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FEATURES OF DEPRESSION DEVELOPMENT IN MYASTHENIA GRAVIS

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Ключевые слова: *миастения, депрессия, класс, QMG, антитела к рецепторам ацетилхолина, мышечно-специфическая тирозин-киназа, длительность заболевания*

Abstract. Features of depression development in myasthenia gravis. Kalbus O.I., Makarov S.O., Shastun N.P., Somilo O.V., Bukreyeva Yu.V. *The relative risk of developing depression in myasthenia gravis is 2.14 times higher than in the general population. The features of depression in myasthenia patients remain poorly understood and need to be clarified. The purpose of this work was to study the features of the development of depression in patients with myasthenia gravis. From 2014 to 2017, 182 patients with myasthenia gravis were examined. 147 (80.8%) patients had a generalized form of the disease, 35 (19.2%) had an ocular form. The clinical examination included assessment of complaints, medical history, neurological examination, as well as MGFA (Myasthenia Gravis Foundation of America) disease class and subclass of the disease determination. The severity of myasthenia gravis has been quantified according to the QMG score (Quantitative Myasthenia Gravis Score). All the patients were examined for the titer of antibodies to acetylcholine receptors (AchR) and muscle-specific tyrosine kinase (MuSK) by enzyme-linked immunosorbent assay (ELISA). Patients were also tested for the presence of antibodies to titin and SOX1 by indirect immunofluorescence. To detect depression the Beck depression inventory (BDI) was used. The mean depression score in the total sample was 16.0 (10.0; 24.0), which corresponds to a moderate depression level. The mean depression score in patients with ocular form was 6.0 (3.0; 11.0) points (ie, depression is absent), whereas in patients with generalized myasthenia gravis – 19.0 (12.0; 29.0) points (corresponds to moderate depression) ($p < 0.001$). The distribution of patients with mild depression was also uneven: significantly bigger part of the patients was recorded with myasthenia gravis of class I (ocular form) – 10 (28.6%), and with myasthenia gravis of class II – 23 (44.2%). Among the patients with myasthenia gravis of class III, only 13 (20.3%) patients were reported with mild depression and 1 (3.2%) with class IV, $p<0.001$. The distribution of patients with moderate depression was the opposite of others: most patients had myasthenia gravis of class II – 12 (18.8%), and there were no patients with myasthenia gravis of class I. A similar tendency is also observed in the case of severe depression: patients with myasthenia gravis of class II – 23 (35.6%) dominated, to a lesser extent - patients with myasthenia gravis of class IV – 6 (19.4%). Among patients with ocular myasthenia gravis, only 1 (2.9%) patient was found to have severe depression. Severe depression was mainly recorded in patients with myasthenia gravis of class IV – 22 (71%) patients. The number of patients with severe depression has been decreased in the class of myasthenia gravis: 13 patients (20.3%) patients with III class, 1 (1.9%) with II class, no patients with class I. The degree of depression correlates with the clinical form of myasthenia gravis ($\rho= -0.52$; $p<0.001$), class ($\rho= -0.30$; $p<0.001$) and the subclass of the disease according to MGFA ($\rho= -0.36$; $p<0.001$). A reliable correlation relationship was established between the quantitative evaluation of the severity of myasthenia gravis (according to the QMG score) and the results of the evaluation according to the BDI score in the total sample ($\rho=0.73$; $p<0.001$). The assessment indicators on the QMG score and the BDI score significantly correlated in patients with ocular ($\rho=0.36$; $p<0.05$) and generalized forms ($\rho=0.67$; $p<0.05$). In addition, the level of depression correlates with the presence ($\rho=0.15$; $p=0.040$) and the titer of antibodies to AchR ($\rho=0.42$; $p<0.001$), with the presence ($\rho=0.18$; $p=0.016$) and the titer of antibodies to MuSK-AB ($\rho=0.19$; $p=0.011$). No correlation was found between the presence of antibodies to titin and to SOX1 ($\rho=0.14$; $p<0.05$ and $\rho=0.07$; $p<0.05$, respectively). There are no relationships between the use of anticholinesterase drugs, prednisone, the combined use of prednisone with / without azathioprine with / without anticholinesterase drugs and the development of depression in patients with myasthenia gravis.*

Реферат. Особливості розвитку депресії при міастенії. Кальбус О.І., Макаров С.О., Шастун Н.П., Соміло О.В., Букреєва Ю.В. *Відносний ризик розвитку депресії при міастенії в 2,14 раза вищий, ніж у загальній популяції. Особливості розвитку депресії у хворих на міастенію залишаються вивченими недостатньо та потребують уточнення. Метою цієї роботи було вивчення особливостей розвитку депресії у хворих на міастенію. З 2014 по 2017 рік було обстежено 182 хворих на міастенію. 147 (80,8%) пацієнтів мали генералізовану форму захворювання, 35 (19,2%) – очну. Клінічне обстеження включало оцінку скарг, анамнезу захворювання, неврологічне обстеження, визначення класу та підкласу захворювання за MGFA (Myasthenia Gravis Foundation of America). Ступінь тяжкості міастенії визначали кількісно за шкалою QMG (Quantitative Myasthenia Gravis Scale). Усім хворим визначали титр антитіл до рецепторів ацетилхоліну (AchR) та м'язово-специфічної тирозин-кінази (MuSK) методом імуноферментного аналізу. Хворим також визначали наявність антитіл до титину та SOX1 методом непрямої імунофлюорисценції. Для виявлення депресивних змін хворим проводили оцінку за шкалою депресії Бека (BDI). Середній показник рівня депресії в загальній вибірці становив 16,0 (10,0; 24,0), що відповідає помірному рівню депресії. Середній рівень депресії у хворих на очну форму становив 6,0 (3,0; 11,0) балів (тобто депресія відсутня), тоді як у хворих на генералізовану міастенію – 19,0 (12,0; 29,0) балів (відповідає рівню помірної депресії) ($p<0,001$). Розподіл хворих з легкою депресією був нерівномірним: достовірно більша їх кількість мала клас I міастенії (очна форма) – 10 (28,6%) осіб, а також клас II міастенії – 23 (44,2%) особи. Серед хворих з класом III міастенії легка депресія реєструвалася лише в 13 (20,3%) пацієнтів, а з класом IV – в 1 (3,2%), $p<0,001$.Розподіл хворих з помірною депресією був протилежно іншим: більшість хворих мали клас III міастенії – 12 (18,8%), а хворих з класом I міастенії не було взагалі. Подібна тенденція прослідковується й у випадку вираженої депресії: за кількістю домінували хворі з класом III міастенії – 23 (35,6%) особи, дещо меншою мірою – хворі з класом IV міастенії – 6 (19,4%) осіб. Серед хворих з очною формою міастенії виявився лише 1 (2,9%), що мав виражену депресію. Тяжка депресія здебільшого реєструвалася у хворих з класом IV міастенії – 22 (71%) пацієнти. Кількість хворих, що мали тяжку депресію, зменшувалася зі зменшенням класу міастенії: 13 хворих (20,3%) хворих з класом III, 1 (1,9%) – з класом II, жодного хворого – з класом I. Рівень депресії корелює з клінічною формою міастенії ($\rho=-0,52$; $p<0,001$), класом ($\rho=-0,30$; $p<0,001$) та підкласом захворювання за MGFA ($\rho=-0,36$; $p<0,001$). Встановлено достовірний кореляційний зв'язок між показниками кількісної оцінки тяжкості міастенії (за шкалою QMG) та результатами оцінки за шкалою депресії Бека в загальній вибірці ($\rho=0,73$; $p<0,001$). Показники оцінки за шкалою QMG та шкалою депресії Бека також достовірно корелювали у хворих з очною ($\rho=0,36$; $p<0,05$) та генералізованою формою ($\rho=0,67$; $p<0,05$). Крім того, рівень депресії корелює з наявністю ($\rho=0,15$; $p=0,040$) та титром антитіл до AchR ($\rho=0,42$; $p<0,001$), з наявністю ($\rho=0,18$; $p=0,016$) та титром антитіл до MuSK ($\rho=0,19$; $p=0,011$). Не встановлено кореляцій між наявністю антитіл до титину та до SOX1 ($\rho=0,14$; $p>0,05$ та $\rho=0,07$; $p>0,05$ відповідно). Не встановлено зв'язків між прийомом антихолінестеразних препаратів, преднізолону, комбінованого прийому преднізолону з/без азатіоприном з/без антихолінестеразними засобами та розвитком депресії у хворих на міастенію. Не встановлено зв'язку між тривалістю міастенії та тяжкістю депресії.*

Myasthenia gravis is a neurological autoimmune disease of unknown etiology, which is based on damage of the postsynaptic terminal of the neuromuscular synapse. The pathogenesis of myasthenia is associated with the appearance of autoantibodies to acetylcholine receptors (AchR) or muscle-specific tyrosine kinase (MuSK). As a result, pathological fatigue and weakness of the striated muscles (skeletal) develop, which is the main clinical manifestation of the disease [7].

According to the epidemiological studies, the expected prevalence of myasthenia gravis is 20 cases per 100 thousand population per year, and the overall one reaches 150-200 cases per 1 million population per year, with a twofold prevalence of the disease among young women [4, 5, 6, 8, 11]. Among older persons, the disease dominates in men [16]. In Ukraine, the prevalence of myasthenia gravis reaches 5.16 cases per 100 thousand population per year [1]. Mortality caused by myasthenia gravis (mainly from crises) has been dramatically decreased over the past 40 years from 75% to 4.5% as a result of improved diagnostic and treatment options [16].

Today, in most countries in the routine practice, myasthenia gravis classification is done according to MGFA (Myasthenia Gravis Foundation of America, 2001), and accordingly 5 classes of the disease have been identified. Class I – an ocular myasthenia; class II-V – a generalized myasthenia. When conducting scientific research, a quantitative assessment of myasthenia gravis, namely, QMG (Quantitative Myasthenia Gravis Scale) is used to quantify symptoms [7].

Clinical manifestations of myasthenia gravis affect various aspects of patients' lives (family, social, personal, professional). Like most other chronic diseases, myasthenia gravis is associated with the development of depression, pathological anxiety, mainly due to the nature of the course of the disease itself (unpredictable progression, varying severity of symptoms during the day, spontaneous development of the complications, etc.) [2, 15].

The depression incidence risk ratio in patients with myasthenia gravis is up to 2.14 times higher than in the general population [15]. Moreover, depression and increased anxiety can cause the development of the so-called "pseudo-decompensations" (patient complaints do not correspond to the objective examination data) and lead to independent uncontrolled increase in doses of anticholinesterase drugs by patients. This, in turn, may lead to the development of cholinergic crises and even to death.

Features of the development of depression in patients with myasthenia remain poorly studied and still need to be clarified.

The aim of this work was to study the features of the development of depression in patients with myasthenia gravis.

MATERIALS AND METHODS OF RESEARCH

182 patients with myasthenia gravis have been examined. 147 (80.8%) patients had a generalized form of the disease, 35 (19.2%) – an ocular form.

The clinical examination included evaluation of complaints, medical history, and neurological examination. The clinical form, class, and subclass of myasthenia gravis have been defined according to the MGFA classification. The severity of myasthenia gravis has been quantified according to the QMG score.

All the patients were examined for the titer of antibodies to acetylcholine receptors (AchR) and muscle-specific tyrosine kinase (MuSK) by enzyme-linked immunosorbent assay (ELISA). Patients were also tested for the presence of antibodies to titin and SOX1 by indirect immunofluorescence.

To detect depressive changes, the patients were examined according to the Beck depression inventory (BDI).

For mathematical processing, non-parametric statistics methods were used in connection with the deviation of the distribution of quantitative data from the normal law (Shapiro-Wilk law). Average values have been presented as median (Me) and interquartile range (25%; 75%). Statistical processing of the research findings was carried out using Microsoft Excel software products (Microsoft Office 2016 Professional Plus, Open License 67528927), STATISTICA 6.1 (StatSoftInc., Serial No. AGAR909E415822FA).

The participants in the study took part in the research on the basis of informed consent meeting international standards of medical ethics.

RESULTS AND DISCUSSION

The age of the patients included in the study ranged from 18 to 83 years at the time of the examination and in average was 52.0 (34.0; 65.0) years.

Among the examined sick persons, there were 128 (70.3%) women and 54 (29.7%) men. The ratio of women to men was 2.37:1. A statistically significantly larger proportion of men was determined in patients with the generalized form of the disease in compare to an ocular one ($p=0.027$). However, statistically significant differences in the overall structure of the examined by gender were not found between classes and subclasses of the disease ($p<0.05$).

AchR antibodies were detected in 124 (68.1%) patients, incl. in 108 (73.5%) – with generalized form and in 16 (45.7%) - with ocular form.

Antibodies to MuSK were detected in 16 (10.9%) patients with generalized myasthenia gravity, and none was detected in any patient with ocular myasthenia gravis.

Antibodies to titin were detected in 53 (29.1%) persons, thus in almost every third person examined. These antibodies were also not detected in patients with ocular myasthenia gravis.

Antibodies to SOX1 were not detected also in patients with ocular myasthenia gravis, but were diagnosed in 10 (6.8%) with generalized form.

The results of clinical and neurological examination of patients with evaluation according to the QMG scale are presented in Table 1.

When conducting intensive tests according to the QMG scale (0-9 points – mild; 10-16 points – moderate, 17 points or more – expressed) it turned out that in all patients of class I and the overwhelming proportion (90.4%) of class II a mild degree of the disease was determined; while in patients of class III and IV the severity of myasthenia gravis was predominantly moderate (87.5% and 51.6%) (g.<0.001).

The average degree of depression in the total sample was 16.0 (10.0; 24.0), which corresponds to a moderate degree of depression. The average degree of depression was determined according to Beck depression inventory (BDI), was in patients with ocular form 6.0 (3.0; 11.0) points (that is, depression is absent), while the patients with generalized form – 19.0 (12.0; 29.0) points (corresponds to the degree of moderate depression) ($p<0.001$).

Separately, the degree of depression was evaluated in patients with different classes and, accordingly, subclasses of generalized myasthenia gravis according to MGFA. The average level of depression in patients with myasthenia gravis of class II was 11.5 (8.5; 15.5), in subclass II-A – 11.0 (8.0; 15.0), in subclass II-B – 14.0 (9.0; 20.0). The indicators between subclasses do not significantly differ ($p> 0.05$). The level of depression in the group of patients with myasthenia gravis of class II corresponds to mild depression.

Table 1

The QMG Scale assessment results

Study Group	QMG (points)	The age of the first symptoms, years	Age of diagnosis establishing, years	Time from the first symptoms to diagnosis establishment, months
Total sample, n=182	**10.0 (5.0; 14.0)**	**45.0 (26.0; 61.0)**	**46.5 (28.0; 62.0)**	**4.0 (2.0; 12.0)**
Ocular form (Class I), n=35	**4.0 (3.0; 6.0)**	**44.0 (22.0; 61.0)**	**44.0 (22.0; 61.0)**	**2.0 (1.0; 3.0)**
Generalized form, n=147	**11.0 (7.0; 14.0)**	**45.0 (29.0; 62.0)**	**48.0 (29.0; 62.0)**	**5.0 (3.0; 12.0)**
p*	***<0.001***	***0.410***	***0.305***	***<0.001***
II–A, n=37	**6.0 (4.0; 7.0)**	**38.0 (29.0; 58.0)**	**39.0 (30.0; 58.0)**	**3.0 (3.0; 10.0)**
II–B, n=15	**5.0 (4.0; 8.0)**	**46.0 (29.0; 70.0)**	**51.0 (29.0; 71.0)**	**10.0 (3.0; 24.0)**
Class II, n=52	**6.0 (4.0; 7.5)**	**38.5 (29.0; 59.5)**	**40.0 (29.5; 60.5)**	**4.0 (3.0; 12.0)**
III–A, n=35	**12.0 (11.0; 14.0)**	**48.0 (25.0; 63.0)**	**49.0 (27.0; 63.0)**	**5.0 (3.0; 24.0)**
III–B, n=29	**11.0 (10.0; 14.0)**	**49.0 (30.0; 59.0)**	**49.0 (30.0; 59.0)**	**6.0 (3.0; 12.0)**
Class III, n=64	**12.0 (11.0; 14.0)**	**48.0 (26.0; 61.5)**	**49.0 (27.0; 62.0)**	**5.5 (3.0; 16.0)**
IV–A, n=14	**16.5 (15.0; 18.0)**	**48.5 (33.0; 58.0)**	**50.5 (40.0; 58.0)**	**9.0 (6.0; 24.0)**
IV–B, n=17	**16.0 (15.0; 21.0)**	**40.0 (29.0; 63.0)**	**40.0 (29.0; 63.0)**	**3.0 (1.5; 5.0)**
Class IV, n=31	**16.0 (15.0; 19.0)**	**46.0 (33.0; 63.0)**	**49.0 (33.0; 63.0)**	**5.0 (3.0; 12.0)**
p	***p**<0.001; p_{I-II}=0.085; p_{I-III}<0.001; p_{I-IV}<0.001***	***0.789***	***0.667***	***p**<0.001 p_{I-II}=0.001 p_{I-III}<0.001 p_{I-IV}=0.002***
p*	***p**<0.001; p_{I-IIA}=0.402; p_{I-IIB}=0.845; p_{I-IIIA}<0.001; p_{I-IIIB}<0.001; p_{I-IVA}<0.001; p_{I-IVB}<0.001; $p_{IIA-IIB}$=0.10; $p_{IIA-IIIA}$<0.001; $p_{IIA-IIIB}$<0.001; $p_{IIA-IVA}$<0.001; $p_{IIA-IVB}$<0.001;$p_{IIB-IIIA}$<0.001; $p_{IIB-IIIB}$<0.001; $p_{IIB-IVA}$<0.001; $p_{IIB-IVB}$<0.001; $p_{IIIA-IIIB}$=0.100; $p_{IIIA-IVA}$=0.001; $p_{IIIA-IVB}$<0.001; $p_{IIIB-IVA}$=0.001; $p_{IIIB-IVB}$<0.001; $p_{IVA-IVB}$=0.967***	***0.824***	***0.654***	***p**<0.001 p_{I-IIIA}=0.001 p_{I-IIIB}=0.025 p_{I-IVA}<0.001 p_{I-IVB}=0.006***

Notes: *p** – differences between the forms of myasthenia gravis according to the Mann-Whitney criterion (U); *p*** –differences between classes of myasthenia gravis and *p* ** - differences between class I of myasthenia gravis and subclasses of classes II-IV of the generalized form of myasthenia gravis by Kruskel-Wallis non-parametric analysis of variance (KW-H). Pairwise comparison of groups in accordance with the designation of the class / subclass of the disease according to the Dunn index.

The average level of depression in patients with myasthenia gravis of class III was 21.0 (15.5; 25.0), in subclass III-A – 20.0 (15.0; 25.0), in subclass III-B – 21.0 (16.0; 25.0). The indicators between subclasses do not significantly differ ($p>0.05$). The level of depression in the group of patients with myasthenia gravis of class III corresponds to moderate depression. The average levels of depression in patients with myasthenia gravis of class II were significantly higher compared with the corresponding indicators of patients with myasthenia gravis of class II ($p<0.001$).

The average level of depression in patients with myasthenia gravis of class IV was 32.0 (26.0; 49.0), in the IV-A subclass – 32.0 (24.0; 47.0), in the IV-B subclass - 46, 0 (31.0; 49.0). The indicators between subclasses significantly differ ($p<0.001$). The level of depression in the group of patients with myasthenia gravis of class IV corresponds to severe depression.

Separately, the evaluation of the distribution of patients according to the degree of depression, depending on the clinical form of myasthenia gravis was conducted (Tab. 2).

Table 2

Distribution of patients with ocular and generalized myasthenia gravis depending on the level of depression

Indicators	Total sample n=182	Ocular form n=35	Generalized form n=147
No depression (up to 9 points), n (%)	43 (23.6)	24 (68.6)	19 (12.9)*
Mild depression (10-15 points), n (%)	47 (25.8)	10 (28.6)	37 (25.2)*
Moderate depression (16-19 points), n (%)	18 (9.9)	0 (0)	18 (12.2)*
Expressed depression (20-29 points), n (%)	38 (20.9)	1 (2.9)	37 (25.2)*
Severe depression (≥30 points), n (%)	36 (19.8)	0 (0)	36 (24.5)*

Notes. * – $p<0.001$, differences between the forms of myasthenia gravis according to the non-parametric variance analysis of Kruskal-Wallis for average indices, for relative indices according to the $\chi 2$ criterion, including those with Yates's correction at values close to 0.

As shown in Table 2, a significant number of patients with ocular myasthenia gravis (68.6%) did not have any depressive changes, and its mild form prevailed among patients with depression. Most patients with generalized myasthenia gravis were recorded with depression. Only 12.9% of patients had no depression.

For more in-depth analysis of the obtained data, the distribution of patients with different classes and subclasses of myasthenia gravis according to MGFA was separately studied depending on the level of depression (Tab. 3).

Table 3

Distribution of patients with different classes of myasthenia gravis depending on the level of depression

Indicators	Class I n=35	II–A n=37	II–B n=15	Class II n=52	III–A n=35	III–B n=29	Class III n=64	IV–A n=14	IV–B n=17	Class IV n=31	*p*
No depression (up to 9 points), n (%)	24 (68.6)	12 (32.4)	4 (26.7)	16 (30.8)	3 (8.6)	0 (0)	3 (4.7)	0 0)	0 (0)	0 (0)	*ip1<0.001 p2<0.001*
Mild depression (10-15 points), n (%)	10 (28.6)	16 (43.2)	7 (46.7)	23 (44.2)	6 (17.1)	7 (24.1)	13 (20.3)	1 (7.1)	0 (0)	1 (3.2)	*p1<0.001 p2<0.001*
moderate depression (16-19 points), n (%)	0 (0)	4 (10.8)	0 (0)	4 (7.7)	7 (20)	5 (17.2)	12 (18.8)	1 (7.1)	1 (5.9)	2 (6.5)	*p1<0.001 p2<0.001*
Expressed depression (20-29 points), n (%)	1 (2.9)	4 (10.8)	4 (26.7)	8 (15.4)	13 (37.1)	10 (34.5)	23 (35.9)	4 (28.6)	2 (11.8)	6 (19.4)	*p1<0.001 p2<0.001*
Severe depression (≥30 points), n (%)	0 (0)	1 (2.7)	0 (0)	1 (1.9)	6 (17.1)	7 (24.1)	13 (20.3)	8 (57.1)	14 (82.4)	22 (71)	*p1<0.001 p2<0.001*

Notes: Differences between the groups according to the non-parametric variance analysis of Kruskal-Wallis for average indicators, for relative indicators according to the $\chi 2$ criterion, including with the Yates's correction at values close to 0: p1 - between subclass II-A and other subclasses of II-IV classes of the generalized form of myasthenia gravis; p2 - between classes of myasthenia gravis.

As shown from Tab. 3, in patients with myasthenia gravis of class III, there were only 3 (4.7%) patients who did not have depression, and there were no patients without depression at all in class IV patients.

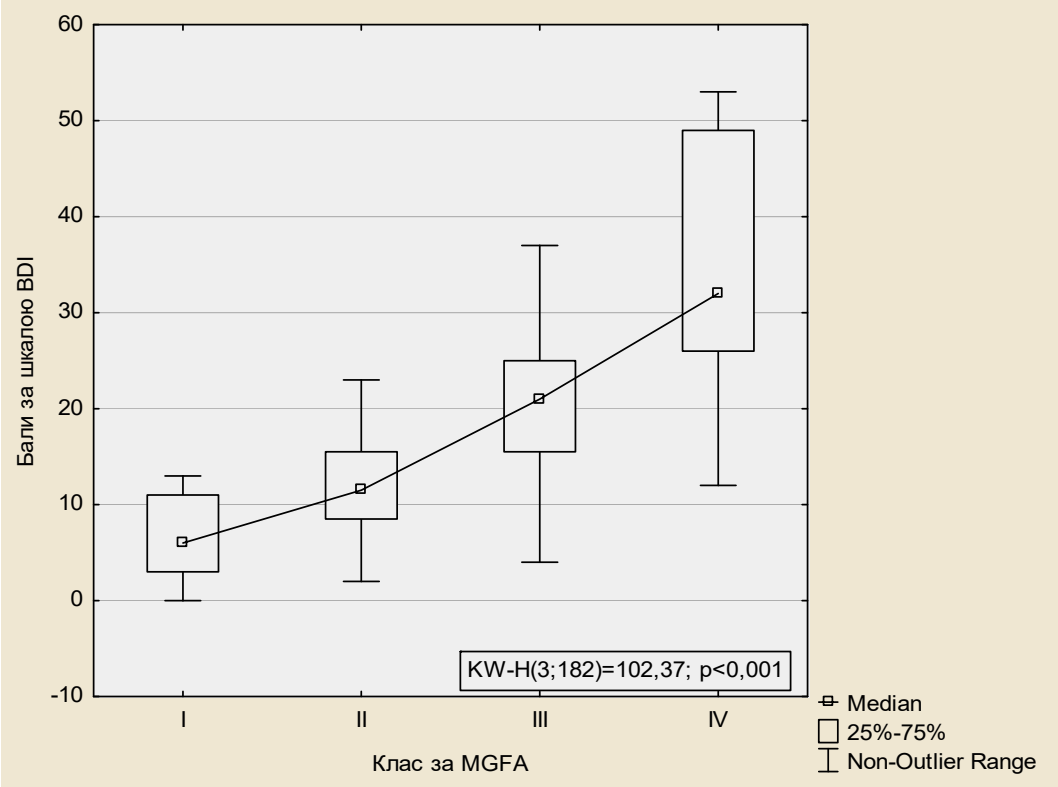
The distribution of patients with mild depression was also uneven: significantly bigger part of the patients was recorded with myasthenia gravis of class I (ocular form) – 10 (28.6%), and with myasthenia gravis of class II – 23 (44.2%). Among the patients with myasthenia gravis of class III, only 13 (20.3%) patients were reported with mild depression and 1 (3.2%) with class IV, $p<0.001$.

The distribution of patients with moderate depression was the opposite of others: most patients had myasthenia gravis of class II – 12 (18.8%), and there were no patients with myasthenia gravis of class I.

A similar tendency is also observed in the case of severe depression: patients with myasthenia gravis of class II – 23 (35.6%) dominated, to a lesser extent – patients with myasthenia gravis of class IV – 6 (19.4%). Among patients with ocular myasthenia gravis, only 1 (2.9%) patient was found to have severe depression.

Severe depression was mainly recorded in patients with myasthenia gravis of class IV – 22 (71%) patients. The number of patients with severe depression has been decreased in the class of myasthenia gravis: 13 patients (20.3%) patients with III class, 1 (1.9%) with II class, no patients with class I.

Thus, it can be indirectly concluded that the degree of depressive disorders in patients with myasthenia gravis depends on the class of myasthenia according to MGFA (Fig.), and, therefore, on the depth of clinical manifestations of myasthenia gravis.



The average level of depression in patients with myasthenia gravis according to Beck depression inventory (BDI) depending on the class of the disease (median, interquartile range, scope of all values without outliers, KW-H - Kruskal-Wallis test)

For more in-depth analysis of the factors affecting the development of depression in patients with myasthenia gravis, some comparisons were made using the Spearman's Rank correlation coefficient. The degree of depression correlates with the clinical form of myasthenia gravis ($\rho= -0.52$; $p<0.001$), class ($\rho= -0.30$; $p<0.001$) and the subclass of the disease according to MGFA ($\rho= -0.36$; $p<0.001$). A reliable correlation relationship was established between the quantitative evaluation of the severity of myasthenia gravis (according to the QMG score) and the results of the evaluation according to the BDI score in the total sample ($\rho=0.73$; $p<0.001$). The assessment indicators on the QMG score and the BDI score

significantly correlated in patients with ocular (ρ=0.36; p<0.05) and generalized forms (ρ=0.67; p<0.05). In addition, the level of depression correlates with the presence (ρ=0.15; p=0.040) and the titer of antibodies to AchR (ρ=0.42; p<0.001), with the presence (ρ=0.18; p=0.016) and the titer of antibodies to MuSK-AB (ρ=0.19; p=0.011). No correlation was found between the presence of antibodies to titin and to SOX1 (ρ=0.14; p<0.05 and ρ=0.07; p<0.05, respectively).

When comparing the age of the first symptoms of the disease, the age of diagnosis, the duration of the disease and the Beck depression inventory, no reliable correlation was found (ρ=0.07; p>0.05; ρ=0.09; p>0.05 and ρ=0.08; p>0.05, relatively). Despite this, there was a significant weak correlation between the Beck Depression Score and the time from the first symptoms to diagnosis (ρ=0.15; p=0.047).

No significant correlation was established between treatment type – no treatment, symptomatic treatment – anticholinesterase drugs (anti-ChEs), prednisolone with / without anti-ChEs, prednisolone + azathioprine with / without anti-ChEs (ρ=0.07, p>0.05; ρ=0.06, p>0.05; ρ=0.04, p>0.05 and ρ=0.05, p>0.05, respectively).

Therefore, the work addresses the development of depression in patients with myasthenia gravis. The study confirmed the hypothesis of the severity of depression on the degree of clinical manifestations of myasthenia gravis. These findings reflect the results in other studies [9, 12].

In our study, the hypothesis about the effect of the duration of the disease on the development of depression was not confirmed: for example, when comparing the Beck score with the duration of the disease, statistically significant connections were not found. The above data do not coincide with the findings of several other studies. In the study [3] it is indicated that the development of depression is reliably associated with the duration of myasthenia gravis and the frequency of hospitalizations. The authors of other studies have come to similar conclusions [15].

In our opinion, it turned out to be an interesting fact that none of the 182 examined patients had active complaints of any manifestations of depression (tearfulness, sleep disturbance, apathy, sexual problems, etc.). At the same time, 139 (76.4%) patients from the total sample appeared to have depression when had been examined according to the Beck score. This suggests the need to evaluate the psycho-emotional state, in particular depression in patients with myasthenia gravis. It is important to bear in mind the significant effect of depression on somatic manifestations of chronic diseases in general, and depression in particular.

To date, the literature provides guidance on the effect of anticholinesterase, prednisolone and azathioprine on the development of depression [9, 10, 12, 13]. According to our study, this effect has not been confirmed. However, our study did not examine the relationship between doses of these drugs and the development of depression. This requires further study, because, for example, a dose-dependent effect of corticosteroid intake on the development of psycho-emotional changes has been established [10, 12].

In our study, reliable correlation relationships between antibody titers to AchR, MuSK, and depression have been found. The obtained data are contradictory, though. Yet, Suzuki Y.et al., 2011, also indicate a correlation between the presence of antibodies to AchR and the level of depression, but when conducting univariate logistic regression analysis of HF (odds ratio – OR) of depression in the presence of antibodies to AchR were HF (CI): 1.0 (1.0; 1.01), p=0.28 [9].

CONCLUSIONS

1. The severity of depression depends on the degree of clinical manifestations of myasthenia gravis regardless of the form of the disease.
2. The severity of depression correlates with the presence and titer of antibodies to AchR and MuSK.
3. There is no connection between the duration of myasthenia gravis and the severity of depression.
4. There are no relationships between the use of anticholinesterase drugs, prednisone, the combined use of prednisone with / without azathioprine with / without anticholinesterase drugs and the development of depression in patients with myasthenia gravis.

A conflict of interest. The authors note the absence of a conflict of interest.

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