

STRUCTURE OF ANXIETY DISORDERS IN PATIENTS WITH CHRONIC MIGRAINE AND ABDOMINAL OBESITY

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Introduction. In Ukraine, on average, 30 % of people are obese and 25 % are overweight. In parallel with the increase in the number of overweight patients, the percentage of people with migraine is increasing. The prevalence of migraine is high, it affects 12-15 % of the population. Both diseases negatively affect not only the function of internal organs, but also the nervous-psychological state of patients, leading to anxiety and depressive disorders.

The aim of the study was to analyze the features of the structure of anxiety disorders in obese patients with chronic migraine.

Materials and methods: 180 patients (90 women and 90 men) were examined and divided into two clinical groups: 1st group – 60 persons with chronic migraine with an average BMI=23.5.8±1.10 kg/m²; 2nd group – 60 obese patients with chronic migraine, BMI=34.6±1.42 kg/m². The control group consisted of 60 patients without a headache and with average BMI=19.5±0.7 kg/m². The ICHD-3 criteria were used to diagnose migraine. The DSM-5 criteria were used to diagnose anxiety disorders. The patient's level of anxiety was measured using Taylor Manifest Anxiety Scale (TMAS). Statistical processing was performed using dispersion and correlation analysis.

Results: Phobic anxiety disorders were in 1.5 times more common in 2nd group patients ($\chi^2=9.81$, $p<0.001$) than in 1st group patients; panic disorder was in 1.8 times more frequent in 2nd group ($\chi^2= 11.99$, $p<0.001$) than in the 1st group, generalized anxiety disorder was in 2 times ($\chi^2=13.08$, $p<0.0001$) less common in patients with chronic migraine than in comorbid patients. The total number of patients with anxiety disorders in patients with chronic migraine on the background of abdominal obesity was twice folds higher ($\chi^2=20.93$, $p=0.00001$) than in 1st group patients.

Conclusions: the presence of concomitant abdominal obesity in patients with chronic migraine, not only increases the total number of anxiety disorders, but also affects their structure. Therefore, in addition to basic anti-migraine therapy, non-medicinal therapy in the form of a balanced diet, an individual exercise program and 10-12 sessions of cognitive-behavioral therapy (CBT) should be supplemented for the treatment of such patients.

Key words: migraine, obesity, body mass index, anxiety disorders, triggers

INTRODUCTION

No other disease people get sick as often as obesity. According to the latest WHO estimates, more than 1 billion people in the world are overweight [1]. This problem is relevant regardless of social and professional affiliation, area of residence, age and gender. In economically developed countries, almost 50 % of the population is overweight, of which 30 % are obese [2, 3]. In Ukraine, on average, 30 % of people of working age are obese and 25 % are overweight. The number of obese children and adolescents is increasing every year also. WHO sees obesity as a global epidemic reaching millions

of people. Obese people are prone to many diseases. The relationship between obesity and such life-threatening diseases as type 2 diabetes mellitus, arterial hypertension, atherosclerosis, some types of tumours, reproductive disorders, gastrointestinal and musculoskeletal diseases has been absolutely proven [4, 5].

The prevalence of migraine is high, affecting 12-15 % of the population [6, 7]. A quarter of the world's population has experienced a migraine attack at least once in their lifetime. WHO experts suggest that in the future the incidence of migraine will increase. The pathogenesis of migraine is unclear. The trigeminovascular system is

considered to be the anatomical and physiological substrate from which nociceptive transmission originates and yields the perception of migraine pain. A peripheral origin of migraine attacks is believed to involve direct or indirect activation and sensitization of first order trigeminovascular neurons. Indirect effects are likely mediated by dilation of intracranial arteries and corresponding efflux of potassium, which yields mechanical and chemical stimulation that activates and sensitizes the perivascular trigeminal

nerve endings. A central origin of migraine attacks is hypothesized also to involve cortical spreading depression, hypothalamic activation, and/or brain stem activation (fig.1). Cortical spreading depression is widely regarded as the physiological substrate underlying migraine aura- It is characterized by a self-propagating wave of extensive depolarization across the cerebral cortex which disrupts ionic gradients and is followed by cerebral hypoperfusion [8,9, 10].

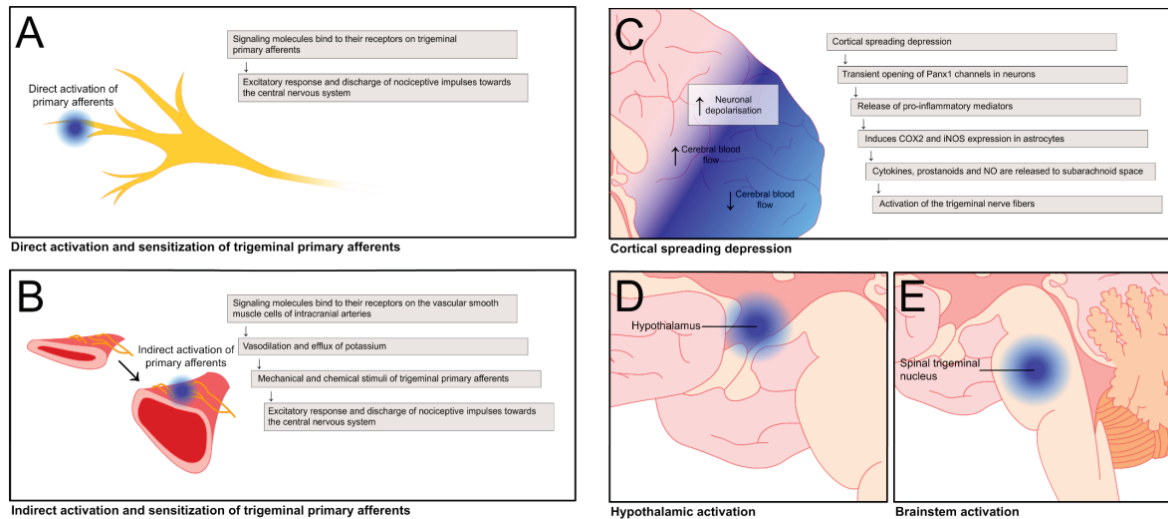


Fig. 1. Possible mechanisms of migraine attack [8]

Randomized trials demonstrate that patients with episodic headache and obesity have a 5-fold higher risk of chronic migraine. Obesity is the background for migraines and risk correlates with weight gain, particularly in those of reproductive age. The American cohort study involved 15.105 people aged 35 to 74 years. As a result of the study, scientists identified a statistically significant association between daily migraine and obesity (odds ratio 1.86; 95 % confidence interval: 1.12-3.09). The presence of abdominal obesity alone did not demonstrate such an association, but the association between daily migraine and obesity in general remained pronounced in the analysis in the absence of the diagnosis of abdominal obesity, especially among 35-49 years of age [11].

Both diseases have a negative impact not only on the function of the internal organs and systems of the body, but also on the neuropsychiatric state of patients. Obesity can lead to anxiety disorders in different ways. For example, weight-related discrimination and stigmatization can cause profound disorder in obese people; furthermore, from this perspective, the negative impact of obesity on health and quality of life is important. Both factors can subsequently lead to anxiety disorders. So, for example, there is evidence that the presence of obesity is associated with an increase in the risk of developing anxiety disorders by 25 % [12].

Migraine is often combined with anxiety-depressive disorders. In a study on migraine comorbidity, it was noted

that with episodic migraine, anxiety was detected in 55.8 % of cases, anxiety-depressive disorders – in 38 % [13].

THE AIM OF THE STUDY

To determinate the structure of anxiety disorders in patients with chronic migraine and abdominal obesity.

MATERIALS AND METHODS

180 people (90 women and 90 men) were examined at the University Clinic of the Black Sea National University. The age of women ranged from 19 to 65 years (the average age was 42.0 ± 0.8 years). Patients were divided into two clinical groups: 1st group- 60 patients with chronic migraine with average BMI= $23.5.8 \pm 1.10$ kg/m²; 2nd group – 60 patients with migraine and abdominal obesity, average BMI= 34.6 ± 1.42 kg/m². The control group – 60 patients without headache and with an optimal BMI of 19.5 ± 0.76 kg/m².

The criteria for inclusion in the studies were: the presence of headache for more than 15 days per month for > 3 months, in which headache attacks had signs of migraine and were observed at least 8 days per month, as well as the effective relief of attacks with a specific antimigraine agent (triptans or ergotamines).

The studies did not include patients with cluster headache and secondary headaches (after traumatic brain

injuries; vascular headaches; headaches with non-vascular intracranial lesions; a headache related to mental illness).

The examination of patients included: a detailed history (information on the increased onset of migraine, the presence of heredity, the number of migraine attacks, the need to take and the lack of efficacy of antimigraine drugs was clarified); physical examination of neurological status was carried out to exclude organic neurological symptoms and the possible symptomatic nature of headache; anthropometric study included: determination of body height and weight; calculation of body mass index (kg/m²); measurement of waist and hip circumference; «waist circumference/hip circumference» index (WC/HC); BMI was assessed according to the criteria of WHO: normal body weight – BMI < 25.0 kg/m², overweight – BMI 25.0-29.9 kg/m², obesity – BMI ≥30,0 kg/m².

Laboratory tests were included: a comprehensive general blood test with the calculation of the leukocyte formula, a biochemical blood test (general protein, amylase, creatinin, K⁺, Na⁺, AST and ALT), a lipidogram (cholesterol, triglycerides, high density lipoprotein, low-density lipoproteins, very low-density lipoprotein), determined carbohydrate metabolism indicators, i. e., blood glucose and glycosylated haemoglobin. All patients were performed instrumental examinations: electrocardiogram (ECG); ultrasound of abdominal organs (US), during which the thickness of the subcutaneous fat layer was measured. MRI of the brain was performed 5 patients with aphasic and hemiplegic type of migraine with the purpose of differential diagnosis.

The ICHD-3 criteria were used to diagnose migraine. Diagnostic and Statistical Manual on Mental Disorders (DSM-5) used for clinical diagnosis of anxiety disorders. The Taylor Manifest Anxiety Scale (TMAS) was used to assess the patient's level of anxiety.

Ethical issues. All participants were informed about the aims, organization, methods of the study and signed an informed consent to participate in it, and all measures were taken to ensure patient anonymity. The study was approved by the commission on ethics and bioethics of Medical Institute of the Petro Mohyla Black Sea National University. The study was conducted in accordance with the basic bioethical norms of the Helsinki Declaration of the World Medical Association on Ethical Principles of Scientific and Medical Research, as amended (2000, amended in 2008), the Universal Declaration on Bioethics and Human Rights (1997), the Council of Europe Convention on Human Rights and Biomedicine (1997).

The statistical processing was performed using software STATISTICA 13.0 (TIBCO, USA), the parametric methods of assessing the reliability of the results of the mean value and the standard deviation. Intergroup differences of qualitative characteristics were assessed using the Pearson's criterion (χ² test). The difference was considered reliable at a significance level of p<0.05. The correlation analysis was carried out using the Spearman coefficient. The strength of the relationship was interpreted as follows: very weak – 0-0.3; weak-0.3-0.5; medium strength-0.5-0.7; strong-0.7-0.9; very strong-0.9-1.0.

RESULTS AND DISCUSSION

During the study, it was established that the main triggers of migraine were: psychological factors (stress, depression, fatigue) in 41 (34.1 %) patients, weather changes in 12 (9.7 %) persons; hormonal imbalance (menstruation, ovulation) – 17 (13.9 %) patients; nutrition factors (hunger, excessive consumption of caffeine and serotonin-containing products, tough diets) – 7 (5.5 %) people; alcohol intake (especially red wine) – 24 (20.0 %); sleep disorders – 20 (16.8 %) (Fig.2).

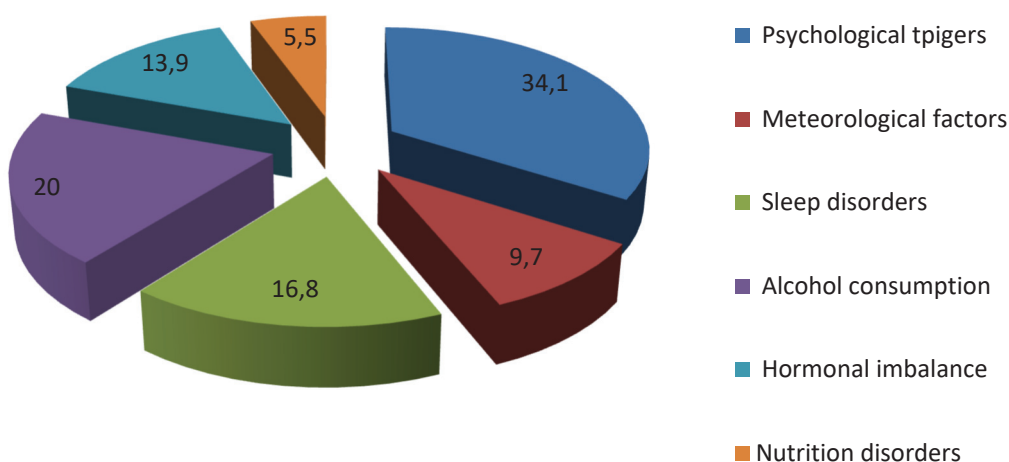


Fig.2. The main triggers of the occurrence of chronic migraine among patients of various clinical groups

The results of the study showed that phobic anxiety disorders were in 1.5 times more common in 2nd group patients ($\chi^2=9.81$, $p=0.000004$) than in 1st group patients; panic disorder was in 1.8 times more frequent in 2nd group ($\chi^2= 11.99$, $p=0.00001$) than in the 1st group, and generalized anxiety disorder was in 2 times ($\chi^2=13.08$, $p= p=0.00001$) less common in patients with chronic migraine than in comorbid patients. The total number of

patients with anxiety disorders in patients with chronic migraine on the background of abdominal obesity was in twice folds higher ($\chi^2=20.93$, $p=0.00001$) than in 1st group patients. Thus, the presence of concomitant obesity not only contributes to an increase in the total number of patients with anxiety disorders, but also affects the structure and course of anxieties (table 1).

Table 1

The structure of anxiety disorders in patients of different clinical groups

Types of anxiety disorders	1 st group 60 patients with chronic migraine, with average BMI = 23.5.8±1.10 kg/m ²		2 nd group 60 with chronic migraine and abdominal obesity, average BMI=34.6± 1.42 kg/m ²		The difference between the 1st and 2nd groups	
	n	%	n	%	χ^2	p-value
Absence of anxiety disorders	16	26.7	5	8.3	20.93	0.00001*
F 40. Phobic anxiety disorders	14	23.3	21	35	9.81	0.000004*
F 41.0 Panic disorder (episodic panic attack)	6	10	11	18.3	11.99	0.00001*
F 41.1 Generalized anxiety disorder	5	8.3	10	16.7	13.08	0.00001*
F 42. Obsessive-compulsive disorder	5	8.3	3	5	0.47	0.56
F 43. Reaction to severe stress and adaptation disorders	6	10.0	4	6.7	0.43	0.51
F 44. Dissociative (conversion) disorders	4	6.7	3	5	0.13	0.15
F 44.8 Other dissociative (conversion disorders): Hanser syndrome, psychogenic confusion of consciousness, etc.	4	6.7	3	5	0.13	0.15

* The difference is considered reliable when $p<0.05$

In patients with chronic migrane predominated psychological symptoms of anxiety, while in patients with comorbid pathology (chronic migraine and abdominal obesity) predominate somatic component of anxiousness. Strong correlation in the 1st group, white established between the disturbance of concentration of attention

($r=0.71$, $p=0.002$) and sleep disturbance ($r=0.71$, $p=0.001$). In the 2nd group a strong correlation was established between tremor ($r=0.72$, $p=0.001$), increased heartbeat ($r=0.7$, $p=0.03$), sweating ($r=0.71$, $p=0.001$), sensation and discomfort in the chest ($r=0.8$, $p=0.04$) (table 2).

Table 2

Intergroup correlation between the main symptoms of anxiety and concomitant disease

Main symptoms of anxiety	Intergroup correlation			
	1 st group 60 patients with chronic migraine, with average BMI = 23.5.8±1.10 kg/m ²		2 nd group 60 with chronic migraine and abdominal obesity, average BMI=34.6 ± 1.42 kg/m ²	
	r	p-value	r	p-value
Feelings of fear and dark feelings	0.59	0.03*	0.4	0.02*
Irritability	0.66	0.04*	0.55	0.03*
Sleep disorder	0.7	0.001*	0.49	0.04*
Muscle tension	0.4	0.08	0.33	0.09
Poor concentration of attention	0.71	0.002*	0.36	0.2
Tremor	0.43	0.2	0.72	0.001*
Reduction of libido	0.39	0.1	0.39	0.08
Heartbeat	0.43	0.09	0.7	0.03*
Weakness	0.49	0.08	0.44	0.08
Discomfort in chest	0.29	0.31	0.8	0.04*
Urgent urination	0.34	0.07	0.68	0.02*
Sweating	0.36	0.09	0.71	0.001*

* The strength of the relationship was interpreted as follows: very weak – 0-0.3; weak-0.3-0.5; medium strength-0.5-0.7; strong-0.7-0.9; very strong-0.9-1.0. The difference is considered reliable when $p<0.05$.

Thus, chronic migraine on the background of abdominal obesity is most often associated with panic disorders, mainly in women, as well as with specific phobia and social phobia; generalized anxiety disorder. Patients with generalized disorder complained of feelings of excessive anxiety and agitation about various life situations or events that did not match self-control and were present for more than ≥ 6 months. The excitement was manifested by: motor anxiety, excitement, nervousness; increased fatigue, difficulty concentrating attention; irritability, muscle tension; anxious sleep.

Patients with panic attacks complained of recurring panic seizures for more than 1 month, in which patients silenced persistent anxiety associated with the fear of a recurrence of exacerbation; patients showed disadaptive behavioral responses to panic attack (e.g. a desire to avoid being in the company of other people, whether during sports such as exercise or at secular activities to try to prevent recurrent attacks).

Social phobias were characterized by the fact that the same social situations almost always caused fear or anxiety, so patients actively tried to avoid such situations. Among the most common specific phobias in patients with chronic migraine and abdominal obesity were the fear of animals (zoophobia), height (acrophobia) and thunderstorms (astaphobia). Patients significant persistent (≥ 6 months) severe fear or anxiety lasting more than 6 months.

CONCLUSIONS

The results of the study confirmed that the presence of concomitant abdominal obesity, not only increases the total number of patients with anxiety, but also affects the structure and type of anxieties. Therefore, in addition to basic antimigraine therapy, before treating such patients should be supplemented with non-medicinal therapy in

the form of a balanced rational diet, an individual exercise program and 10-12 sessions of cognitive-behavioural therapy (CBT). Elements of CBT: should include cognitive restructuring; breathing training with expressed hyperventilation component in anxiety structure; applied relaxation; training on concern awareness (with records of the time and content of disturbing thoughts); training aimed at awakening and overcoming your own low tolerance to uncertainty; training designed to develop problem-solving behaviour skills.

PERSPECTIVES OF FURTHER STUDIES

The obtained results of the study are the basis for further development of algorithms of administration and rendering of medical care to patients with anxiety disorders in patients with chronic migraine and obesity.

FUNDING AND CONFLICT OF INTEREST

The authors state that there is no conflict of interest. Funding: at the authors' own expense.

COMPLIANCE WITH ETHICAL STANDARDS

All participants were informed about the goals, organization, methods of the study and signed the informed consent to participate in it, and all measures were taken to ensure the anonymity of the patients. The study was approved by the commission on ethics and bioethics of the Medical Institute of Petro Mohyla Black Sea National University. The study was conducted in accordance with the basic bioethical norms of the Helsinki Declaration of the World Medical Association on Ethical Principles of Scientific and Medical Research, as amended (2000, amended in 2008), the General Declaration on Bioethics and Human Rights (1997), the Council of Europe Convention on the Rights of man and biomedicine (1997).

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Резюме

СТРУКТУРА ТРИВОЖНИХ РОЗЛАДІВ У ХВОРИХ НА ХРОНІЧНУ МІГРЕНЬ ТА АБДОМІНАЛЬНЕ ОЖИРІННЯ Юрій М. Ворохта, Надія В. Беляєва

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Актуальність. В Україні в середньому 30 % осіб працездатного віку мають ожиріння та 25 % – надмірну масу тіла. Паралельно зі збільшенням кількості пацієнтів із надмірною вагою зростає відсоток людей з мігренню. Поширеність мігрені висока, на неї страждає 12-15 % популяції. Обидва захворювання негативно впливають не тільки на функцію внутрішніх органів, але й на нервово-психічний стан пацієнтів, призводячи до тривожних та депресивних розладів.

Мета дослідження – проаналізувати особливості структури тривожних розладів у пацієнтів з хронічною мігренню на фоні абдомінального ожиріння.

Матеріали та методи: було обстежено 180 пацієнтів (90 жінок та 90 чоловіків), які були розподілені на дві клінічні групи: 1 група – 60 осіб з хронічною мігренню (ХМ) з $IMT_{ср.} = 23,58 \pm 1,10$ кг/м²; 2 група – 60 пацієнтів з ХМ та абдомінальним ожирінням з $IMT_{ср.} = 34,6 \pm 1,42$ кг/м². Контрольну групу склали пацієнти без головного болю та з $IMT_{ср.} = 19,5 \pm 0,7$ кг/м². Мігрень діагностували за критеріями ICHD-2. Для встановлення клінічного діагнозу тривожних розладів використовували критерії Діагностичного і статистичного посібника з психічних розладів (Diagnostic and Statistical Manual of Mental Disorders (DSM-5)). Для оцінки рівня тривоги пацієнта використовували шкалу проявів тривоги Тейлора (Taylor Manifest Anxiety Scale, TMAS). Статистичну обробку проводили за допомогою дисперсійного та кореляційного аналізу.

Результати: фобічні тривожні розлади зустрічалися в 1,5 рази частіше у пацієнтів 2 групи ($\chi^2 = 9,81$, $p < 0,0001$), ніж у пацієнтів 1 групи; панічний розлад, фіксували в 1,8 рази частіше у 2-й групі ($\chi^2 = 11,99$, $p = p < 0,0001$), ніж у 1-й групі, а генералізований тривожний розлад був в 2 рази ($\chi^2 = 13,08$, $p < 0,0001$) рідше зафіксований у пацієнтів з ХМ, ніж у пацієнтів із супутніми ожирінням. Загальна кількість хворих на тривожні розлади у 2-й групі пацієнтів була вдвічі більшою ($\chi^2 = 20,93$, $p < 0,0001$), аніж у осіб 1-ї групи.

Висновки: наявність супутнього абдомінального ожиріння у пацієнтів з ХМ, збільшує не лише загальну кількість тривожних розладів, але й впливає на їх структуру. Тому крім базової протимігренної терапії, до лікування таких пацієнтів повинна додатково призначатись немедикаментозна терапія у вигляді: збалансованого раціонального харчування, індивідуальної програми з фізичного навантаження та 10-12 сеансів когнітивно-поведінкова терапії (КПТ).

Ключові слова: мігрень, ожиріння, індекс маси тіла, тривожні розлади, тригери