Оригінальні дослідження

CONNECTION BETWEEN COMORBID PRIMARY HEADACHE, DEPRESSION AND ANXIETY IN PATIENTS WITH MULTIPLE SCLEROSIS

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SUMMARY. Multiple sclerosis (MS) is a chronic autoimmune disorder of central nervous system that affects young people and progresses to physical disability. Among patient with MS risk of excessive anxiety and depression is quite common. One of the frequent comorbidities of MS is primary comorbid headache. Depression and anxiety might be more prominent on patients with pain comorbidity of MS.

The aim – to show the prevalence and frequency of depression and anxiety in a population of patients with MS, with special attention to the group of patients with primary comorbid headache.

Material and Methods. MS was confirmed according to the McDonald criteria 2017. Questionnaires Beck Depression Inventory (BDI) for assessment of depression and The Spielberger State-Trait Anxiety Inventory in Hanin`s interpretation (STAI), version for evaluation of reactive anxiety were used.

Results. 130 patients with MS were examined with disease duration 8.63±7.49 years. 36.2 % of males (n=47) and 63.8 % of females (n=83) were included. Average score of patients with MS was 40.22±8.89 points that indicates moderate reactive anxiety. BDI score accounted for 14.15±7.58 points that interpretates as mild-to-moderate depression. Patients with MS and comorbid primary headache received the average points of the STAI in Hanin's interpretation – 42.41±7.49 (moderate anxiety); patients with MS without comorbid primary headache – 37.42±9.31 (low or moderate anxiety), but generally this difference did not show statistical significance (p=0.39). Among MS course scores of anxiety was similar between groups, depression score was the highest in group with primary progressive MS (PPMS).

Conclusion. The average score of anxiety and depression showed moderate severity among patients with MS. There were not found significance between patients with primary headache comorbidity and without it, although scores between course disease subgroups showed higher points in patients with comorbid primary headache.

KEY WORDS: multiple sclerosis; headache; comorbidity; anxiety; depression; pain syndrome.

Introduction. Multiple sclerosis (MS) is a chronic autoimmune demyelinating disease of the central nervous system [1, 2]. This is the most common neuro-immunological disease that affects and over time leads to the disability of young people [1, 3, 4]. One of the frequent comorbid conditions in multiple sclerosis is headache [2]. It is known that comorbidity can affect the course of the disease and contribute to the development of depression or anxiety [5]. There is evidence that half of patients with multiple sclerosis in the population will have signs of low mood, which may meet the criteria for depression [1, 5, 6]. Moreover, a group of researchers such as Giordano et al. found that 11 % of patients were diagnosed with depression at the onset of the disease [7]. There is also a noticeable connection with the assessment according to the main scale for measuring the degree of disability Expanded Disability Status Scale (EDSS). With a higher score, there is a higher risk of anxiety-depressive disorder [8], but some researchers still do not consider it unambiguous. [9, 10]. Anxiety is also a common symptom among MS patients. In the general healthy population, anxiety occurs in 29.6 %, and in patients with multiple sclerosis – 35.6 % [1, 5]. Of course, depression and anxiety have a negative impact on the quality of life [11]. In particular, in the presence of a comorbid primary headache, such symptoms will worsen the intensity of the pain syndrome

and, of course, the severity of the course of the underlying disease [12].

The aim of the study – to show the prevalence and frequency of depression and anxiety in a population of patients with MS, with special attention to the group of patients with primary comorbid headache.

Material and Methods. 130 patients with MS were examined in the Department of Neurology in Vinnytsia National Pirogov Memorial Medical University. Diagnosis Multiple sclerosis was confirmed according to the McDonald criteria 2017. Primary headache was classified according to the International classification of headache disorders 3 (ICHD-3). 2 clinical groups were created – MS+comorbid primary headache and MS without comorbid primary headache. Also we structured patients regarding to the course of MS – relapsing-remitting MS (RRMS) and progressive MS (included primary progressive MS (PPMS) and secondary progressive MS (SPMS)). Questionnaires Beck Depression Inventory (BDI) for assessment of depression and The Spielberger State-Trait Anxiety Inventory in Hanin`s interpretation (STAI), version for evaluation of reactive anxiety were used. The STAI in Hanin's interpretation for reactive anxiety has 20 questions, the answer to each of which is evaluated in the corresponding points. The total score can range from 20 to 80 points. The high-

er the score, the higher the level of anxiety, respectively. We interpreted the obtained data according to the following ratings: "no or low anxiety" (20–37), "moderate anxiety" (38–44), and "high anxiety" (45–80) [13]. BDI includes 21 questions. Each answer is scored from 0 to 3 points. Received points of less than 10 = no or minimal depression, 10–18 = mild-to-moderate depression, 19–29 = moderate-to-severe depression, 30+ = severe depression [13]. The research was carried out into account the principles of the Helsinki Declaration of the World Medical Association "Ethical Principles of Medical Research with the participation of a person as an object of research".

Statistical data was analyzed by SPSS statistics program, version 26.0.0 with elements of descriptive statistical methods, assessment of reliability according to the Student`s criterion. The level of significance was taken to be equal to 0.05.

Results and Discussion. 130 patients with MS were proposed to answer questionnaires regarding low mood and anxiety. Average of MS duration in our study accounted for 8.63±7.49 years. Gender differentiation was the next – 36.2 % of males (n=47) and 63.8 % of females (n=83). Demographics and disease duration divided into course of MS is presented in Table 1.

Table 1. Demographics of patients in the study

Demographic data	RRMS	PPMS	SPMS
% of patients with different MS course	76 % (n=98)	6 % (n=8)	18 % (n=24)
Age (Y)	32.38±7.06	51.75±3.53	46.25±7.45
Gender	Male – 33.6 % (n=33) Female – 66.3 % (n=65)	Male – 62.5 % (n=5) Female – 37.5 % (n=3)	Male – 33.3% (n=8) Female –66.6 % (n=24)
Disease duration (Y)	6.39±4.08	14.5±10.95	15.94±8.31

Notes: MS – multiple sclerosis; RRMS- relapsing-remitting multiple sclerosis; PPMS – primary progressive multiple sclerosis; SPMS – secondary progressive multiple sclerosis.

Average score of examined patients with MS in The STAI in Hanin's interpretation was 40.22±8.89 points that indicates moderate reactive anxiety. BDI score accounted for 14.15±7.58 points that interpretates as mild-to-moderate depression. Patients with MS and comorbid primary headache received the average points of the STAI in Hanin's interpretation – 42.41±7.49 (moderate anxiety) in comparison with patients with MS without comorbid primary headache – 37.42±9.31 (low or moderate anxiety). Despite a slightly higher indicator in patients with comorbidity, generally this difference did not show statistical significance (p=0.39). The same was repeated for evaluation of depression scale. Result of BDI in general group of patients with comorbid primary headache accounted for 14.94±6.80 that indicated mild to moderate depression. This data was compared to score of MS patients without primary comorbid headache who received 13.14±8.43 points. As in case with anxiety no statistical significance was found (p=0.848). Next step in our study included division of examined

patients with MS into groups of different MS courses and presence of comorbid primary headache. Group 1 included RRMS patients with subgroups 1 and 2 with comorbid primary headache and without it respectively. Group 2 included patients with PPMS with subgroups 3 and 4 with comorbid primary headache and without it respectively. Group 3 included patients with subgroups 5 and 6 with comorbid primary headache and without it respectively. General score of the STAI in Hanin's interpretation for Group 1 is 40.15±8.71 points, Group 2 – 41.25±6.73 points, Group 3 – 40.16±10.44 points that confirmed moderate anxiety. Evaluation of groups by BDI revealed the next results: group 1 – 13.61±7.57 points; group 2 – 16.20±7.71 points; group 3 – 13.22±7.91 points that showed mild-to-moderate depression. Table 2 demonstrates received data from questionnaires.

Depression and anxiety are important and quite common problems among patients with MS as a comorbidity or symptom of MS and should be adequately treated and screened [1, 14, 15]. Special attention

Table 2. Average results of depression and anxiety scores among subgroups of patients with MS

Subgroups	BDI	STAI in Hanin's interpretation
Subgroup 1	14.92±6.61	41.6±6.71
Subgroup 2	12.25±8.37	38.29±10.45
Subgroup 3	16.81±6.66	42.72±8.87
Subgroup 4	15.69±8.74	38.0±11.49
Subgroup 5	13.0±7.15	40.0±6.0
Subgroup 6	19.5±6.36	45.0±9.89

Notes: BDI – Beck Depression Inventory; STAI – The Spielberger State – Trait Anxiety Inventory in Hanin's interpretation.

should be paid to such disturbances in the mental sphere in patients with comorbidity and MS, especially comorbid pain syndrome, for example, primary headache. Our study compares different types of MS courses with the presence of comorbid primary headache. According to their own observations, almost every second patient felt some degree of anxiety. In our analysis, anxiety was not significantly associated with comorbid primary comorbid headache. Although MS patients had more anxiety symptoms than depression, there was no significant association with comorbid headache symptoms. However, the literature found a weak but significant association between the number of comorbidities and the severity of anxiety. In a study by Janssens et al. of 101 patients with newly diagnosed MS and their partners found higher levels of anxiety in patients with more functional limitations [16]. In a study of more than 7,000 MS patients in the United Kingdom, female patients with RRMS were more likely to report higher levels of anxiety than patients with PPRS or SPMS, whereas in men, no significant association was found between anxiety and type of MS [62]. In contrast, in a meta-analysis of four different studies, Peres et al. there was no significant difference between the level of anxiety or depression and the course of MS [17]. Our data showed no difference in the course of MS and primary comorbid headache depending on the level of anxiety or depression in patients with MS. Levels of anxiety were almost the same among different types of MS, but the level of depression was highest in patients with PMS. An interesting fact was described in one study [1, 18], where 44.5 % of 742 patients with MS had either a diagnosis of depression or relevant symptoms of depression, but only 14.2 % of these patients were taking antidepressants. We did not look in this direction, but this may be a future avenue for further research, as this finding demonstrates that depression is often overlooked and undertreated in clinical practice among MS patients.

Conclusion. In our study we compared patients with MS and comorbid primary headache and without it depending on the level of anxiety and depression. As literature described, it was confirmed in our research that there was no statistic difference between these two groups. Despite that, we compared subgroups of patients with different MS course and presence or absence of comorbid primary headache. Results showed slight difference between means of different subgroups with increased points of anxiety and depression in subpopulation with headache comorbidity. Among three courses of MS general score of anxiety was generally similar between all group and showed moderate anxiety. In cast of the depression assessment it showed "mild-to-moderate" severity among patient with MS with the highest score in patients with PPMS.

Prospects for further research. Mental health impairment of patients of MS is relevant topic in finding the best approach in management of patients with MS. It might have an impact on quality of life of patients. The direction of future research could be concentrated on comparisons of quality of life of patients with comorbid primary headache and MS with increased levels of anxiety and depression with inclusion of clinical assessment of disability of patients with MS.

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ЗВ'ЯЗОК МІЖ КОМОРБІДНИМ ПЕРВИННИМ ГОЛОВНИ БОЛЕМ, ТРИВОГОЮ ТА ДЕПРЕСІЄЮ СЕРЕД ПАЦІЄНТІВ З РОЗСІЯНИМ (МНОЖИННИМ) СКЛЕРОЗОМ

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РЕЗЮМЕ. Розсіяний (множинний) склероз (РС) – це хронічне автоімунне захворювання центральної нервової системи, яке вражає молодих людей і прогресує до фізичної інвалідності. Серед пацієнтів з РС ризик надмірної тривоги та депресії досить поширений. Одним із частих супутніх захворювань РС є первинний коморбідний головний біль. Депресія та тривога можуть бути більш помітними у пацієнтів із супутньою патологією та РС.

Мета дослідження – показати поширеність і частоту депресії та тривоги в популяції пацієнтів з РС, приділяючи особливу увагу групі пацієнтів із первинним коморбідним головним болем.

Матеріал і методи. РС підтверджено відповідно до критеріїв McDonald 2017. Опитувальники депресії Бека (Beck Depression Inventory (BDI)) та шкала Спілбергера в модифікації Ханіна (The Spielberger State-Trait Anxiety Inventory in Hanin`s interpretation (STAI)), версія для оцінки реактивної тривоги було використано.

Результати. Обстежено 130 пацієнтів з РС із тривалістю захворювання (8,63±7,49) років. Було включено 36,2 % чоловіків (n=47) і 63,8 % жінок (n=83). Отриманий бал шкали тривожності серед пацієнтів з РС складав (40,22±8,89) балів, що свідчить про помірну реактивну тривожність. Індекс депресії склав (14,15±7,58) балів, що трактується як легка чи помірна депресія. Пацієнти з РС та коморбідним первинним головним болем отримали середні бали за шкалою тривожності – 42,41±7,49 (помірна тривожність); пацієнти з РС без коморбідного первинного головного болю – 37,42±9,31 (низька або помірна тривожність), але в цілому ця різниця не мала статистичної значущості (p=0,39). Загалом рівень тривоги при різних типах перебігу РС був подібним між групами, а от показник депресії був найвищим у групі з первинно-прогресуючим РС.

Висновок. Середній бал тривоги та депресії показав помірну тяжкість серед пацієнтів з РС. Не було виявлено значущості між пацієнтами з головним болем та без нього, хоча показники між підгрупами захворювання показали вищі бали у пацієнтів із коморбідним первинним головним болем.

КЛЮЧОВІ СЛОВА: розсіяний склероз; головний біль; коморбідність; тривога; депресія; больовий синдром.