Patient Health Questionnaire), GAD-7 (Generalized Anxiety Disorder 7-item).

4. Instrumental (determination of oxygen saturation using a pulse oximeter, hand muscle strength using a wrist dynamometer electronic CAMRY EH101, calculation of vital capacity of the lungs using a dry portable spirometer).

5. Laboratory (general blood test to determine leukocyte formula, total protein, albumin, creatinine, urea, alanine aminotransferase, aspartate aminotransferase, bilirubin, creatine phosphokinase, K^+, Na^+, C-reactive protein, D-dimer, fibrinogen, procalcitonin).

Table 1
Interpretation of the NEWS2 scale

Score	Risk grading	Monitoring frequency	Solution
0	No	Every 12 hours	
1—4	Low	Every 6 hours	• Maintain existing monitoring • Increase monitoring frequency • Inform doctor
3	For any individual parameter, the risk is below average	Every 1—2 hours	• Maintain existing treatment • Adjust treatment plan • CCRRT remote consultation
5—6	Medium risk		
≥ 7	High risk	Continuous	CCRRT on-site consultation

CCRRT — Critical Care Rapid Response Team.

6. Statistical (mean, standard deviation, determination of part of the whole, determination of Pearson's correlation coefficient, construction of the decision tree).

The subjects were myasthenia gravis patients diagnosed with COVID-19 and COVID-19 patients without myasthenia gravis.

Results and discussion

The experimental group of patients with MG and COVID-19 included 11 patients (Table 2), 6 female and 5 male patients. The mean age of patients was 60 years (min — 30, max — 82 years, standard deviation (STD) — 17.26). According to the clinical classification of myasthenia gravis MGFA patients were distributed as follows: class IIA — 4 patients, IIB — 2 patients, IIIA — 1 patient, IIIB — 2 patients, class V — 2 patients. Weakness of the torso muscles (subtype A) dominated in 5 patients and weakness of the oropharyngeal muscles (subtype B) in 4 patients.

The prognosis for comorbid infectious pathology was estimated by NEWS2. The mean score in 11 patients was 7, which corresponds to a high potential clinical risk of deterioration in hospitalized patients with COVID-19 [1], in 6 patients NEWS2 was 7 or higher.

The average duration of treatment with COVID-19 was 13 days, min — 3 days (n = 2), max — 20 days, STD — 6.33, the average duration of the entire period of COVID-19 — 25 days, min — 11, max — 44 days, STD — 9.58.

Table 2
Main clinical characteristics of patients with myasthenia gravis and COVID-19 (n = 11)

N	Sex	Age, years	MGFA scale	NEWS2 scale	Duration of treatment for COVID-19, days	Duration of COVID-19, days	The result of treatment	Height, m	Weight, kg	BMI	Duration of myasthenia, years	Basic therapy
1	M	62	V	12	19	32	Extract	1.62	82	31.2	15	Pyridostigmine 60 mg 3 times per day
2	M	30	IIIB	1	3	13	Extract	1.8	65	20.1	2	Pyridostigmine 60 mg 2 times per day and 30 mg once
3	M	69	V	11	16	44	Extract	—	—	—	3	Pyridostigmine 60 mg
4	M	62	IIA	12	3	11	Death	1.85	120	35.1	1	Mofetil mycophenolate 500 mg 2 times per day, pyridostigmine 60 mg 4 times per day
5	F	82	IIA	1	17	24	Extract	1.63	100	37.6	35	Pyridostigmine 60 mg 3 times per day
6	M	62	IIB	13	18	31	Extract	1.74	103	34	10	Methylprednisolone 16 mg once
7	F	65	IIB	8	20	32	Extract	1.64	85	31.6	21	Pyridostigmine 30 mg 4 times per day
8	F	38	IIA	6	6	22	Extract	1.69	69	24	2	Pyridostigmine 30 mg 3 times per day
9	F	80	IIIB	6	14	24	Extract	1.68	120	42.5	—	Pyridostigmine 120 mg 3 times per day and 60 mg once, methylprednisolone 8 mg once
10	F	71	IIA	1	14	28	Extract	—	—	—	40	Pyridostigmine 60—120 mg
11	F	38	IIIA	11	17	17	Extract	1.75	120	39.2	9	Pyridostigmine 60 mg 3 times per day, methylprednisolone 8 mg every other day
μ		60	III	7.5	13.4	25.3		1.7	96	32.8	13.8	

MGFA — Myasthenia Gravis Foundation of America; NEWS2 — National Early Warning Scale 2; COVID-19 — coronavirus disease of 2019; BMI — body mass index; μ — the arithmetic mean; M — the male; F — the female.

Differences in the clinical picture

Prevalence of clinical symptoms in the comorbidity group of myasthenia gravis and COVID-19 can be described as follows:

- 11 patients complained of progression of muscle weakness from mild to severe;
- 10 patients complained of unproductive cough;
- 9 patients reported shortness of breath;
- 5 patients were bothered by nausea;
- 3 patients suffered from diplopia, dysphagia and diarrhea;
- 2 patients reported loss of appetite, chest pain, dizziness, palpitations, sweating, ptosis and dysphonia;
- 1 patient complained of thirst, tinnitus, syncope, shakiness, leg tremor, vomiting, productive cough, difficulty chewing, ear congestion, stomach pain, sore throat, bone pain, bone pain, anosmia.

The control group was characterized by the following complaints:

- progression of muscle weakness from minor to mild (n = 7);
- cough (n = 5);
- shortness of breath (n = 4);
- hyperthermia, sweating (n = 3);
- nausea, sore throat (n = 2);
- syncope, dizziness, vomiting, hoarseness, difficulty breathing, headache, sore throat, bone pain, muscle pain, anosmia (n = 1).

A comparison of the complaints of patients with myasthenia gravis and COVID-19 with the control group (Fig. 1) suggests that the progression of muscle weakness is observed in each group, but the degree of muscle weakness is significantly different, which will be discussed below. Universal symptoms of COVID-19 were found in both groups: cough, shortness of breath, dizziness, nausea, vomiting, hyperthermia, difficulty breathing, bone, muscle pain, and anosmia. Another important feature is the presence in the group of myasthenia gravis of specific complaints of ptosis, diplopia, dysphonia, dysphagia, masticatory muscle weakness, which did not complicate the course of infectious disease in the control group.

The construction of the basic rules for the distribution of the degree of muscle weakness (Fig. 2), operating in the experimental and control groups suggest that if the duration of COVID-19 is less than 12 days, muscle weakness is not higher than 1 point.

In patients without myasthenia gravis, if the duration of COVID-19 was 12—43 days and the result of treatment was «hospital discharge», the muscle weakness was within 1—2 points. However, if the treatment was fatal or the treatment lasted more than 43 days (severe course of the disease), the weakness, even in the COVID-19 group without myasthenia gravis (control group), was 2—4 points. This indicates that the symptom of muscle weakness is pathognomonic for COVID-19 and the severity of the course affects the level of muscle weakness, even in the absence of pathology of neuromuscular transmission.

In the group of patients with myasthenia gravis, the duration of COVID-19 was crucial: with a disease duration of less than 20 or more than 38 days, the weakness was 4 points. This pattern can be explained by the rapid increase in the patient's severity, malignant course of the disease in the short term with the development of severe muscle weakness or long-term resistant progression of the disease, which ultimately leads to decompensation of myasthenia gravis and critical loss of muscle strength. The duration of the disease within 20—38 days in patients with myasthenia gravis was associated with a lower degree of muscle weakness (2—4 points).

The effect of comorbidity on the main indicators of the course of COVID-19 in patients with/without myasthenia

Comorbidity with bronchial asthma (Table 3) correlates with the level of oxygen saturation (SpO_2) when breathing atmospheric air (r = –0.791 — strong

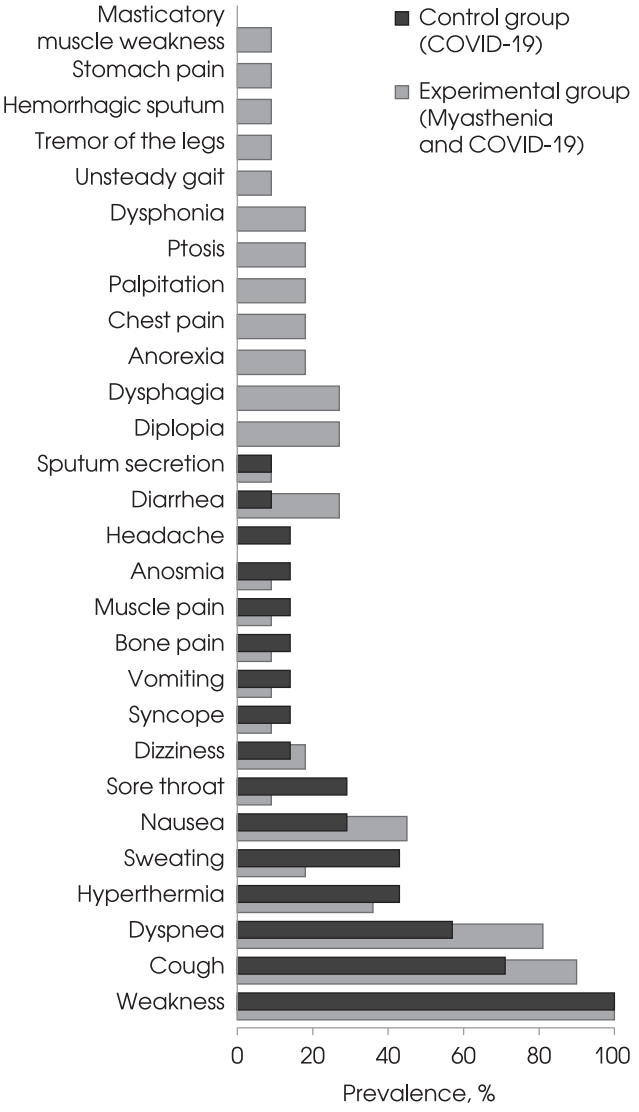

Fig. 1. *Prevalence of complaints of patients from the experimental and control groups*

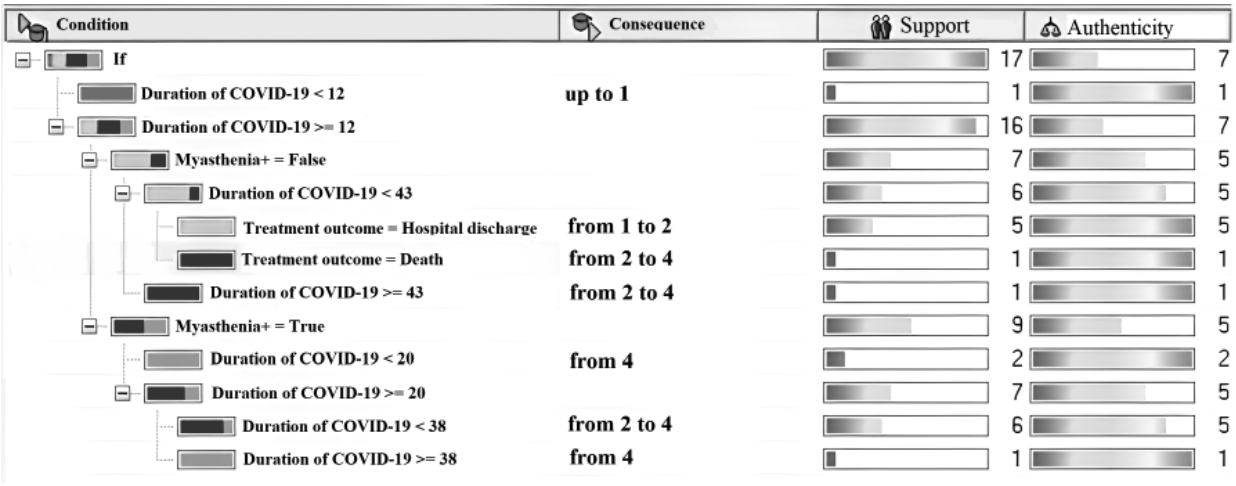

Fig. 2. *Basic rules for the distribution of the degree of muscle weakness in the groups of patients with COVID-19 and COVID-19 with myasthenia gravis (Based on all data obtained, the cases were classified using a decision tree. The degree of muscle weakness (scored from 1 to 4 points) was influenced with a high degree of confidence by the duration of the disease, the presence of myasthenia gravis, and the result of treatment)*

feedback), which attracts special attention to this group of patients, because it was found that the combination of bronchial asthma and COVID-19 in patients with or without myasthenia gravis is a significant factor in the development of oxygen deficiency. Also a SpO_2 level when breathing atmospheric air correlates with the presence of diabetes mellitus (r = –0.553 — medium feedback) and hypertension (r = –0.301 — weak feedback), which predicts a decrease in saturation in patients with impaired carbohydrate metabolism and cardiovascular pathology and requires targeted supervision of such patients.

An interesting was the detection of a direct weak correlation (r = 0.271) the presence of myasthenia gravis and the level of SpO_2 when breathing atmospheric air, which may be due on the one hand to pyridostigmine, which can reduce inflammation in the respiratory system and the risk of respiratory failure (RF), acute respiratory distress syndrome (ARDS), on the other hand, such a correlation may be associated

Table 3

Comorbidity profile of patients with myasthenia gravis and COVID-19 (n = 11)

N	Patient	Obesity	OBPP	CHD	HBP	DM	BA	GSD	Other
1	P	Class 1	+	+	+				
2	B		+						
3	B		+	+				+	Left hydrothorax. Multinodular goiter. Polycystic kidney disease. Condition after splenectomy, slaughter of lungs and heart (car accident in the 1987)
4	M	Class 2	+		+	+			
5	B	Class 2	+	+				+	Dyscirculatory encephalopathy. Autoimmune thyroiditis. Chronic obstructive pulmonary disease
6	F	Class 1	+				+		Anemia medium degree
7	R	Class 1	+		+				
8	Y		+						
9	B	Class 3	+	+	+				Consequences of ischemic stroke
10	P		+	+					
11	S	Class 2	+		+	+			Ovarian adenocarcinoma, condition after ovarian and hysterectomy, chemotherapy. Secondary systemic osteoporosis. Generalized anxiety disorder. Panic disorder. Depressive episode. Otitis media.
Share of all, %		63	100	45	45	18	9	18	9

OBPP — outpatient bilateral polysegmental pneumonia; CHD — coronary heart disease; HBP — high blood pressur/hypertension; DM — diabetes mellitus; BA — bronchial asthma; GSD — gallstone disease.

with less muscle mass in patients with myasthenia gravis, which is one of the main consumers of oxygen, as well as less ability to involve muscles to work through the development and intensification of specific myasthenic dynamic muscle weakness, as the level of muscle weakness at almost the same level with the diagnosis of myasthenia gravis correlated with the level of SpO_2 when breathing atmospheric air ($r = -0.278$). However, it should be noted that the strength of the identified link can not be a substantial basis for drawing definitive conclusions, so further studies of the correlation between myasthenia gravis and SpO_2 levels, as well as the risk of RF and ARDS are necessary.

Analysis of the correlation between NEWS2 and parameters of the study and control group confirmed the presence of an increased risk of prognostic adverse course of COVID-19 with diabetes mellitus ($r = 0.501$), asthma ($r = 0.483$), obesity ($r = 0.376$)), hypertension ($r = 0.352$) and, to a lesser extent, with the presence of multinodular goiter ($r = 0.204$), unilateral hydrothorax ($r = 0.204$) and myasthenia gravis ($r = 0.120$).

Detection of correlation of the main indicators of the course of COVID-19 in patients with/without myasthenia gravis

A strong feedback relationship was found between SpO_2 when breathing atmospheric air and NEWS2 ($r = -0.610$) in the experimental group (patients with myasthenia gravis and COVID-19) and the control group (patients with COVID-19). This correlation can be explained by the fact that lower levels of oxygen in the capillary blood due to lung damage associated with an increased risk of developing RF and severe COVID-19.

There was found a correlation between the duration of treatment for COVID-19 with BMI ($r = 0.523$ — average direct connection), age ($r = 0.504$ — average direct connection), taking pyridostigmine as a basic therapy ($r = -0.243$ — weak feedback) and patient weight ($r = 0.228$ — weak direct connection) in the experimental group of patients with myasthenia gravis and COVID-19.

The study of the correlation between the prediction of the severity of intercurrent pathology — NEWS2 in the group of patients with myasthenia gravis and COVID-19 revealed an association with pyridostigmine ($r = -0.386$ — mean reverse), weight ($r = 0.355$ — mean direct) and BMI ($r = 0.256$ — weak line).

Thus, according to our preliminary data, in a small cohort of patients with myasthenia gravis and COVID-19 it has been found that constitutional features, namely lower BMI and weight (modifiable factors) may help reduce the duration of treatment, in addition, pyridostigmine intake may reduce not only duration of treatment, but also NEWS2.

The effect of pyridostigmine can be explained by anti-inflammatory effects, cellular and humoral immunosuppression. The results of a study in mice show that treatment with pyridostigmine after 72 h reduces the number of macrophages and lymphocytes, inhibits the levels of TNF, IL-1β, IL-6 and IFN-γ in bronchoalveolar lavage and blood plasma of mice with ARDS [2]. A recent preprint of a randomized, double-blind, placebo-controlled, PISCO study (Pyridostigmine in the treatment of adults with severe SARS-CoV-2 infection) found that adding pyridostigmine to standard treatment significantly reduced mortality among patients hospitalized for severe COVID-19 [5].

Correlation analysis of disease rates in patients with myasthenia gravis and COVID-19

The correlation analysis of the severity of myasthenia gravis and COVID-19 in the experimental group (Fig. 3) revealed a direct strong correlation between treatment duration and heart rate (HR) ($r = 0.757$), which may be due to compensatory tachycardia against the background of respiratory failure and more severe disease, which are the basis for longer treatment of the patient in the hospital.

The strong direct correlation between the duration of treatment with obesity ($r = 0.572$) and BMI ($r = 0.526$) coincides with the results of recent meta-analyzes [14], which indicate the development of a more severe course of COVID-19 in obese patients because obesity and metabolic syndrome can cause organ damage and dysfunction [3, 13]. Obesity is accompanied by increased expression of ACE2 (Angiotensin converting enzyme 2), which binds strongly to S protein and makes adipose tissue a portal for invasion *virus* [4], and makes the lungs and heart vulnerable to viral attack [9]. Obesity is accompanied by hyperactive inflammation and immune response, which can lead to excessive inflammation and exhaustion

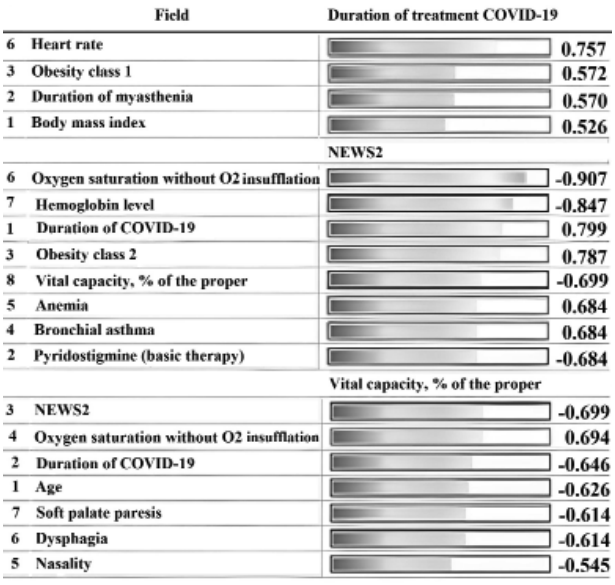

Fig. 3. *Correlation analysis of some indicators of the severity of myasthenia gravis and COVID-19 (duration of treatment, NEWS2 and lung vital capacity) (n = 6)*

of the immune response in COVID-19. Additionally, obese patients have high abdominal pressure, limited expansion and movement of the chest, as well as insufficient respiratory compensatory function [7].

Another significant indicator that correlated with the duration of COVID-19 treatment was the duration of myasthenia gravis (r = 0.570). It can be argued that the longer a patient suffers from myasthenia gravis, the greater the risk of prolonged treatment with COVID-19. This trend may be due to the older age of patients with a long history of myasthenia gravis, their comorbidity and prolonged respiratory dysfunction due to myasthenia gravis, leading to changes in respiratory parameters, respiratory failure and longer inpatient treatment for COVID-19.

Correlation analysis of the NEWS2 revealed a strong inverse relationship between this indicator of worsening and the level of SpO_2 when breathing atmospheric air (r = –0.907), hemoglobin level (r = –0.847) and the inverse mean relationship with the level of vital capacity (VC) (r = –0.699). The detected pattern may be due to the influence of the level of SpO_2 during respiration of atmospheric air on the score on the NEWS2 scale, as saturation is used to calculate NEWS2. However, the important role of saturation, hemoglobin and VC in the functioning of the respiratory system and the implementation of tissue gas exchange has been additionally confirmed. These indicators are one of the main prognostic markers in diseases affecting the respiratory system, especially COVID-19.

There was also a direct strong correlation between NEWS2 and COVID-19 duration (r = 0.799), which can be explained by a longer period of COVID-19 treatment in the presence of signs of severe respiratory damage, oxygen deficiency, RF, which are taken into account in the NEWS2 scale assessment.

The presence of obesity (r = 0.787), anemia (r = 0.684) and bronchial asthma (BA) correlated with the level of NEWS2, because this comorbidity profile involves the respiratory system and gas exchange function in the pathological process, leads to RF and NEWS2 score increasing.

Promising in the direction of further management of patients was the detection of inverse mean correlation of NEWS2 and the use of pyridostigmine as a basic therapy (r = –0.684), which can be interpreted as a potentially positive effect of this anticholinesterase agent not only on muscle strength but also on prognosis clinical course of COVID-19 on the NEWS2 scale.

One of the most informative methods of examining patients with myasthenia gravis was the determination of VC (% of normal) by spirometry in patients with myasthenia gravis and COVID-19. The obtained correlation indicates the presence of average feedback between the presence of bulbar syndrome and the level of VC: soft palate paresis (r = –0.614), dysphagia (r = –0.614) and nasality (r = –0.545) correlated with a decrease of VC, which has value in terms of predicting RF in patients with oropharyngeal muscle weakness.

It was important to identify the correlation between VC and NEWS2 (r = –0.699), which reflects the prognosis. So it can be argued that a decrease in VC may result in increased NEWS2 and, consequently, the risk of severe disease. Higher saturation in atmospheric oxygen respiration correlated with higher VC (r = 0.694), which may be useful in terms of indirect evaluation of VC using available pulse oximetry.

The duration of COVID-19 (r = –0.646) and the patient's age (r = –0.626) were correlated with VC (mean feedback), which is why targeted surveillance of elderly patients with long-term COVID-19 in the presence of myasthenia gravis will be justified, because this cohort of patients has a high chance of reducing VC, which may resulting in critical RF.

Fatal case of myasthenia gravis and COVID-19

A detailed study of the anamnesis of a patient from the experimental group, whose disease led to a fatal outcome, made it possible to draw attention to some difficult problems in the management of patients with myasthenia gravis and COVID-19.

A 62-year-old patient independently applied to the emergency department of the hospital on the 8th day of illness. He complained about severe shortness of breath, cough, and moderate muscle weakness. BMI was 35.1, which corresponds to obesity class 2. The comorbidity profile included hypertension, type 2 diabetes mellitus. From the basic therapy the patient took a combination of cytostatics mycophenolate mofetil 500 mg twice per day, pyridostigmine 60 mg 4 times per day. The duration of myasthenia gravis was 1 year. During the stay in the department, dyspnea and general weakness progressively increased, the trend towards a decrease in SpO_2 when breathing moist oxygen through a mask was due to the constant refusal to continue oxygen therapy.

The patient was assessed on the scales of depression and anxiety: PHQ-9-10 points, GAD-7-4 points, IAPT phobia scale — 6 points. The following results were obtained on specific scores for myasthenia gravis: MGFA — IIA, MG-QOL15-24 points, MG-ADL and QMGS — 0 points. NEWS2-12 points, indicating a severe course of COVID-19 and high risk.

Despite the ongoing treatment, on the 3rd day of hospital stay, biological death was ascertained. It remains unclear what was the main factor in the death of the patient, but it can be argued that the appearance of COVID-19 and new symptoms in the form of severe shortness of breath and persistent unproductive cough, progression of muscle weakness in combination with a decrease in the quality of life due to myasthenia gravis (24 points according to MG-QOL15) led to a critical decrease in hope for recovery and the development of signs of moderate depression (10 points on PHG-9), which could prompt the patient to remove the mask and stop oxygen

therapy. On the other hand, worsening and critical progression of RF against the background of untimely drug treatment (day 8 of illness), severe course of COVID-19 (12 points according to NEWS2), complicated by hypertension, type 2 diabetes mellitus, and grade 2 obesity cannot be excluded.

Conclusions

Thus, the study showed that myasthenia gravis during the accession of acute intercurrent disease — COVID-19 tends to worsen the course, progression of muscle weakness, the development of RF and hypoxia.

Aggravating factors are the age of patients, the duration of myasthenia gravis, the duration of COVID-19, BMI, comorbidity profile (diabetes, hypertension, coronary heart disease, bronchial asthma, obesity and anemia).

An important factor is the use of pyridostigmine as a basic therapy, as according to preliminary data, the use of this anticholinesterase agent tends to reduce inflammation, RF and improve the prognosis.

Significance

Further research is needed in patients with myasthenia gravis in the event of COVID-19 accession, since the identification of reliable patterns and effects of therapy is of paramount importance in the context of the COVID-19 pandemic.

Conflicts of interest: none.

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Міастенія гравіс, ускладнена розвитком COVID-19: аналіз клінічних випадків

Міастенія гравіс (МГ) — автоімунне захворювання, що характеризується підвищеною динамічною м'язовою слабкістю. Пацієнтів з міастенією об'єднує феномен погіршення клінічного стану після приєднання інфекції, відмови від лікування або прийому деяких препаратів, проведення хірургічного втручання, перебування в умовах спеки та стресу. В умовах пандемії коронавірусної хвороби — 2019 (COVID-19) дослідження пацієнтів з міастенією та новим інфекційним захворюванням може виявити нові патогенетичні закономірності та змінити терапевтичну стратегію.

Мета — виявити клініко-параклінічні, терапевтичні закономірності у пацієнтів з МГ у разі приєднання COVID-19.

Матеріали і методи. Проаналізовано перебіг МГ на тлі COVID-19 у 11 пацієнтів у період з квітня 2021 р. до листопада 2021 р. Контрольну групу утворено із 7 пацієнтів з COVID-19 без МГ. Використано загальноклінічні, неврологічні, інструментальні, лабораторні та статистичні методи обстеження, шкали Myasthenia Gravis Foundation of America (MGFA), The Quantitative Myasthenia Gravis Score (QMGS), Myasthenia Gravis Activities of Daily Living (MG-ADL), The National Early Warning Score 2 (NEWS2), а також анкети.

Результати. В дослідній та контрольній групі виявлено обернено пропорційний зв'язок між рівнем SpO_2 при диханні атмосферним повітрям та наявністю бронхіальної астми (БА) (r = –0,791), цукрового діабету (ЦД) (r = –0,553), гіпертонічної хвороби (ГХ) (r = –0,301), прямо пропорційний зв'язок — між наявністю міастенії та рівнем SpO_2 при диханні атмосферним повітрям (r = +0,271), що може бути зумовлено прийомом піридостигміну та меншою масою м'язової системи у пацієнтів з МГ, а також між показником NEWS2 із ЦД (r = +0,501), БА (r = +0,483), ожирінням (r = +0,376), ГХ (r = +0,352), багатовузловим зобом (r = +0,204), гідротораксом (r = +0,204) та міастенією (r = +0,120). У дослідній групі — зв'язок між тривалістю лікування з приводу COVID-19 та індексом маси тіла (IMT) (r = +0,523), віком (r = +0,504), прийомом піридостигміну (r = –0,243), масою тіла (r = +0,228), між NEWS2 і прийомом піридостигміну (r = –0,386), масою тіла (r = +0,355) та IMT (r = +0,256). Тривалість лікування COVID-19 була пов'язана з тривалістю міастенії (r = +0,570), ожирінням (r = +0,572) та IMT (r = +0,526), NEWS2 корелював із рівнем SpO_2 при диханні атмосферним повітрям (r = –0,907), гемоглобіну (r = –0,847) та життєвої ємності легень (ЖЕЛ) (r = –0,699), ожирінням (r = +0,787), анемією (r = +0,684) та БА, прийомом піридостигміну (r = –0,684). Парез м'якого піднебіння (r = –0,614), дисфагія (r = –0,614), гнусавість (r = –0,545), тривалість COVID-19 (r = –0,646) та вік пацієнта (r = –0,626) корелювали з ЖЕЛ.

Висновки. Міастенія у разі приєднання COVID-19 має тенденцію до погіршення перебігу, прогресування м'язової слабкості, розвитку дихальної недостатності та гіпоксії. Обтяжувальними чинниками є вік, тривалість міастенії та COVID-19, IMT, коморбідність (ЦД, ГХ, БА, ожиріння і анемія). Конституційні особливості (менші IMT та маса тіла) можуть сприяти скороченню тривалості лікування. Прийом піридостигміну може зменшити не лише тривалість лікування, а й ризик погіршення стану, що може бути зумовлено інгібуванням запального процесу при прийомі антихолінестеразного засобу.

Ключові слова: міастенія, міастенія гравіс, міастенічний криз, антитіла до ацетилхолінових рецепторів, AChR, м'язово-специфічна тирозинкіназа, MuSK, COVID-19, SARS-CoV-2, MGFA, NEWS2, піридостигмін.

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