The Significance of Some Risk Factors in The Development of Discirculatory Encephalopathy in Patients with Type 2 Diabetes Mellitus

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ABSTRACT

The aim of the study was to evaluate risk factors for the development of dyscirculatory encephalopathy in patients with type 2 diabetes mellitus.

Materials and methods. 60 patients were examined, 48 women (80.0%), 12 men (20.0%) suffering from type 2 diabetes who were being treated in the endocrinology department of the 3rd TMA clinic. The age of the patients was 56.5±8.7 years, body mass index (BMI) 32.3±3.8 kg/m2, with a duration of DM 6.8± 3.7 years. Among men, 6 active smokers, with an average experience of 5.3 ± 1.1 years. The diagnosis of type 2 diabetes and the degree of compensation of carbohydrate metabolism was established according to WHO recommendations. In all patients, anthropometric parameters were evaluated with the calculation of BMI according to the Quetelet formula, blood pressure was measured for the diagnosis of hypertension, carbohydrate metabolism was studied – fasting blood glucose, postprandial glycemia and glycated hemoglobin (HbA1c). Also, total blood cholesterol was examined for the diagnosis of hypercholesterolemia. To determine the symptoms of anxiety and the degree of their severity, the Spielberger anxiety scale was used (the test is an informative way to self-assess the level of anxiety at the moment (reactive anxiety as a condition) and personal anxiety) - Spielberger State and Trait Anxiety Scale. Hemodynamics in the main arteries of the head was studied by ultrasound Dopplerography in pulsating and continuous modes. Risk factors for the development of DE were calculated according to the recommendations of L.A. Ponomareva.

Results. The results showed that the patients' carbohydrate metabolism indicators were significantly increased in comparison with the control group. In patients with compensation, anxiety was absent in 60% of cases, and was moderate in the remaining 40% of patients. In patients with decompensated DM, only 16% of patients had no anxiety, in the remaining 84% of patients moderate anxiety prevailed, while in these patients the average Spielberg scale score was 38.4± 5.8 points. It should be noted that personality anxiety prevailed in 80% of patients. Integrated analysis of the risk of DE in patients with type 2 diabetes showed that the leading risk factors in the occurrence of DE in patients with type 2 diabetes are: smoking men, hypercholesterolemia, by gender - women, duration of hypertension, age group 54-60 years, by severity of anxiety-moderate anxiety, BMI 30 kg/m2.

Conclusions. The results showed that patients with type 2 diabetes have a decrease in speed characteristics, an increase in peripheral resistance indices, which indicate a progressive decrease in the elastic-tonic properties of the vascular wall, which ultimately contributes to a decrease in cerebral blood flow and the development of dyscirculatory encephalopathy. The severity of anxiety disorders depends on the degree of diabetes compensation, while in 84% of patients with diabetes decompensation moderate anxiety prevailed, while the average Spielberg scale was 37.4± 5.8 points.

Integrated risk analysis of DE in patients with type 2 diabetes showed that the leading risk factors in the occurrence of DE in patients with type 2 diabetes are: smoking, hypercholesterolemia, the sex of patients is women, the severity of anxiety - moderate anxiety prevails, BMI and the age of patients 54-60 years.

Keywords:	type 2 diabetes mellitus, dyscirculatory encephalopathy, dopplerography of cerebral vessels, Spielberg-Khanin scale.

The incidence of type 2 diabetes mellitus (DM) in the XXI century has reached an epidemic level. Type 2 diabetes is often characterized by a low-symptomatic or asymptomatic course, so the disease is often diagnosed late, when patientsalready have micro- and macrovascular complications.

According to the International Diabetes Federation, in 2017 there were 415 million adult patients with diabetes mellitus (DM) in the world, and more than 90% of them were patients with type 2 diabetes. About half of the patients do not know about their diagnosis. This number is projected to grow to 643 million by 2030 and to 784 million by 2045 [1,10].

According to the World Health Organization, in economically developed countries up to 4-6% of the population has diabetes. In Europe, the proportion of such patients is about 4%. WHO states that diabetes mellitus predetermines an increase in The presence and severity of diabetic angiopathy determine the prognosis of the disease and the fate of the patient [8]. Changes in small vessels (arterioles mortality by 2-3 times and reduces life expectancy by 10-30%) [10]. According to the World Health Organization, in economically developed countries up to 4-6% of the population has diabetes. In Europe, the proportion of such patients is about 4%. WHO states that diabetes mellitus predetermines an increase in mortality by 2-3 times and reduces life expectancy by 10-30% [10].

Along with the increase in the number of patients with diabetes, the number of patients suffering from complications of this terrible disease, which are the main cause of disability and mortality, is increasing. DM is characterized by a generalized lesion of both small vessels (microangiopathy) and medium- and large-caliber vessels (macroangiopathy), which has received the collective name "diabetic angiopathy"., capillaries, venules) are specific for diabetes, in large ones they are regarded as early and widespread atherosclerosis. It is important that diabetic macroangiopathy has no specific differences from atherosclerotic changes in people without diabetes. However, atherosclerosis in patients with DM develops 10-15 years earlier than in people without it. He does not spare young and middle-aged people, especially with a long-term course of the disease. If patients with atherosclerosis without DM are predominantly affected by coronary, cerebral or peripheral vessels, then with DM, atherosclerosis affects most arteries, which is explained by metabolic disorders predisposing to vascular lesions. DM by the nature of metabolic disorders is a natural model of atherosclerosis. The prevalence of the atherosclerotic process in DM is promoted by microangiopathy. Such features of vascular system damage in DM explain the significant prevalence of cardiovascular diseases, including cerebrovascular diseases, in this pathology. Dyscirculatory encephalopathy (DE), or chronic cerebral ischemia, is a syndrome of progressive multi-focal or diffuse brain damage, clinically manifested by neurological and/or mental disorders and caused by chronic cerebral vascular insufficiency and/or repeated episodes of acute cerebral circulatory disorders [2,4]. Risk factors such as age, duration, presence of cardiovascular diseases, dyslipidemia, smoking and many others are important in the development and progression of DE [6]. There is a mutual influence between many FRS, leading to a more significant increase in the likelihood of developing vascular disorders in patients with type 2 diabetes. The study and early prevention of FR DE in patients with type 2 diabetes leads to an improvement in the quality of life, a decrease in the frequency of cerebral complications in the form of stroke and dementia.

The aim of the study was to evaluate risk factors for the development of dyscirculatory encephalopathy in patients with type 2 diabetes mellitus.

Materials and methods.

60 patients were examined, 48 women (80.0%), 12 men (20.0%) suffering from type 2 diabetes who were being treated in the endocrinology department of the 3rd TMA clinic. The age of the patients was 56.5±8.7

years, body mass index (BMI) 32.3±3.8 kg/m2, with a duration of DM 6.8± 3.7 years. Among men, 6 active smokers, with an average experience of 5.3 ± 1.1 years. The diagnosis of type 2 diabetes and the degree of compensation of carbohydrate metabolism was established according to WHO recommendations. In all patients, anthropometric parameters were evaluated with the calculation of BMI according to the Quetelet formula, blood pressure was measured for the diagnosis of hypertension, carbohydrate metabolism was studied – fasting blood glucose, postprandial glycemia and glycated hemoglobin (HbA1c). Also, total blood cholesterol was examined for the diagnosis of hypercholesterolemia. The patients were comparable in age, BMI, HbA1c levels, fasting blood glucose and postprandial glycemia. The patients were also examined by an ophthalmologist to determine the presence and severity of diabetic retinopathy. Patients who had suffered acute vascular diseases, with chronic heart and kidney failure were not included in the study.

A clinical neurological study was conducted to objectively assess the severity of sensorimotor disorders in accordance with the NDSm scale. At the same time, the presence of the Achilles reflex and sensitivity thresholds were assessed

• * tactile using a monofilament that exerts pressure on the skin with a force of 10 g/cm2;
* temperature control using Theo-term thermal tip;
* vibratory with a graduated neurological tuning fork that vibrates at a frequency of 128 Hz.

The calculation of the sum of points was carried out as follows: 0 - norm, 1 - reduction, 2 - absence for each side. Therefore, the maximum total score could be 10.

At the same time, the sum of points from 0 to 1 indicated the absence or presence of initial signs of peripheral sensorimotor polyneuropathy in the patient, from 3 to 5 points — moderate, from 6 to 8 — moderate severity, from 9 to 10 - severe neuropathy.

To determine the symptoms of anxiety and the degree of their severity, the Spielberger anxiety scale was used (the test is an informative way of self-assessment of the level of anxiety at the moment (reactive anxiety as a condition) and personal anxiety) - Spielberger State and Trait Anxiety Scale [11] (the test indicators were interpreted according to the following orientational estimates: up to 30 points - low, 31-44 points - moderate, 45 and more – high anxiety).

Hemodynamics in the main arteries of the head was studied by ultrasound Dopplerography in pulsating and continuous modes [7]. The general, external and internal carotid arteries, vertebral arteries were examined using a sensor with a frequency of 4 MHz. The signal was evaluated using a fast Fourier converter and displayed on the screen as a spectrogram consisting of dots of different colors, the totality of which gave a spectrum of velocities in the cross-section of the arteries during the cardiac cycle.

Risk factors for the development of DE were calculated according to the recommendations of Ponomareva L.A. et al. [5]. Knowing the possible risk factors, it is possible to predict adverse consequences taking into account the complex impact of numerous factors, which allow not only to take into account the degree of probability of such consequences, but also to isolate from the many risk factors those that seem to be the most significant [5].

The control group consisted of 20 healthy individuals of comparable age and gender.

Statistical processing of the material was carried out using the Excel program. The reliability of the differences was assessed by the Student's t-criterion. The correlation coefficient was calculated using the Spearman rank method. The statistical significance of the results was confirmed at $p<0.05$.

Results and their discussion

For the diagnosis of DE, clinical, anamnestic and instrumental signs of brain damage were included. The main complaints of DE in patients with type 2 diabetes were: headaches, dizziness, noise in the head, fatigue, decreased attention, instability when walking, sleep disorders, anxiety and depression, minor

memory disorders, cognitive activity are also often detected.

Characteristic of patients in this category were persistent cephalgic syndrome (86%), dizziness (60%), sleep disturbance (58%), noise in the head (45%), memory impairment (45%), anxiety (40%) and a high percentage of prevalence (90%) of astheno-neurotic manifestations.

All patients took oral hypoglycemic drugs before being included in the study. Diabetic sensory symmetric neuropathy was diagnosed in all examined patients. At the same time, the NDSm averaged 8.6±0.3 points.

When analyzing carbohydrate metabolism, we revealed that 18 (30.0%) were diagnosed with compensation and 42 (70.0%) patients had decompensation. As can be seen from Table 1, the BMI data of the studied patients did not significantly differ from the control group. At the same time, there is a significant increase in the indicators of carbohydrate metabolism in the examined patients compared with the control group. Thus, HbA1c was increased by 36% in the compensation group, and by 48% in the decompensation group compared to the control group (p<0.05), compared to the studied groups by 23% (p<0.05), which reflects the decompensation of diabetes. An increase in OH was revealed in the group with compensation by 29%, in the decompensation group by 38% (p<0.05), and there was also a slight increase in this indicator compared to the studied groups. The indicators of SAD and DAD were increased in the examined groups, which indicates concomitant hypertension.

Table 1

Indicators of carbohydrate metabolism, BMI, blood pressure in patients with type 2 diabetes

Indicator	Control group n-10	compensation n-18	decompensation n-42
BMI, kg/m2	30,3±4,5	34,5±2,9	33,9±3,3
HbA1c, %	4,3±0,5	6,4±0,4*	9,3±0,8*,**
Fasting blood glucose, mmol/l	4,8±0,9	6,8±0,2*	9,8±0,9*
Postprandial glycemia, mmol/l	5,9±0,5	9,8±0,7*	14,9±3,0*
Blood cholesterol, mmol/l	4,2±0,5	5,9±0,7*	6,9±3,0*,**
Systolic blood pressure, mmHg	117,6±7,7	148,6±12,7*	159,8±11,3*
Diastolic blood pressure, mmHg	78,7±10,7	88,0±10,3	97,8±9,1*

Note: n is the number of examined patients;
*-the presence of reliability (P<0.05) compared to the control;
**-the presence of reliability (P<0.05) in comparison with the studied groups.

When analyzing the Dopplerographic examination of the brachiocephalic and vertebrobasilar arteries, we revealed: atherosclerotic changes in the vertebral arteries, common, internal and external carotid arteries. The majority of 30 (68.2%) have atherosclerotic changes with a decrease in the laminar velocity of blood flow through the vertebral arteries. The remaining 14 (31.8%) had atherosclerosis of the carotid arteries. In patients, there was a significant decrease in the speed characteristics of cerebral blood flow and an increase in peripheral resistance in the vertebral arteries. The same trends took place in the medullary artery, without reaching the level of statistical significance, however, a significant increase in intravascular resistance in the medullary artery with compensated

diabetes mellitus was noted. Differences in the thickness of intima-media (TIM) in decompensated diabetes compared with

compensated (p=0.03) were significant (Table 2).

Table 2
UZDG-characteristics of cerebral blood flow in patients suffering from DM2, depending on the degree of compensation of the disease

Groups	Control group n-20	compensation n-18	decompensation n-42
PA Vs(d), cm/sec.	48,3±2,9	47,5±3,9	46,5±20,6*
PA Vs(d), cm/sec .	19,1±4,4	18,1 ±4,1	15±4,8*
PA Pi(d), conl.ed.	1,0±0,17	0,93 ±0,09	0,88±0,14*
PA Pi(d), conl.ed.	0,68±0,03	0,63±0,1	0,57 ±0,2*
PA SB(d), conl.ed.	2,70±0,4	2,69 ±0,7	2,33±0,6
PA SB(d), conl.ed.	41,7±14,6	41,7±15,4	42,5±16,9
SMA Vs(d) cm/sec.	87,5±14,2	90,5±16,8*	90±17,7*
SMA Vd(d), cm/sec.	36,5 ±3,1	35,5±3,7	39±9,5*
SMA Vm(d), cm/sec.	56,5±13,1	54,5±7,1	59 ±9,1*
SMA Pi(d), conl.ed.	0,78±0,03	0,95±0,08*	0,98±0,1*
SMA iR(d), conl.ed.	0,57±0,01	0,59±0,09*	0,6±0,13*
TIM, mm	0,8±0,13	0,8±0,19	0,9±0,2

Note: n is the number of examined patients;

*-the presence of reliability (P<0.05) compared to the control;

Notes: PA is the vertebral artery, SMA is the middle cerebral artery, Vs is the maximum value of the spectrum during systole, Vd is the maximum value of the spectrum during the final diastole, Vm is the average value of the spectrum, TIM is the thickness of the intima media, iR is the ratio between the difference of systolic and diastolic velocities (from peak to peak) with an average velocity, the Purcello Pi index is the ratio between the difference between systolic and diastolic velocities (from peak to peak) and systolic velocity.

When analyzing the parameters of dopplerography of brachiocephalic and vertebrobasilar vessels, we revealed: UZDG

signs of atherosclerosis in carotid and paravertebral vessels. In 9 (20.4%) patients, stenosing atherosclerosis was detected along the left vertebral artery, in 11 (25%) - along the left external carotid artery. Critical cerebral vascular ischemia was not detected in the examined patients. In these patients, there is an increase in the linear velocity of blood flow of a compensated nature. Another clinical manifestation of DE in patients with type 2 diabetes is a state of anxiety. The presence of anxiety-depressive disorders increases the risk of developing and progressing complications of diabetes: arterial hypertension, coronary heart disease and stroke, which are the main cause of

death in these patients. However, the problem of detecting anxiety disorders in patients with DM in the early stages is far from being resolved [12,13].

Given the fact that many patients have diabetic complications and comorbid, this is often complicated by a state of anxiety. An anxious state can be either reactive or situational and personal. To identify situational and personal anxiety, we used the Spilbereg questionnaire. The level of anxiety on the Spilbereg scale in the examined patients varied from 32 to 42 points, on average - 37.1 ± 5.5 points, i.e. moderate anxiety was detected. The

dependence of anxiety on the degree of diabetes compensation was also studied. It was found that in patients in the compensation stage, anxiety was low by 26% (P<0.05), in comparison with the group of patients in the decompensation state, where moderateanxiety. It is known that poor glycemic control leads to the development and progression of vascular complications of diabetes and their adverse outcomes. Anxiety disorders are often associated with the development of DE with all clinical manifestations, as well as with an increased risk of stroke [9,12].

Table 3
The structure of anxiety disorders in the examined patients depended on the state of carbohydrate metabolism compensation.

Group	Control group n-20	Compensation n-18	Decompensation n-42
Scores	19,5±1,9	24,5±5,6*	38,4±5,8*,**

Note: n is the number of examined patients;
*-the presence of reliability (P<0.05) compared to the control;
**-the presence of reliability (P<0.05) in comparison with the studied groups.

According to literature data, poor metabolic control leads to the development and progression of micro- and macrovascular complications in patients with diabetes mellitus. The basis of brain damage in patients with type 2 diabetes mellitus are macro- and microangiopathies involving extracranial and cerebral arteries of large and small caliber and microcirculation disorders [6,8]. Based on the available information about the risk of subsequent development of depression and anxiety in patients with DE, timely and early diagnosis of the latter prevents the development of acute vascular catastrophes [3,13]. In order to determine the state of anxiety, patients, depending on the degree of compensation, were divided into 2 groups: 1gr.-these are patients with compensation, 2gr.-with decompensation of diabetes. In patients with compensation, anxiety was absent in 60% of cases, and was moderate in the remaining 40% of patients. In patients with decompensated DM, only 16% of patients had no anxiety, in the remaining 84% of patients moderate anxiety prevailed, while in these

patients the average Spielberg scale score was 38.4± 5.8 points. It should be noted that personality anxiety prevailed in 80% of patients. Also, in patients with predominance of atherosclerosis in the vertebral arteries, anxiety was more pronounced - 35.4 ± 2.8 points, compared to those with predominant atherosclerosis in the carotid arteries. The average score was 30.5±2.9 points.

The development of DE is a consequence of the interaction of risk factors (duration and severity of diabetes, hypertension, dyslipidemia, hypercoagulation, age, smoking). Knowing the possible risk factors, it is possible to predict adverse consequences taking into account the complex impact of numerous factors, which allow not only to take into account the degree of probability of such consequences, but also to isolate from the many risk factors those that seem to be the most significant [5].

In each patient, we assessed the following factors: gender, age, BMI, smoking, duration of hypertension, hypercholesterolemia, severity of anxiety. At

the same time, the patients were divided according to the duration of the disease: group 1 included patients with a duration of 2 to 5 years – 22 (36.6%), group 2 – 5-8 years - 38 (63.4%). Among the examined patients, 32 patients were diagnosed with hypertension, while according to the duration of hypertension, patients were divided into 2 groups: 1-5 years – 14 (23.4%) and more than 5 years – 18 (30.0%). Among them, stage 1 hypertension had 8 (25%) patients, stage 11 - 13 (40.6%) and 2 (34.3%) had stage 3 hypertension.

For each factor in both groups (the studied main and control), likelihood coefficients were calculated (P osn. To do this, the probability of the indicator of each gradation of factors (absolute number) was divided by the total number of observations in each group of factors.

Below is a prognostic matrix regarding the formation of DE in patients with type 2 diabetes by risk factors for its development (Table 3).

Table 4

Integrated and prognostic assessment of risk indicators of DE in patients with type 2 diabetes

Groups Factors	Gradations of factors	Main group n-36		Control Group n-20		Likelihood ratio	Range Risk	
		abs.	P1	abs.	P2		min	max
		36	P1=pi/n	20	P2=pi/n	P1/P2	P Int	P Int
Gender	Male	18	0,30	7	0,35	0,71	0,70	2,08
	Female	42	0,70	13	0,65	2,05		
Age, years	38-44	8	0,11	5	0,25	0,44	0,39	1,49
	44-54	25	0,39	8	0,4	0,98		
	54-60	27	0,5	7	0,35	1,43		
Hypercholesterolemia, mmol/l	5,3-6,1	22	0,19	17	0,37	1,26	1,19	2,35
	5,8-7,3	38	0,47	3	0,48	2,21		
Duration of AH, years	1-5	14	0,17	11	0,45	0,42	0,19	1,47
	5 or more	18	0,81	9	0,55	1,40		
Smoking in men	No	6	0,06	4	0,2	0,95	1,47	2,94
	Есть	6	0,19	3	0,25	2,54		
Severity of anxiety	Low	10	0,54	4	0,21	0,48	0,50	1,97
	Moderate	10	0,69	2	0,28	1,61		
BMI, kg/m2	Overweight	28	0,48	4	0,29	0,56	0,44	1,87
	Obesity	32	0,78	3	0,32	1,12		
Total score							4,88	14,21

As can be seen from Table 4, the greatest risk of developing DE in patients with type 2 diabetes are: gender-women (Rint= 2.08), age group 54-60 years (Rint= 1.49), hypercholesterolemia (Rint= 2.35), smoking men (Rint= 2.94), according to the severity of anxiety-moderate anxiety (Rint= 1.97), duration of hypertension (Rint= 1.47), BMI 30 kg / m2 (Rint=1.87).

Thus, DPN was diagnosed in patients with type 2 diabetes according to the subjective and objective NDSm scale. Dopplerography data of bracheocephalic and vertebrobasilar vessels showed that in patients with widespread atherosclerosis of the above vessels, atherosclerosis of the vertebral arteries with vertebrobasilar insufficiency prevails. At the same time, the severity of the anxiety state depends on the state of diabetes compensation and on the severity of damage to the vertebral arteries. Also, an assessment of the integrated and prognostic assessment of

risk factors for the development of DE showed that the leading factor is in descending order - smoking, hypercholesterolemia, the sex of patients is women, the severity of anxiety - moderate anxiety prevails, BMI and the age of patients 54-60 years.

Conclusions:

1. In patients with type 2 diabetes, a decrease in speed characteristics, an increase in peripheral resistance indices indicate a progressive decrease in the elastic-tonic properties of the vascular wall, which ultimately contributes to a decrease in cerebral blood flow and the development of dyscirculatory encephalopathy

2. The severity of anxiety disorders depends on the degree of diabetes compensation, while in 84% of patients with diabetes decompensation moderate anxiety prevailed, while the average Spielberg scale was 37.4 ± 5.8 points.

3. Evaluation of integrated and prognastic assessment of risk indicators of DE in patients with type 2 diabetes showed that the leading risk factors in the occurrence of DE in patients with type 2 diabetes are: smoking men (Rint=2.94), hypercholesterolemia (Rint=2.35), by gender - women (Rint=2.08), duration of hypertension (Rint=1.47), by severity of anxiety-moderate anxiety (Rint=1.97), BMI 30 kg/m2 (Rint=1.87) and age group 54-60 years (Rint=1.49).

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