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Clinical and demographic data and the significance of various dysfunctions and severity indicators in multiple sclerosis patients

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Introduction: Visual and oculomotor disorders are frequent manifestations of nervous system damage in multiple sclerosis. Multiple sclerosis is associated with an increased risk of falls, degeneration of sensory organization, and a possible increased reliance on vision for balance control.

The clinical picture of multiple sclerosis is characterized by numerous neurological symptoms, among which visual and oculomotor disorders occupy a significant place. This is because the consequences of inflammation, demyelination, and neurodegeneration often negatively affect both the afferent and efferent parts of visual function, significantly worsening the quality of life of patients with multiple sclerosis.

Objective: To determine the clinical and demographic characteristics, the significance of nervous system dysfunction and disability, the degree of visual and oculomotor impairment, severity of pain, fatigue, depression, and cognitive impairments, quality of life indicators in patients with multiple sclerosis and to identify the peculiarities of their course in terms of comorbidity.

Materials and methods: A total of 216 patients with various forms of multiple sclerosis were examined. Clinical-demographic data, paraclinical characteristics of nervous system dysfunction and disability, severity of pain, fatigue, depression, cognitive disorders and quality of life indicators were analyzed.

Patients were assessed using the Functional System Scale (FS), Expanded Disability Status Scale (EDSS), an extended neuropsychological examination.

The presence and duration of comorbid diseases were clinically determined through laboratory and instrumental studies, as well as examinations by other specialists (ophthalmologist, therapist, cardiologist, rheumatologist, urologist, and dentist).

Results: When conducting a study of patients with multiple sclerosis of the general sample, symptoms associated with pyramidal functions impairment were in 191 patients (88.4%), symptoms caused by the cerebellar functions impairment - in 178 patients (82.4%), symptoms caused by brainstem and cranial nerve dysfunction – in 161 patients (74.5%), symptoms associated with impaired sensitivity functions – in 169 patients (78.2%), symptoms due to pelvic disorders – in 187 patients (87.0%), symptoms caused by impaired visual functions – in 116 patients (53.7%), symptoms associated with impaired cerebral (mental) functions – in 184 patients (85.2%).

In total, visual disorders were recorded in 116 (53.7%) patients with multiple sclerosis, among them - in 46 (21.3%) patients of I group (without comorbidity) and in 70 (32.4%) patients of II group (with presence of comorbidity), and oculomotor disorders - in 168 (77.8%) patients with multiple sclerosis, among them - in 77 (35.6%) patients of group I (without comorbidity) and in 91 (42.1%) patients of group II (with presence of comorbidity).

In patients with multiple sclerosis, according to the data of the FS-3 FS scale (oculomotor disorders), the average indicators were as follows: group I - 1.4 ± 0.3; group II - 1.6 ± 0.3, and according to the FS-6 FS scale (visual disorders), the average indicators were as follows: group I - 0.8 ± 0.2, group II - 1.4 ± 0.3.

Conclusions: 1. The prevalence of visual disorders of patients with multiple sclerosis was 56.0%, and oculomotor disorders - 85.2%.

2. Oculomotor disorders were more widely represented in patients with multiple sclerosis, which, in our opinion, is associated with damage to the structures of the posterior longitudinal bundle, which is often affected in multiple sclerosis due to the "dissemination in space" characteristic of the disease.

3.It was found that in patients with multiple sclerosis visual disorders were most clearly correlated with the level of depression and cognitive impairment. Oculomotor disorders in patients with multiple sclerosis were most clearly correlated with levels of fatigue.

4. In the group of patients with multiple sclerosis with comorbid pathology, visual and oculomotor disorders were significantly more prevalent.

Key words: *multiple sclerosis; clinical and demographic characteristics; visual disorders; oculomotor disorders; severity of pain; severity of fatigue; severity of depression; severity of cognitive impairment; quality of life indicators; comorbidity*

Introduction

Multiple sclerosis (MS) is a degenerative disease of the nervous system, the basis of the pathological mechanisms of which is the process of progressive demyelinating damage, primarily of the central nervous system. The clinical picture of MS is characterized by a wide range of neurological symptoms, among which visual and oculomotor disorders occupy a significant place because the consequences of inflammation, demyelination, and neurodegeneration often negatively affect both the afferent and efferent parts of visual function, significantly worsening the quality of life of patients with MS [1, 2, 3, 4, 5].

Retrobulbar neuritis is often one of the earliest manifestations of MS. Visual disorders, or afferent visual abnormalities — including decreased visual acuity and contrast sensitivity, binocular vision defects, visual field disturbances, changes in color perception due to retrobulbar neuritis in MS are frequent symptoms of exacerbation, occurring in 14-50% of patients with MS [5, 6, 7], while 77% of patients have subclinical changes in visual function [4]. As a result of acute retrobulbar neuritis, central scotomas usually appear in the affected eye, which leads to a decrease in visual acuity and contrast sensitivity, as well as a narrowing of the field of vision [2, 3]. Jasse L. et al., 2013 [8] showed, that more than a third of patients with MS have persistent visual disturbances. Hemianopsia may also occur in patients with MS; the degree of recovery varies depending on the degree of initial disturbance of the field of vision [2].

Medical treatment of acute retrobulbar neuritis can shorten the time of recovery of visual functions, but ultimately does not affect the quality and completeness of recovery [8]. Although in the case of acute retrobulbar neuritis there are often quite effective courses of methylprednisolone pulse therapy, sometimes in combination with plasmapheresis, which can accelerate the recovery of vision in approximately 70% of MS patients [9], the results of the treatment of visual function disorders in MS are generally contradictory [10]. Some researchers believe that there is no procedure or method of treatment that can improve visual functions in general. This unsatisfied need for the treatment of visual disorders in MS requires the development of new treatment methods that have a neuroprotective effect and are able to restore impaired functions in patients with MS [3, 4, 5].

Oculomotor disorders (efferent visual abnormalities) are also symptoms in MS patients, and may occur temporarily or permanently, appearing in parallel with visual disturbances or independently of them. Oculomotor disorders are more common in patients with a progressive course of MS (compared with relapsing), may be an indicator of demyelinating damage to the structures of the posterior cranial fossa representing a more difficult neurological prognosis [2, 3, 4, 5]. Oculomotor deficiency is most often associated with MS with internuclear ophthalmoplegia, which leads to diplopia [2]. All types of nystagmus can occur in MS patients, along with saccadic eye movements, oscillopsia (immovable objects appear to patients as moving), blurred vision or its blurring, ocular dysmetria and gaze paresis [2, 5].

Low efficiency of in the treatment in terms of restoration of visual and oculomotor functions is observed in patients with MS in the presence of comorbid diseases, cognitive disorders, depressive disorders, fatigue and premorbid visual disorders [11, 12, 13, 14].

Objective: To determine clinical and demographic characteristics, significance of nervous system dysfunction and disability, degree of visual impairment, degree of oculomotor impairment, severity of pain, severity of fatigue, severity of depression, severity of cognitive impairment, quality of life indicators in patients with MS and to find out the peculiarities of their course in terms of comorbidity.

Materials and methods

Study participants

A total of 216 patients with MS were examined. The research was carried out at the Department of Neurology and Reflexotherapy of the Shupyk National Healthcare University of Ukraine. The research was conducted in accordance with the Helsinki Declaration of Human Rights (1964), the Council of Europe Convention "On Human Rights and Biomedicine" (1997), and current regulatory legal acts of Ukraine. Informed consent to participate in the examination and treatment was obtained from all patients. The research protocol was approved by the local ethics committee (Ethics Committee of the Shupyk National Healthcare University of Ukraine, minutes of the KE No. 9 dated October 1, 2012).

Inclusion criteria

The inclusion criterion was diagnosis of "multiple sclerosis" with indicators of the course of the disease, such as the frequency of clinically pronounced exacerbations and the rate of neurological deficit progression. The survey did not include patients with MS aged under 18 or over 65 years of age, as well as with a degree of disability of more than 5.5 points on the Expanded Disability Status Scale (EDSS). The criteria for excluding patients from observation were: refusal of the patient or his relatives to participate in the study; inability to be observed throughout the entire period.

216 patients with multiple sclerosis with various forms of course who underwent complex outpatient or inpatient treatment in the period from 2007 to 2016 were monitored. The diagnosis of "Multiple Sclerosis" was made in accordance with the updated criteria of McDonald (2005; 2010) [15, 16], and the accompanying pathology was recorded in the outpatient chart by the relevant specialist or detected during the examination or through a questionnaire. Due to the fact that the study was conducted in the period from 2007 to 2016, all patients were evaluated according to the McDonald criteria 2005 (for patients with MS who were included in the study in 2007-2010) while the 2010 criteria were used for MS patients enrolled between 2011 and 2016 for the diagnosis of multiple sclerosis. The 2017 revision of the McDonald criteria was not used in this study.

Group characteristics

All 216 patients with MS examined by us with different forms of the course, depending on the presence or absence of comorbid pathology, were divided into 2 groups: group I - patients without any concomitant

disease (109 patirents); group II- patients with one or more concomitant diseases (107 patients).

Group II consisted of 107 patients with MS, who at the time of examination had a clinically significant comorbid pathology, the data of which were revealed through a detailed survey of patients during an objective examination and analysis of medical records. At the same time, in group II 40 (18.5%) patients with MS had one comorbid pathology, 27 (12.5%) patients had two comorbid pathologies, 21 (9.7%) patients had three comorbid pathologies, and 19 (8.8%) patients had four or more comorbid pathologies.

The average age in the study group was 39.9 ± 9.7 years. The gender ratio (female/male) was approximately 7:4 (141 females/75 males), which confirms the data of modern researchers about the predominance of women among patients with MS. Regarding the marital status of patients with MS, married people prevailed in the study group - 60.7% (131: 85).

Among 216 patients, 96 (44.4%) with relapsing course of MS, the stage of exacerbation of the disease of various degrees of severity was registered, and in 43 (19.9%) patients – the stage of remission. Among patients with a progressive course of MS, 54 (25.0%) had a gradual deterioration of neurological deficit with slow dynamics, and 23 (10.7%) had a more rapid progression of symptoms.

Research design

A prospective comprehensive examination was conducted: clinical-neurological, neuropsychological, electrophysiological, ultrasound, MRI, laboratory examination of 216 patients (75 men and 141 women) aged 21 to 62 years (mean age 39.9 ± 9.7 years) diagnosed with MS according to the McDonald criteria (2005; 2010) with various forms of course (remitting and progressive) with a degree of disability ranging from 1 to 5.5 points on the EDSS scale (mean score 3.8 ± 1.3), with and without comorbid diseases, who underwent comprehensive outpatient or inpatient treatment at the clinical base of the Department of Neurology and Reflexotherapy (neurological departments of the Kyiv Regional Clinical Hospital) in the period from 2007 to 2016. The duration of observation for each patient was two years.

The clinical condition of the patients was described in accordance with the FS scale, and the degree of severity of neurological deficit - based on research data on the EDSS [17].

For the convenience of generalizing the symptoms of MS and adequately assessing the picture of the disease, the functional system lesion classification, proposed by J. F. Kurtzke, was used, which contains 7 sections for the assessment of: 1) pyramidal functions; 2) cerebellar functions; 3) brain stem and cranial nerves functions; 4) sensitivity functions; 5) bowel and bladder functions; 6) visual functions; 7) cerebral (mental) functions.

Each category is scored based on the severity of dysfunction, from less pronounced to more pronounced. The number of points is estimated for each scale separately (from FS-1 to FS-7). The use of this scale allows not only to obtain an in-depth clinical characteristic, but also to conduct dynamic monitoring of the course of the disease in patients with MS. We determined the level of disability using EDSS. During the neurological examination of patients with MS, we found the presence or absence of visual and oculomotor disorders, as well as in the anamnesis, after the diagnosis of multiple sclerosis, their nature was clarified. When determining the degree of FS-6 impairment (visual functions), the evaluation was performed on the more affected eye. Before determining the degree of damage to the FS-6, a mandatory ophthalmologic evaluation was performed, including measurement of visual acuity (with and without correction), fundus examination, and assessment of visual fields ***(Table 1)***.

Table 1. Assessment of visual and oculomotor functions according to the FS-6 and FS-3 scales by J. Kurtzke

Assessment of the degree of impaired functions in points	**Points**	**FS-3 Brain stem and cranial nerves functions**	**FS-6 (visual functions)**
	0	Norm	Norm
	1	Signs of dysfunction without disability	Scotoma with visual acuity (corrected) better than 0.6 (20/30); pallor of the temporal halves of the discs of the optic nerves
	2	Moderate nystagmus or other mild disorders	In the worse eye, scotoma and maximum visual acuity (corrected) from 0.6 (20/30) to 0.35 (20/59)
	3	Pronounced nystagmus, pronounced weakness of the oculomotor muscles or moderate impairment of other cranial nerves functions	In the worse eye, a large scotoma or moderate narrowing of the visual field, but the maximum visual acuity (with correction) from 0.35 (20/60) to 0.15-0.2 (20/99)
	4	Marked dysarthria or other significant impairments	In the worse eye, there is a marked narrowing of the field of vision and the maximum visual acuity (with correction) from 0.2 (20/100) to 0.1 (20/200); 3rd degree impairment plus maximum visual acuity in the better eye no more than 0.35 (20/60)
	5	Inability to swallow or speak	In the worse eye, the maximum visual acuity (with correction) is less than 0.1 (20/200); 4th degree impairment plus maximum visual acuity in the better eye no more than 0.35 (20/60)
	6	-	Disturbance of the 5th degree plus maximum visual acuity in the better eye no more than 0.35 (20/60)

A neuropsychological study was also conducted: manifestations of fatigue according Fatigue Severity Scale (FSS), pain according to the Visual Analogue Scale (VAS), level of depression according to the Beck Depression Inventory-II (BDI-II), cognitive function disorders according to the Mini-Mental-State-Examenations (MMSE) and indicators of quality of life were determined according to the SF-36.

Statistical analysis

For the purpose of statistical analysis of the study results, variational statistics methods were used to calculate the frequency characteristics of the studied indicators (%), average values (arithmetic mean – X) and estimate their variability (standard deviation – SD). To assess the statistical significance of clinical results and estimate the 95% confidence interval (CI), the mean error (m) was determined. In case of correspondence of the primary data to the parameters of the normal distribution, statistical analysis was performed using the Student's test, and in case of discrepancy – by generally accepted non-parametric methods: for quantitative indicators – the sum of Mann-Whitney ranks for two independent groups, Kruskal-Wallis rank analysis of variance for three independent groups, Dunnett's test (for comparison with the control group); for qualitative indicators – classical Pearson χ^2 -criterion with Yates' and Bonferroni corrections (for multiple comparisons), two-sided Fisher's exact criterion. To evaluate the data in dynamics, the Wilcoxon criterion (for comparing the indicators of one group) and the Kruskal-Wallis criterion (for comparing the indicators of several groups) were used. The assessment of the relationship between indicators was carried out by correlation analysis with Pearson's correlation coefficient. To compare observations before and after treatment, the Wilcoxon criterion was used for two dependent groups. The level of statistical significance was taken as $p < 0.05$. Statistical analysis was carried out using the standard SPSS software version 8.0.0 and Statistica 6.0.

Results

A total of 216 patients with MS were examined. An analysis of the entire patient cohort was performed. General clinical and demographic characteristics of patients are shown in ***Table 2***.

Clinical and demographic characteristics of patients with MS in connection with division into groups (comorbidity) are given in ***Table 3***.

Table 2. General clinical and demographic characteristics of patients

No.	Indicator	A general group of examined patients with MS (n = 216)
1	Average age, years (mean ± SD)	39.9 ± 9.7
2	Average age of onset of multiple sclerosis, years (mean ± SD)	28.7 ± 7.6
3	Duration of the disease, years (mean ± SD)	6.4 ± 3.5
4	Gender ratio (women / men, %)	62.3 / 37.7
5	Marital status (married, %)	60.7
6	Degree of disability for the EDSS, %	
	light	46.8
	average	53.2
	severe	-
	group average, points (mean ± SD)	3.8 ± 1.3
Type of course of multiple sclerosis		
7	Remitting, %	64.4
	Relapsing-remitting MS, %	42.6
	Relapsing-progressive MS, %	21.8
8	Progressive, %	35.6
	Primary progressive MS, %	20.8
	Secondary progressive MS, %	14.8
9	The presence of visual disorders, abs. (%)	116 (53.7)
10	The presence of oculomotor disorders, abs. (%)	168 (77.8)

Table 3. Clinical and demographic characteristics of patients with MS in connection with division into groups

No.	Indicator	A general group of examined patients with MS (n = 216)	
		group I (n = 109)	group II (n = 107)
1	Average age, years (mean ± SD)	36.9 ± 9.3	42.3 ± 10.4
2	Average age of onset of multiple sclerosis, years (mean ± SD)	28.4 ± 7.3	29.1 ± 7.9
3	Duration of the disease, years (mean ± SD)	5.3 ± 1.9	7.4 ± 2.0
4	Gender ratio (women/men, %)	66.1 / 33.9	64.5 / 35.5
5	Marital status (married, %)	57.8	63.5
6	Degree of disability by the EDSS, %		
	light	51.4	42.1
	average	48.6	57.9
	severe	-	-
	group average, score (mean ± SD)	3.4 ± 1,2	4.3 ± 1.4
7	VAS pain assessment, score (mean ± SD)	3.1 ± 1.3	4.8 ± 1.6
8	FSS fatigue assessment, score (mean ± SD)	3.3 ± 0.9	4.5 ± 1.3
9	Assessment of depression according to the Beck Depression Inventory-II (BDI-II), points (mean±SD)	11.5 ± 1.6	16.1 ± 1.9
9	Assessment of cognitive functions, (MMSE), score (mean ± SD)	27.93 ± 1.4	25.12 ± 2.3
10	Assessment of quality of life, SF-36, generalized indicators, scores (mean± SD)	PCS 43.1 ± 13.7 MCS 47.8 ± 12.5	PCS 32.2 ± 16.8 MCS 38.7± 11.5
11	The presence of visual disorders, abs. (%)	46 (21.3)	70 (32.4)
12	The presence of oculomotor disorders, abs. (%)	77 (35.6)	91 (42.1)

Note. PCS – physical component of health, MCS – mental component of health.

Ophthalmological examination revealed a decrease in visual acuity in 95 (44.0%) patients, visual field disturbances in 72 (33.3%), and change in color perception in 29 (13.4%). In 87 (40.3%) patients there was pallor of the temporal halves of the discs of the optic nerves. In total, visual disturbances occurred in 116 (53.7%) patients with MS of both groups, among them in group I - 46 (21.3%) patients, while in group II - 70 (32.4%). At the same time, in patients with MS according to the data of the FS-6 FS scale (visual disorders), the average indicators were as follows: group I - 0.8 ± 0.2; group II - 1.4 ± 0.3; and according to the severity of visual disturbances, the gradations were as follows: group I: 0 points – 63 (29.2%), 1 point – 21 (9.7%), 2 points – 14 (6.5%), 3 points – 11(5.1%); group II: 0 points – 37 (17.1%), 1 point – 30 (13.9%), 2 points – 18 (8.3%), 3 points – 16 (7.4%), 4 points – 6 (2.8%). According to the data of the FS-3 FS scale (oculomotor disorders), the average indicators were as follows: group I - 1,4 ± 0,3; group II - 1,6 ± 0,3; and according to the severity of visual disturbances, the gradations were as follows: group I: 0 points – 32 (14.8%), 1 point – 30 (13.9%), 2 points – 29 (13.4%), 3 points – 18 (8.3%); group II: 0 points – 16 (7.4%), 1 point – 40 (18.5%), 2 points – 32 (14.8%), 3 points – 19 (8.8%) ***(Table 4)***.

During the clinical and neurological examination, the presence of complaints of diplopia was recorded in 39 (18.1%) patients with MS, blurred vision or its clouding - in 63 (29.2%) patients.

Oculomotor deficiency was also manifested by vertical or horizontal nystagmus - in 117 (54.2%) patients, convergence and accommodation insufficiency - in 125 (57.9%) patients, uncoordinated movements of the eyeballs - in 48 (22.2%) patients, disparity eyeballs vertically (or horizontally) – in 29 (13.4%) patients, saccades – in 72 (33.3%) patients, oscillopsia – in 8 (3.7%) patients, eye dysmetria – in 10 (4.6%) patients, gaze paresis - in 6 (2.8%) patients. In total, oculomotor disorders occurred in 168 (77.8%) patients with multiple sclerosis of both groups, among them in group I - in 77 (35.6%) patients, while in group II - in 91 (42.1%) patients.

The average level of prevalence of neurological symptoms in the patients with multiple sclerosis, caused by dysfunction of other cranial nerves brain stem, was as follows: 129 patients (59.7%).

Involvement of the trigeminal nerve was recorded in 63 patients (29.2%), including paresthesias and/or dysesthesias in the facial area (36 patients, 16.7%), odontogenic facial pain (10 patients, 4.6%), trigeminal neuralgia (7 patients, 3.2%), trigeminal sensory neuropathy (3 patients, 1.4%), arthrogenic facial pain due to temporomandibular joint arthropathy (7 patients, 3.2%).

Facial nerve was involved in 66 patients (30.6%), which included myofascial facial pain (4 patients, 1.9%), xerostomia (dryness in the mouth) (37 patients, 17.1%), facial paresis (29 patients, 13.4%).

We performed an analysis of neurological disorders in the debut of the disease ***(Table 5)***: in 171 (79.2%) patients, the debut of MS was monosymptomatic, and in 45 (20.8%) patients, multifocal symptoms were detected as the first manifestations of the disease.

A predominance of pyramidal motor disorders (in the form of pyramidal insufficiency, central para-, mono-, hemi-, paraparesis of one degree or another) was established in the debut of MS - in 32 (14.8%) patients, visual disorders - in 36 (16.7%), oculomotor disorders - in 47 (21.8%) and polysymptomatic onset of MS - in 45 (20.8%) patients.

Table 4. Analysis of visual and oculomotor disorders in patients with MS according to data from the FS-3 and FS-6 scales by J. Kurtzke

Groups of patients with multiple sclerosis	Average indicators on the FS-3 and FS-6 scales (mean ± standard deviation)		Characteristics of the point assessment of the degree of impaired functional systems FS-3 and FS-6	
	FS-3 (mean ± SD)	FS-6 (mean ± SD)	FS-3, abs. (%)	FS-6, abs. (%)
group I (n = 109)	1.4 ± 0.3	0.8 ± 0.2	0 points – 32 (14.8)	0 points – 63 (29.2)
			1 point – 30 (13.9)	1 point – 21 (9.7)
			2 points – 29 (13.4)	2 points – 14 (6.5)
			3 points – 18 (8.3)	3 points – 11 (5.1)
group II (n = 107)	1.6 ± 0.3	1.4 ± 0.3	0 points – 16 (7.4)	0 points – 37 (17.1)
			1 point – 40 (18.5)	1 point – 30 (13.9)
			2 points – 32 (14.8)	2 points – 18 (8.3)
			3 points – 19 (8.8)	3 points – 16 (7.4)

Table 5. Analysis of symptoms of debut in patients with MS

Debut symptoms of MS	Number of patients with MS (abs.,%)		
	group I (n = 109), abs. (%)	group II (n=107), abs. (%)	Total (n=216), abs. (%)
Pyramidal disturbances	15(6.9)	17 (7.9)	32 (14.8)
Visual disorders	17 (7.9)	19 (8.8)	36 (16.7)
Oculomotor disorders	22(10.2)	25(11.6)	47 (21.8)
Coordination disorders	4 (1.9)	3 (1.4)	7 (3.2)
Vestibular disorders	3 (1.4)	2 (0.9)	5 (2.3)
Disorders of general sensitivity	5 (2.3)	7 (3.2)	12 (5.6)
Mild facial paresis	7 (3.2)	8 (3.7)	15 (6.9)
Trigeminal neuralgia	-	6 (2.8)	6 (2.8)
Psychoemotional disorders	2 (0.9)	4 (1.9)	6 (2.8)
Pelvic disorders	2 (0.9)	3 (1.4)	5 (2.3)
Polysymptomatic onset	32 (14.8)	13 (6.0)	45 (20.8)

Visual disorders were usually manifested by the clinic of retrobulbar neuritis with a pronounced decrease in visual acuity, disturbances in visual fields and changes in the fundus, and, as a rule, subsequent recovery to one degree or another. In the absolute majority of cases, visual problems were unilateral. In 21 (9.7 %) patients, the onset occurred with damage to other cranial nerves.

Thus, in group I of patients with MS, the disease debuted most frequently with oculomotor disorders, polysymptomatic onset, visual disorders, and pyramidal disorders, while in group II of patients with MS, debut symptoms pyramidal disorders, oculomotor disorders, visual disorders, mild facial paresis.

It should also be noted that in patients of both groups of MS with a remitting course, visual disturbances (23.7%) and polysymptomatic onset (18.8%) were the most frequent in the debut. In patients with a progressive course of MS of both groups, at the onset of the disease, movement disorders were more often observed (27.03%), and to a lesser extent - oculomotor disorders (5.8%) and sensory disorders (5.3%).

Furthermore, it was found that visual and oculomotor symptoms, although responsive to pharmacological treatment—particularly corticosteroid pulse therapy—often leave residual effects. These may include incomplete recovery of visual acuity or visual fields, or persistent symptoms such as facial pain or numbness in the orbital region, even when other exacerbation-related symptoms of MS have fully resolved. The main characteristic feature of MS, described by J. M. Charcot, there is " scattering in time", that is, in the future there is a possibility of new exacerbations of the disease. These exacerbations can include renewed episodes of retrobulbar neuritis, full or partial recurrence of visual disturbances and pain symptoms in the orbit. Taking into account the characteristic features of the course of multiple sclerosis, such as the presence of the syndrome of "instability of clinical manifestations" as a result of adverse environmental influences (primarily, a general or even local increase in temperature: the so-called "hot bath symptom", alimentary factors, etc.), blocking of nerve impulse conduction in partially demyelinated nerve conductors may periodically occur due to shortening of the action potential with the appearance of transient or more persistent symptoms of decreased vision, impaired perception of colors, visual fields defects, orbital pain) even without exacerbation of multiple sclerosis.

It was also possible to show that in older age groups of patients with multiple sclerosis (45 and > years), color perception disorders develop almost twice as often as in younger patients.

When analyzing the correlations between the severity of visual and oculomotor disorders and the FSS, BDI-II, VAS, MSSE and SF-36 indicators, we were able to establish that the closest direct correlations are observed between visual disorders and depression indicators according to the BDI-II (r= 0.28 – group I; r= -0.36 – group II, $p<0.05$) and cognitive functions according to MSSE data (r= 0.21 – group I; r= -0.29 – group II) $p<0.05$), as well as between oculomotor disorders and the degree of fatigue according to FSS data (r= 0.34 – group I; r= -0.56 –group II, $p<0.05$).

Thus, it is clear that the combination of physical, cognitive and psychological symptoms in multiple sclerosis can make a negative contribution to the process of deepening the decrease in the patient's functional activity.

The results of the influence of various types of comorbid pathology in patients with MS on the severity of visual and oculomotor disorders were as follows: the most pronounced visual disorders (in relation to the average of the group II) were observed in patients with gastroenterological comorbidity (1.9±0.4; $p <0.01$) and cerebrovascular comorbidity (2.1 ± 0.5; $p<0.05$); while the most pronounced oculomotor disorders (in relation to the average of the group II) occurred in patients with gastroenterological comorbidity (2.0 ± 0.3; $p<0.05$), and under conditions of polycomorbidity: three concomitant diseases (2.3 ± 0.8; $p<0.05$), four or more concomitant diseases (2.5 ± 0.9; $p<0.05$). Conversely, the least pronounced visual and oculomotor disorders were observed in patients with MS autoimmune comorbidity (1.2±0.3; $p<0.05$).

Considering the fact that special difficulties in stopping visual and oculomotor disorders arise in conditions of comorbidity with MS with diseases of the stomach and hepatobiliary system, cerebrovascular diseases, as well as in conditions of deepening manifestations of fatigue, depression and cognitive disorders, given the frequent residual symptoms of retrobulbar neuritis, the insufficient effectiveness of their drug treatment and stopping of oculomotor disorders, and the possibility of a partial or complete return of the symptoms of exacerbation in the future, it is advisable to use acupuncture methods as part of the complex treatment of MS, in particular, the method of scalp acupuncture with an effect on the areas of the scalp and corporal acupuncture points, capable of enhance the effects of scalp acupuncture.

Discussion

Visual disorders (afferent visual abnormalities) and oculomotor disorders (efferent visual abnormalities) are frequent symptoms in MS patients, and can occur temporarily or permanently, appear parallel to other symptoms of the disease, or independently of them [18, 19, 20, 21, 22].

MS requires complex treatment, both pathogenetic and symptomatic, which is not always sufficiently effective [5, 22, 23, 24]. Although in the case of acute retrobulbar neuritis, courses of pulse therapy with methylprednisolone are often quite effective, sometimes in combination with plasmapheresis, which can accelerate the recovery of vision in approximately 70% of patients [10], the results of treatment of visual disturbances in MS are generally contradictory [5].

In patients with MS with retrobulbar neuritis, even with the condition of complete regression of exacerbation of MS, in the future there is a possibility of a partial return of symptoms of exacerbation (visual, pain) due to incomplete remyelination and negative effects of environmental factors or a new exacerbation [25]. This requires the development of new treatment methods that would have a neuroprotective effect and would be able to restore impaired functions in patients with MS [5, 25, 26]. One of these methods is scalp acupuncture, which is advisable to use as part of the complex treatment of MS patients with visual and oculomotor disorders and pain of various localization [5, 25, 26]. At the same time, individualized acupuncture treatment is necessary, and

in this case it is advisable to use acupuncture diagnostic methods [27].

Researchers indicate that they want to adapt acupuncture diagnostic methods (in particular, syndromic diagnostic methods of traditional Chinese medicine) to specific lesions in MS and determine algorithms for their diagnosis [4, 5, 19, 27]. There is also an opinion that it is advisable to conduct larger studies to assess the effectiveness of acupuncture diagnostic methods for specific lesions in MS, as well as to study the mechanisms of therapeutic influence of acupuncture methods for specific lesions in MS.

So, in one work [25] it is described that special difficulties in stopping visual disturbances and painful symptoms of the orbital area arose under the conditions of comorbidity of MS with diseases of the stomach and hepatobiliary system. The use of acupuncture techniques based on scalp acupuncture and its potentiation with the help of acupuncture points of regular acupuncture meridians and extra-meridian acupuncture points in a complex of therapeutic measures in patients with visual disturbances and facial pain due to retrobulbar neuritis in MS patients made it possible to better treat the above-mentioned disorders with therapy of exacerbation and stop them if they are residual symptoms of exacerbation or occur outside the exacerbation of MS. Another work [4] deals with the treatment of visual and oculomotor disorders in patients with MS using scalp acupuncture.

Thus, it can be noted that acupuncture treatment is a promising non-medicinal remedy for stopping visual and oculomotor disorders in MS (which should be used in a complex of therapeutic measures).

Conclusions

1. The prevalence of visual disorders of patients with MS was 56.0%, and oculomotor disorders - 85.2%.

2. Oculomotor disorders were more widely represented in patients with MS, which, in our opinion, is associated with damage to the structures of the posterior longitudinal bundle, which is often affected in MS due to the "scattering in space" characteristic of the disease.

3.It was found that in patients with multiple sclerosis visual disorders were most clearly correlated with the level of depression and cognitive impairment. Oculomotor disorders in patients with MS were most clearly correlated with levels of fatigue.

4. In the group of patients with MS with comorbid pathology, visual and oculomotor disorders were significantly more prevalent.

Disclosure

Conflict of Interest

The authors declare no conflict of interest.

Ethical Standards

All procedures performed on patients during the study adhered to the ethical standards of the institutional and national ethics committees, as well as the 1964 Helsinki Declaration and its subsequent amendments or comparable ethical standards.

Informed Consent

Written informed consent was obtained from all patients.

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