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PECULIARITIES OF THE COURSE OF SOMATIZED AND ANXIETY DISORDERS IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE ON THE BACKGROUND OF ABDOMINAL OBESITY

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Non-alcoholic fatty liver disease in overweight and obese patients not only complicates the course of chronic somatic diseases, but also increases the risk of non-psychotic mental disorders in this category of patients (depression, anxiety disorders, panic attacks). The purpose of study was to determine the features of non-psychotic mental disorders in obese patients with non-alcoholic fatty liver disease. The Screening for Somatoform Symptoms–2 and the Taylor test were used to assess the presence of non-psychotic mental disorders. Somatized disorders in patients with non-alcoholic fatty liver disease on the background of obesity were recorded 9.6 times more often (D=0.579, p=0.0001<0.05) than in people with normal body mass index, mainly due to gastrointestinal and asthenic symptoms. Very high levels of anxiety were also recorded 2.5 times more often (p=0.007<0.05) than among patients in the control group.

Key words: overweight, obesity, non-psychotic mental disorders, body mass index.

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ОСОБЛИВОСТІ ПЕРЕБІГУ СОМАТИЗОВАНИХ ТА ТРИВОЖНИХ РОЗЛАДІВ У ПАЦІЄНТІВ З НЕАЛКОГОЛЬНОЮ ЖИРОВОЮ ХВОРОБОЮ ПЕЧІНКИ НА ФОНІ АБДОМІНАЛЬНОГО ОЖИРІННЯ

Неалкогольна жирова хвороба печінки у пацієнтів з надлишковою вагою та ожирінням ускладнює не лише перебіг хронічних соматичних захворювань, але й збільшує ризик розвитку непсихотичних психічних розладів у данної категорії пацієнтів (депресій, тривожних розладів, панічних атак). Метою дослідження було визначити особливості непсихотичних психічних розладів у хворих на ожиріння з неалкогольною жировою хворобою печінки. Для оцінки наявності непсихотичних психічних розладів використовували опитувальник соматизованих розладів (Screening for Somatoform Symptoms–2) та тест Тейлора. Соматизовані розлади у хворих неалкогольною жировою хворобою печінки на фоні ожиріння були зафіксовані у 9,6 рази частіше (D=0,579, p=0,0001<0,05), ніж у осіб з нормальним індексом маси тіла, переважно за рахунок шлунково-кишкових та астенічних симптомів. Дуже високий рівень тривоги , також зафіксовано в 2,5 рази частіше (p=0,007<0,05), ніж серед пацієнтів контрольної групи.

Ключові слова: надмірна вага, ожиріння, непсихотичні психічні розлади, індекс маси тіла.

The study is a fragment of the research project "Clinical and pathogenetic substantiation of primary and secondary prevention systems of the most socially significant chronic non-infectious diseases of the internal organs", state registration No. 0120U101641.

Epidemic nature of the prevalence of obesity and related non-communicable diseases – cardiovascular, type II diabetes, musculoskeletal disorders, non-alcoholic fatty liver disease (NAFLD), non-psychotic mental disorders (NPD) [1, 2, 3] in modern medicine [4]. The prevalence of obesity among the female population of Ukraine is 29.7–35.5 % [5, 6], while alimentary-constitutional obesity is almost 95 % [7, 8]. In the urban population of Ukraine, only 29.3 % of the population have a normal body weight, and 70.7 % are overweight and obese I–III degree. Childhood obesity is growing every year and today it is 10 times higher than in the 1970s [9].

Being overweight and obese not only complicates the course of chronic somatic diseases, including non-alcoholic fatty liver disease, but also increases the risk of developing NPD (depression, anxiety disorders, panic attacks). NPD significantly affect physical, mental and social functioning and increase the risk of premature death. NPD make it difficult to meet basic human needs and negatively affects its daily life activities, leading to a significant reduction in quality of life. According to epidemiological studies, NPD causes a number of social dysfunctions that are more severe than the effects of chronic somatic diseases such as angina, arthritis, bronchial asthma and diabetes.

The following are variants of mental disorders that occur in obesity, and are described in the works of various authors: asthenia disorders; endocrine psycho syndrome; anxiety disorders; affective disorders (often depressive); behavioural disorders; cognitive disorders; sleep disorders not caused by depression [10, 11].

Given the great variety of NPD, the study conducted a study on the course of anxiety and somatised disorders in patients with non-alcoholic fatty liver disease on the background of abdominal obesity. This choice is due to the epidemiological dominance of the above disorders, and medical and

socio-economic consequences. Anxiety disorders, along with depression, are among the most common mental disorders. The onset of anxiety disorder occurs, with few exceptions, between the 2nd and 4th decades of life. Almost 60 % of all anxiety disorders manifest for the first time before the age of 21. It is extremely important to pay attention to the hidden potential of chronicity of these disorders: according to the results of research, from the appearance of the first symptoms of anxiety disorder to the beginning of professional psychotherapeutic treatment takes an average of 8 years. Despite a number of studies, the problem of comorbidity in patients with NAFLD on the background of abdominal obesity and the development of NPD is particularly acute for the health care system on a global scale and needs to be addressed urgently.

The purpose of the study was to determine the features of non-psychotic mental disorders in obese patients with non-alcoholic fatty liver disease.

Materials and methods. On the basis of the University Clinic of the Black Sea National University named after Petro Mohyla and the polyclinic of the State Institution "Territorial Medical Association of the Ministry of Internal Affairs of Ukraine in Mykolaiv region" 272 people (136 women and 136 men) were examined. The age of women ranged from 19 to 60 years (mean age was 41.5±11.2 years), the age of men - from 22 to 60 years (mean age – 42.3±12.3 years). All patients were divided into two clinical groups. Group 1 – 90 people (45 women and 45 men) patients with NAFLD and overweight (body mass index (BMI) from 25.8 to 29.3 kg/m^2) 27.5±1.31 kg/m^2), group 2 – 92 people NAFLD (46 women and 46 men) with a degree 1 abdominal obesity (BMI from 30.0 to 33.9 kg/m^2; average 31.74±1.03 kg/m^2). The control group consisted of 90 people (45 women and 45 men) with normal weight (BMI from 19.5 kg/m^2 to 23.9 kg/m^2; average 22.41±1.43 kg/m^2) and healthy liver according to ultrasonography and gastrological results. In each of the groups studied the features of NDP separately in women and men under 45 years and after 45 years.

All patients had anthropometric (height, weight, abdominal circumference, thigh circumference) and physiological (blood pressure, heart rate and respiratory rate) parameters calculated by BMI and waist/thigh index (tab. 1).

Table 1

Anthropometric and physiological parameters of patients of different clinical groups

Indices	Control group (n=90)		Group 1 (n=90)		Group 2 (n=92)	
	Women (n=45)	Men (n=45)	Women (n=45)	Men (n=45)	Women (n=46)	Men (n=46)
Anthropometric indices						
Height (cm)	155–170 (162.51±3.03)	168–180 (174.01±6.03)	157–171 (163.51±2.03)	167–179 (173.01±5.03)	155–172 (164.51±3.03)	168–180 (174.51±6.03)
Weight (kg)	55–70 (67.5±5.21)	65–80 (72.5±4.21)	70–83 (76.52±5.21)	75–89 (82.50±4.21)	80–93 (86.50±6.21)	80–110 95.3±5.21
Waist circum-ference(cm)	60–75 (67.5±2.2)	76–88 (82.2±3.2)	70–85 (77.5±2.3)	80–88 (84.01±4.01)	84–92 (88.5±2.1)	80–88 (89.5±1.1)
Thigh circum-ference (cm)	86–90 (88.0±2.2)	94–96 (95±1)	90–96 (93.0±2.2)	98–101 (99.5±1.0)	94–100 (97.0±2.2)	99–105 (100.5±1.1
Index, waist/hips	0,75–0,80 (0.76±0.04)	0,82–0,84 (0.83±0.01)	0,85–0,90 (0.87±0.04)	0.90–0,95 (0.92±0.01)	94–100 (97.0±2.2)	99–105 (100.5
Physiological indices						
BP	110/65–130/75 (120/70±10/10)	120/65–130/75 (125/75±10/10)	120/75–140/90 (130/82±10/10)	135/75–140/80 (135/82±10/10)	135/75–170/90 (155/92±15/15)	135/75–160/90 148/85±13/12)
HR	64–74 (69±4)	65–75 (70±2)	70–79 (74.5±5.1)	69–82 (75.0±5.2)	72–79 (75.5±5.2)	70–82 (76.3±6.2)
RR	16–18 (17±1)	16–18 (17±1)	18–20 (19±1)	17–19 (18.0±1.2)	18–20 (19±1)	17–19 (18.01±1.02)

To assess the presence of somatized disorders used adapted to the purpose of the study Questionnaire somatized disorders SOMS – 2 (Screening for Somatoform Symptoms). Patients were asked to answer "yes" or "no" to 53 questions about whether these complaints had occurred in the last 2 years (long or short) or whether they existed now. Syndrome-completed somatized disorder was diagnosed with > 20 points for men and >25 points for women.

Anxiety disorders were investigated by the Taylor test, which consisted of 60 statements to which the subject must answer "yes" or "no". The statements were selected from a set of statements from the Minnesota Multifaceted Personality Questionnaire (MMPI). The selection of items for the test was based

on an analysis of their ability to distinguish between persons with "chronic anxiety reactions". The duration of testing was 15–30 minutes. The results were interpreted as follows: 40–50 points – an indicator of a very high level of anxiety; 25–40 points – indicates a high level of anxiety; 15–25 points – about the average (with a tendency to high) level of anxiety; 5–15 points – about the average (with a tendency to low) level of anxiety; 0–5 points – about a low level of anxiety.

Statistical processing of research results was carried out by methods of variation statistics using a standard application package SPSS 13.0 for MS Windows. Descriptive statistics were used for statistical analysis of data; comparison of the average values of the variables was carried out using parametric methods (Student's t-test) with a normal distribution of these features, expressed in the interval scale. Fisher's exact test was used to compare the particle distribution of two or more variables. The difference was considered significant if the achieved significance level (p-value) was lower than 0.05. The Kruscalla-Wallis test was used to establish a correlation.

The study was conducted in accordance with the basic bioethical norms of the Helsinki Declaration of the World Medical Association "Ethical principles of medical research with human participation as an object of study" (1964), as amended, the Universal Declaration on Bioethics and Human Rights of the United Nations (2005), The Council of Europe Convention on Human Rights and Biomedicine (1997). All participants were informed about the goals, organization, research methods and signed an informed consent to participate in it. All measures were also taken to ensure the anonymity of patients.

Results of the study and their discussion. During the study, it was found that with the increase in the weight of patients, the number of NPR increased. The distribution of somatized disorders in patients of different clinical groups is shown in table 2.

Table 2

The difference in the distribution of somatized disorders in patients of different clinical groups, depending on BMI (kg/m^2)

The main somatised disorders	Control group, $BMT_{mid.}$= 22.4 ±1.43 kg/m^2 (n=90)		Group 1, $BMT_{mid.}$= 27.7±1.31 kg/m^2 (n=90)		The difference between the control group and group 1		Group 2, $BMT_{mid.}$= 31.74±1.03 kg/m^2(n=92)		The difference between the control group and group 2		The difference between group 1 and group 2	
	n	%	n	%	D	P	n	%	D	P	D	P
No complaints	58	64.6 %	14	15.6 %	0.489	0.001	6	6.5 %	0.579	0.001	0.09	0.045
Pain in the abdomen and abdomen	4	4.4 %	9	10.0 %	0.056	0.042	12	13.0 %	0.086	0.020	0.03	0.004
Flatulence	5	5.6 %	11	12.2 %	0.067	0.039	12	13.0 %	0.075	0.059	0.0082	0.004
Liquid stool	3	3.3 %	10	11.1 %	0.078	0.038	11	12.0 %	0.086	0.017	0.0085	0.004
Fasten	4	4.4 %	12	13.3 %	0.089	0.031	13	14.1 %	0.097	0.020	0.0080	0.003
Heartbeat, heart failure	4	4.4%	9	10.0 %	0.056	0.042	10	10.9 %	0.067	0.024	0.0087	0.002
Pain in the arms and legs	3	3.3 %	7	7.8 %	0.044	0.154	8	8.7 %	0.054	0.103	0.0092	0.452
Back pain	4	4.4 %	8	8.9 %	0.044	0.190	9	9.8 %	0.053	0.114	0.0089	0.491
Increased fatigue	5	5.6 %	10	11.1 %	0.056	0.044	11	12.0 %	0.064	0.088	0.0085	0.456

Compared to the control group, patients in group 1 were by 4.1 times more likely to complain of somatized disorders (D=0.489, p=0.00<0.05), mainly due to the predominance of gastrointestinal and asthenic symptoms. Thus, in overweight people by 2.3 times more often (D=0.056, p=0.042<0.05) recorded pain in the abdomen and abdomen, by 2.2 times more often flatulence (D=0.067, p=0.039<0.05), by 3.4 times more often loose stools (D=0.078, p=0.038<0.05), by 3.1 times more often constipation (D=0.089, p=0.031<0.05), palpitations and heart failure – by 2.3 times more often (D=0.056, p=0.042<0.05), increased fatigue – by 2.0 times more often (D=0.056, p=0.044<0.05) than in patients of the control group.

Patients in group 2 were by 9.6 times more likely to complain of somatized disorders compared to patients in the control group (D=0.579, p=0.001<0.05), also due to complaints from the gastrointestinal tract and autonomic nervous system. In persons with NAFLD on the background of obesity 3.0 times more often (D=0.086, p=0.020<0.05) recorded pain in the abdomen and abdomen, 2.4 times more often flatulence (D=0.075, p=0.059<0.05), 3.7 times more often loose stools (D=0.086,

p=0.017<0.05), 3.3 times more often constipation (D=0.097, p=0.020<0.05), palpitations and heart failure in 2.3 times more often (D=0.06, p=0.024<0.05), increased fatigue by 2.2 times more often (D=0.064, p=0.088<0.05). That is, patients with NAFLD on the background of overweight and obesity maintain a similar trend: with increasing BMI, the percentage of NPR, especially due to gastrointestinal and asthenic disorders increases.

Low level of anxiety among patients in the control group was recorded in 66.7 % (60/90) patients; in group 1 – in 13.3 % (12/90), group 2 – 8.7 % (8/92). The average level of anxiety among patients in the control group was recorded in 20 % (18/90) of patients; in group 1 – in 44.4 % (39/90), group 2 – 46.7 % (43/92). High level of anxiety among patients of the control group was recorded in 8.9 % (8/90) of patients of the control group, in group 1 in 32.3 % (29/90), in group 2 – 33.7 % (31/92) of patients. A very high level of anxiety in the control group was recorded in 4.4 % (4/90) of patients, group 1 – 10 % (9/90), group 2 – 10.9% (10/92) (fig. 1).

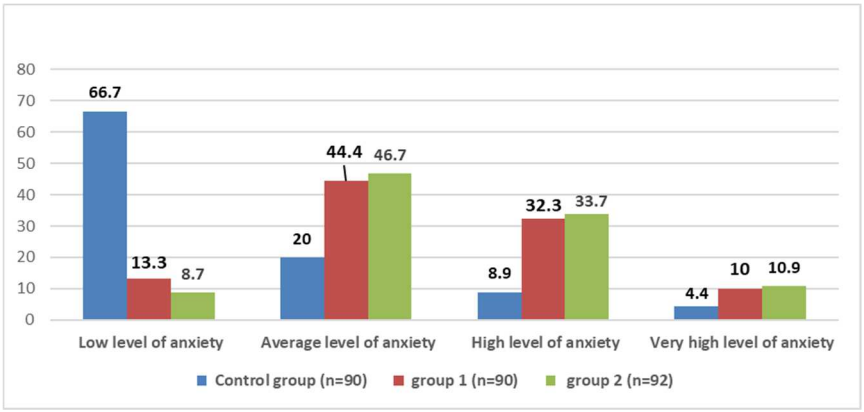

Fig.1. Relationship between the course of anxiety disorders and the weight of patients in different clinical group

Among overweight patients, a very high level of anxiety was recorded 2.3 times more often (x^2=29.143, p=2.09e-06<0.05) than among patients with normal body mass index. In obese individuals, anxiety disorders of a very high level were recorded 2.5 times more often (x^2=12.065, p=0.007<0.05) than in patients in the control group.

Anxiety disorders occurred equally among patients of different sexes and ages. Significant statistical differences, depending on the gender and age characteristics of patients were not found (all p> 0.05) (fig. 2).

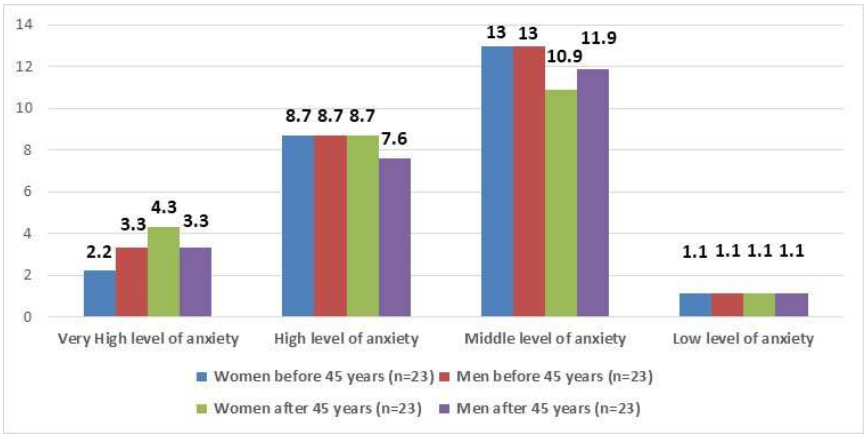

Fig.2. Distribution of anxiety disorders in patients with NAFLD on the background of obesity, depending on the gender and age characteristics of patients

The development of non-psychotic mental disorders in liver disease, in our opinion, is due to a violation of deamination processes: decreased urea levels and glutamine synthesis in the liver, which causes an increase in the concentration of ammonia in the blood. Non-alcoholic fatty liver disease is accompanied by a deficiency of endogenous ademethionine, which is a major participant in methylation processes in the body. Ademethionine deficiency can lead to the development of fatigue in patients with liver disease due to impaired liver detoxification function. At the same time, ademethionine in the form of a drug restores the deficiency of endogenous ademethionine in liver diseases, the structure and function of hepatocytes with a rapid clinical outcome. The results of randomized studies [2] show that already on the 7th day of therapy ademethionine reduced the severity of symptoms of fatigue, a positive trend was also observed in reducing anxiety.

Another cause of NPR in patients with hepatobiliary pathology is likely to be impaired intestinal barrier permeability. The presence of metabolic and microbial endotoxemia can cause anxiety, mood swings, depression, cognitive impairment and social behavior. Today, endotoxemia of the intestinal microbiome and its effect on a number of diseases are being actively studied. It is assumed that the reasons for the development of endotoxin aggression may be the lack of intestinal and hepatic barriers (indicators

of endotoxin aggression levels of lipopolysaccharides and endogenous ethanol in the blood in liver disease are always elevated) [4].

Conclusions

1. Non-alcoholic fatty liver disease on the background of abdominal obesity and non-psychotic mental disorders are interrelated and interdependent. With increasing BMI, the percentage of NPD increases, especially due to somatised and anxiety disorders.

2. Somatised disorders in patients with NAFLD on the background of overweight were recorded 4.1 times more often (D=0.489, p=0.0001<0.05) and in patients with NAFLD with obesity 9.6 times more often (D=0.579, p=0.0001<0.05) than in individuals with a normal body mass index, mainly due to the predominance of gastrointestinal and asthenia symptoms.

3. Among patients with NAFLD on the background of overweight and obesity, a very high level of anxiety was recorded 2.3 times (x^2=29.143, p=2.09e-06<0.05) and 2.5 times more often, p=0.007<0.05) than among patients with normal body mass index.

4. According to the results of the study, the influence of gender and age on the course of anxiety disorders was minimal and occurred equally among patients of different sexes and ages. No significant statistical differences, depending on the gender and age characteristics of patients (all p>0.05)

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