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ASSESSMENT OF COGNITIVE STATUS IN CEREBRAL DISORDERS IN PATIENTS WITH DIABETES MELLITUS

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ABSTRACT

Diabetes mellitus is one of the most significant risk factors for the development of cerebrovascular disorders, which can lead to a decrease in cognitive functions. This study examines the relationship between diabetes mellitus and cognitive impairment due to cerebral changes.

Key words: Mini-Cog test, cognitive status, diabetes mellitus, cerebral disorders.

INTRODUCTION

Background. Stroke is a leading cause of death worldwide. A strong inflammatory response characterized by activation and release of cytokines, chemokines, adhesion molecules, and proteolytic enzymes contributes to brain injury after stroke. Stroke outcomes are worse in diabetics, resulting in increased mortality and disability. Diabetes induces chronic inflammation manifested by the formation of reactive oxygen species, expression of proinflammatory cytokines, and activation/expression of other inflammatory mediators. The increase in proinflammatory processes due to diabetes appears to be further accelerated after

cerebral ischemia, leading to increased ischemic injury. Hypoglycemia is a side effect of glucose-lowering therapy in diabetics and is known to induce proinflammatory changes and aggravate brain injury in experimental stroke. Here, we review the available literature on the influence of neuroinflammation on increased ischemic brain injury in diabetics. We also describe the role of diabetes mellitus in neuroinflammation and ischemic brain injury in diabetics. Understanding the role of neuroinflammatory mechanisms in worsening stroke outcomes in diabetics may help limit ischemic brain injury and improve clinical outcomes.

The aim of the work is to assess the cognitive status of patients with diabetes mellitus under conditions of various degrees of cerebral impairment. The study included patients with diabetes mellitus type 1 and 2, who underwent neuropsychological diagnostics, assessment of metabolic parameters, and neuroimaging methods (MRI/CT of the brain). The data obtained will allow us to identify early signs of cognitive deficit, establish its relationship with the severity of cerebral impairment and the duration of diabetes, and develop approaches to the prevention and correction of higher mental function impairment in this category of patients.

To determine the cognitive status, we used the Mini-Cog test, in which the subjects scored the following points: the control group - 5 points, group 1 - 3.8±0.05 points, which confirms the presence of moderate cognitive disorders, patients of group 2 scored 4.2±0.05 points, which corresponds to mild cognitive disorders (Table 1.1).

Table 1.1

Assessment of cognitive status using the Mini-Cog test, M±m

	Control group	1 group	2 group
Mini-Cog test	5.0±0.03	3.8±0.05***	4.2±0.05**

Note: * - differences relative to the control group data are significant (*** - P< 0.001), ** - P< 0.01, *- P< 0.05

After identifying cognitive disorders in the subjects, we moved on to a more detailed study of the cognitive sphere using a neuropsychological test such as MoCA, as well as the “Schulte table” method to determine the speed of information processing.

The test results showed that groups 1 and 2 had cognitive impairment to varying degrees.

a MoCA test score of 29.1±0.2 points, the patients in group 1 scored 22±0.2 points on the MoCA test, and the patients in group 2 scored 24±0.3 points on the MoCA test (Table 1.2).

Table 1.2

Results of cognitive status using the MoCA test , M±m

	Control group	1 group	2 group
MoCA test	29.1±0.2	22±0.2***	24±0.3***

Note: * - differences relative to the control group data are significant (*** - P< 0.001), ** - P< 0.01, *- P< 0.05

The results of the sensorimotor reaction according to the Schulte table showed the following indicators. The control group showed no impairment in the cognitive sphere and the Schulte test was - 36.2±0.5¢¢, while in patients of group 1 the speed of the sensorimotor reaction according to the Schulte test was - 56.4±0.8¢¢, and in patients of group 2 the speed was - 42.2±0.6¢¢ (Table 1.3).

Table 1.3

Results of sensorimotor reaction according to the Schulte table, M±m

	Control group	1 group	2 group
Schulte test	36.2±0.5	56.4±0.8***	42.2±0.6***

Note: * - differences relative to the control group data are significant (*** - P< 0.001), ** - P< 0.01, *- P< 0.05

The identified disturbances in the cognitive sphere, especially in patients of group 1, confirm the fact that diabetes insidiously damages the cortical and subcortical structures of the brain and worsens intellectual and mnemonic processes, which in turn leads to a slowdown in the rate of sensorimotor reactions and a decrease in the speed of switching attention.

Next, we examined the activity of attention and memory using the “Memorizing 10 Words” test according to the method of A. R. Luria (Table 1.4).

Table 1.4

Results of attention and memory activity using the “Memorizing 10 words” test according to the A. R. Luria method, M±m

"10 Words Memorization" Test	Control group	1 group	2 group
Short-term memory	8.9±0.1	3.9±0.2***	5.8±0.2***
Long-term memory	9.2±0.1	4.7±0.2***	6.8±0.2***
Productivity of memorization	91.8±0.8	53.8±0.8***	72.6±0.5***

Note: * - differences relative to the control group data are significant (*** - P< 0.001), ** - P< 0.01, *- P< 0.05

In patients of group 1, the CP was 3.9±0.2 words, DP - 4.7±0.2, and PZ was 53.8±0.8, i.e. these indicators were 2.28 (P< 0.001); 1.95 (P< 0.001) and 1.70 (P< 0.001) times lower than the values of the control group, respectively.

In patients of the 2nd group, the values of CP and DP, as well as PZ were 5.8±0.2; 6.8±0.2 and 72.6±0.5, respectively. These values are 1.53 (P< 0.01); 1.35 (P< 0.01) and 1.26 (P< 0.01) times lower than the indicators of the control group of individuals.

Thus, the neuropsychological test for memorizing 10 words that we conducted revealed a more pronounced decrease in the indicators of both CP and DP, as well as PZ in patients of both groups. Compared with the indicators of group 2, in patients of group 1 the above indicators were significantly lower by 1.48 (P< 0.01); 1.45 (P< 0.01) and 1.35 (P< 0.01) times, respectively. The volume of short-term reproduction is significantly reduced compared to the norm, which indicates a violation of short-term verbal memory, more pronounced in patients with CCI with type 2 diabetes.

Next, we examined the concentration and stability of attention in patients of both groups using the Bourdon correction test (Table 1.5).

Table 1.5

Average indicators of concentration and attention stability according to the Bourdon correction test in the examined patients and control group, M±m

Indicators	Control group	1 group	2 group
Concentration of attention	500.6±12.2	187.2±6.8***	248.1±4.2***
Sustainability attention	4.6±0.05	3.1±0.02***	3.9±0.02***

Note: * - differences relative to the control group data are significant (*** - P< 0.001), ** - P< 0.01, *- P< 0.05

The study revealed that in the control group, attention concentration was 500.6±12.2, and attention stability was 4.6±0.05.

In patients of group 1, the concentration of attention was 187.2±6.8, and the stability of attention was 3.1±0.02.

These indicators were statistically significantly lower by 2.67 (P< 0.001) and 1.48 (P< 0.01) times compared to the values of the control group.

In patients of group 2, these indicators were equal to 248.1±4.2 and 3.9±0.02 (P< 0.001) (Fig. 1.4).

These indicators were statistically significantly lower by 2 times (P< 0.001) and 1.17 (P< 0.05) times compared to the values of the control group. Cognitive dysfunction with its wide spectrum, from mild cognitive impairment (MCI) to dementia, is one of the chronic complications of diabetes mellitus [4,6]. Both diabetes and cognitive impairment are more common in old age.

There is strong evidence that type 2 diabetes increases the risk of developing dementia in the form of multi-infarct dementia and mixed dementia [5, 10]. There are some strong associations between diabetes and vascular dementia over 100%-160% compared to Alzheimer's disease, which is 45% to 90% [1,3]. The long-term risk of dementia is doubled in patients with diabetes [12]. Even in the prediabetic state; there is an increased risk of dementia that is not associated with the future development of diabetes [151, 104-106]. Patients with diabetes have a more rapid deterioration in cognitive function than older people without diabetes [2, 8]. Diabetes is associated with a 1.5- to 2-fold increased risk of cerebrovascular accidents [7], and the relative risk of stroke increases by 1.15 (95% CI: 1.08-1.23) for every 1% increase in HbA1C [8,11].

In recent years, the association of diabetes with memory impairment has been well established. In 2016, Moulin S and colleagues [9] published the results of their comprehensive prospective study with a large sample from 1992 to 2007. Patients in this cohort were examined at baseline and five times during the 15 years of the study. During each assessment, participants were given a screening interview for dementia as part of a home visit. They followed 1702 subjects and showed that diabetes reduces their cognitive abilities due to cardiovascular impairment [7,11].

The results of the Edinburgh Type 2 Diabetes Study, which was conducted to assess this correlation, were published in 2013, and examined terminal brain natriuretic peptide (NT- proBNP) [1,7,8]. Seven neuropsychological tests were also performed at baseline and after 4 years. They found that stroke and subclinical markers of cardiovascular disease and atherosclerosis were associated with cognitive decline in older patients with type 2 diabetes [11,12].

In 2019, a recent collaboration between the Mayo Clinic and Shanghai was reported. In this study involving a significant number of patients, the impact of diabetes on patients' cognitive function was obvious. This was, of course, independent of patients' gender, age, and possible cardiovascular risk factors [7,8].

One study assessed the association between type 2 diabetes and cognitive impairment, and patients with diabetes had lower MMSE scores than those without diabetes ($P < 0.01$) [205, 2411–2412]. Diabetes was also associated with increased odds of cognitive decline as measured by MMSE [odds ratio (OR) 1.9; 95% CI: 1.01–3.6]. There was also a statistically significant correlation between disease duration and cognitive dysfunction ($P = 0.001$). The same correlation was found for the quality of diabetes control ($P = 0.002$).

In another study conducted by Tan R. et al . [2, 5] on 4206 subjects, they investigated whether and to what extent vascular and degenerative brain lesions mediate the association of diabetes with poor cognitive performance. They assessed cortical and subcortical infarcts and higher white matter lesion volume. They also assessed neurodegenerative processes on magnetic resonance imaging. The results of this cross-sectional study showed that patients with diabetes had significantly lower processing speed and executive functions than others. However, their memory function score was also not better [6,9,10].

The role of diabetes in neurodegeneration has been confirmed by neuroimaging and neurological studies [9]. MRI studies have shown that type 2 diabetes is closely associated with brain atrophy [4,9,13]. The rate of global brain atrophy in type 2 diabetes is 3 times higher than in normal aging [12].

Summary: Subjective complaints were significantly more common in patients of group 1; patients more often complained of cephalgia, vertigo, and tingling in the arms and legs.

During the objective examination of neurological symptoms in patients of group 1, the following signs were revealed: 45 (38.7%) patients had mild pyramidal insufficiency; 58 (51.3%) patients had oral automatism reflexes; 78 (67.2%) patients had central paresis of the VII and XII pairs of cranial nerves; 27 (23.3%) patients had convergence weakness; 65 (56.0%) patients had signs of impaired motor coordination in the form of instability in the Romberg pose, while patients of group 2 had fewer symptoms.

The study of cognitive status showed that the Mini-Cog test scores corresponded to moderate cognitive impairment in patients of group 1 and mild cognitive impairment in patients of group 2. A detailed analysis of the cognitive sphere using the MoCA neuropsychological test , as well as the "Schulte table" method for determining the speed of information processing, were significantly lower in patients of group 1 compared to patients of group 2 and the control group.

The results of the “Memorizing 10 words” test according to the A. R. Luria method, with the help of which it is possible to evaluate the activity of attention and memory, revealed that short-term and long-term memory, as well as memorization productivity, were reduced in patients of the 1st group.

A study of concentration and attention stability in patients of both groups using the Bourdon correction test established that in patients of group 1 these indicators were significantly reduced, compared with the control group and patients of group 2.

Thus, in conclusion, it can be said that chronic cerebral ischemia, which arose as a result of chronic cerebrovascular accident itself leads to the development of certain disorders of the cognitive sphere. Patients who have diabetes mellitus suffer doubly from a decrease in cognitive function, due to the development of atherosclerosis and metabolic disorders.

CONCLUSION

Our study supports the hypothesis that MF/MS cancers are biologically more aggressive than monofocal tumors. This type of cancer has a high tendency to metastasize and predicts the unfavorable outcome of the disease.

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