



SPECIFIC CHANGES IN THE NERVOUS SYSTEM IN PATIENTS WITH TYPE 2 DIABETES

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Abstract

Cerebrovascular diseases and diabetes mellitus are among the leading medical and social problems. The main factor causing the development of polyneuropathy, angiopathy and brain damage in patients with diabetes mellitus is chronic hyperglycemia. Diabetic polyneuropathy is recognized as the most frequent specific complication of diabetes mellitus. Its diagnosis in the presence of sensory, motor, cognitive and speech disorders in patients with cerebrovascular pathology can be difficult. Modern strategies for the treatment of diabetic polyneuropathy involve the prescription of antioxidant drugs, primarily alpha-lipoic acid. The article discusses the possibilities and prospects for the use of alpha-lipoic acid in diabetic polyneuropathy and cerebrovascular diseases.

Keywords: Diabetes, cerebrovascular disease, microcirculation, dementia, neurodegenerative process.

Cerebrovascular diseases are one of the most pressing medical and socio-economic problems. In the structure of total mortality, acute cerebrovascular accidents make up 21.4%, and disability after a stroke reaches 3.2 per 10 thousand of the population, ranking first among all causes of primary disability (1).

In terms of mortality, cerebrovascular diseases are second only to heart diseases and tumors. The costs of treatment, medical rehabilitation of patients with cerebrovascular pathology, and losses in production are damaging the economies of many developed countries. In Russia, the number of such patients is 4 times higher than in the United States and Western Europe (3). Therefore, the main tasks at the present stage are to reduce the incidence of cerebrovascular disorders and the provision of effective medical care.

Diabetes mellitus (DM) is one of the most important risk factors for stroke. Currently, diabetes is a global medical and social threat, the growth rate of which has reached the scale of a global epidemic [5]. The International Diabetes Federation (IDF) estimates that there are 463 million people with diabetes in the world, 63% of them of working age. At the same time, at least half of the cases of diabetes were not diagnosed [6].





In the context of the global epidemic of diabetes, the problem of acute stroke and chronic CVD in such patients is becoming more and more medico-social. The presence of diabetes increases the risk of stroke in all age groups, but to the greatest extent in the working-age population under 65 years of age. In this case, the relative risk of stroke increases up to 1.8 - 3.8 times [3]. In total, patients with ischemic stroke (IS) and diabetes mellitus are younger, more often have a history of myocardial infarction (MI), suffer from arterial hypertension (AH) and dyslipidemia than patients without diabetes [9].

The measures taken by the medical community to correct risk factors for vascular diseases over the past decades are aimed at a significant reduction in the frequency of IS. However, along with significant successes in normalizing systolic blood pressure (BP) and reducing the prevalence of smoking, the progressive increase in the incidence of diabetes played a negative role in this positive trend.

According to Rawshani A. et al. (2018), even when all factors are controlled, the risk of stroke in diabetic patients increases by 22% at the age of less than 55 years. In the presence of other risk factors, the likelihood of stroke in persons with T2DM at the age of 55-65 increases by 2.79 times, in persons under 55 years of age - by 6.23 times. The most significant predictors of stroke are elevated levels of glycated hemoglobin (HbA1c) and systolic blood pressure, long duration of diabetes mellitus, physical activity, and atrial fibrillation (AF). Currently, there is no doubt about the role of type 2 diabetes mellitus (type 2 diabetes) in the occurrence of vascular pathology of the brain. Having type 2 diabetes increases the likelihood of developing a stroke by 2-6 times. In the MRFIT (The Multiple Risk Factor Intervention Trial), the risk of death from stroke among patients with diabetes was 2.8 times higher than in patients without diabetes, while the risk of death from ischemic stroke was 3.8 times higher. from subarachnoid hemorrhage - by 1.1 times and intracerebral hemorrhage - by 1.5 times [1]. The main mechanisms of the development of cerebral vascular pathology in type 2 diabetes are atherosclerotic lesions of large and small cerebral arteries, microcirculation disorders [2-4].

It has been established that not only hyperglycemia is a risk factor for cardiovascular diseases, but also insulin resistance is closely associated with an increased risk of cerebral stroke [7, 8]. Violation of insulin sensitivity is more often observed in young patients with overweight; it is associated with lacunar cerebral infarction and stroke with persistent neurological deficit [9].

Insulin is directly involved in the implementation of a number of cognitive functions, and disorders of its metabolism are accompanied by the emergence of a number of syndromes of impaired neurological functions and cognitive disorders [10, 11]. Insulin





is involved in the regulation of the production of protein - the precursor of amyloid and the product of its metabolism - amyloid beta - the main component of amyloid deposits. Insulin regulates phosphorylation of tau protein, which is the basis of neurofibrillary formations in patients with cognitive impairments [12].

It is believed that insulin is involved in the exchange of beta-amyloid and reduces the rate of its degradation processes (inhibiting the corresponding enzymes), thereby contributing to the accumulation of abnormal proteins in the brain tissue and the progression of Alzheimer's disease. To a certain extent, this is confirmed by the high incidence of insulin resistance in patients with Alzheimer's disease [13].

Over the past two decades, the concept of risk factors for cerebrovascular complications has expanded significantly. These factors, along with traditional ones (arterial hypertension, dyslipidemia, smoking), began to include an increase in the thickness of the intima / media of the common carotid arteries, asymptomatic stenosis of the main arteries of the head, markers of inflammation, hyperfibrinogenemia and other disorders in the hemostatic system [4].

Clinical features of cerebrovascular diseases in type 2 diabetes In addition to the fact that type 2 diabetes is a risk factor for cerebrovascular diseases, disorders of carbohydrate metabolism largely determine the clinical features and severity of neurological symptoms in patients with cerebrovascular accidents. It was found that a high level of glucose in the acute stage of the disease is significantly associated with a higher mortality rate and severe disability in patients with ischemic stroke, especially in the case of extensive infarction or total cerebral ischemia [10]. Fasting glucose levels exceeding 6.1 mmol / L and glycemic levels at any time during the day exceeding 7.2 mmol / L at the time of hospitalization are independent significant risk factors for death and insignificant recovery of neurological functions. The likelihood of death due to stroke in patients with type 2 diabetes is as high as in patients with recurrent stroke, and the presence of concomitant cardiovascular diseases significantly increases the likelihood of death from stroke [8].

It is noteworthy that hyperglycemia in patients on admission to hospital for subarachnoid hemorrhage is also associated with higher mortality and less complete recovery of neurological functions [9].

It should be noted that the clinical features of ischemic stroke are also closely associated with the glucose level at the time of its development. There is evidence that the effectiveness of selective thrombolysis using tissue plasminogen activator (tPA) was lower in patients with initially higher blood glucose levels (more than 7.8 mmol / L)



The presence of type 2 diabetes predisposes to the development of certain types of stroke [1]. Analysis of the results of observation of 4064 patients with stroke for an average of 5.3 years made it possible to establish that intracerebral hemorrhages were relatively less common in patients with type 2 diabetes compared with individuals with normal carbohydrate metabolism, and lacunar strokes caused by the pathology of small arteries were significantly more frequent. and atherothrombosis, while there were no significant differences in the incidence of cardioembolic stroke [9]. At the same time, in another series of observations, which included 937 patients with type 2 diabetes out of a total of 4537 patients with stroke from 7 European countries, an association was established between the presence of type 2 diabetes and a more pronounced neurological deficit by the end of the 3rd month of the disease [3]. In addition, these patients had a more severe disability. The authors noted the prevalence of lacunar infarctions in patients with disorders of carbohydrate metabolism, clinically manifested by paresis of the extremities and dysarthria.

At present, the problem of cerebral infarctions, not accompanied by a clear focal neurological deficit of transferred infarctions in the deep or periventricular parts of the white matter, caused by ischemia in the areas of blood supply of small perforating arteries, is of great interest. There is evidence that cerebral infarctions, despite the absence of clear clinical manifestations, are closely associated with the unfavorable course of various forms of cerebral vascular pathology, in particular, with repeated strokes and progressive vascular dementia [4]. The risk of developing cerebral infarctions increases sharply with a combination of type 2 diabetes and arterial hypertension, and the presence of multiple postischemic foci is observed in such patients much more often than in single patients [5]. It is noteworthy that the frequency of cerebral infarctions is determined, first of all, by the presence of type 2 diabetes and to a lesser extent depends on the severity of arterial hypertension. The frequency of detection of postischemic foci is higher in patients with diagnosed type 2 diabetes and insulin resistance [7]. At the same time, the point of view about the role of type 2 diabetes as an independent cause of cerebral infarction has not been confirmed in all studies [8].

Diffuse white matter lesion is leukoaraiosis, according to Hijdra et al. [3], significantly more often observed in patients with type 2 diabetes compared with individuals with normal carbohydrate metabolism. This dependence has not been confirmed in other studies [13].

In recent years, it has been established that type 2 diabetes is a risk factor not only for cerebral stroke, but also for chronic disorders of cerebral circulation, as well as processes accompanied by a progressive decline in cognitive functions. The results of



population studies indicate a significant relationship between the presence of type 2 diabetes and the risk of both vascular dementia and Alzheimer's disease [4].

There is a certain genetic predisposition to the development of Alzheimer's disease in patients with type 2 diabetes. Thus, the combination of type 2 diabetes and the ApoE4 allele approximately doubles the risk of developing Alzheimer's disease compared to individuals with only the ApoE4 allele [5]. By itself, the presence of type 2 diabetes does not lead to the deposition of amyloid and the development of the clinical picture of Alzheimer's disease, but the available data indicate a significant increase in the number of neurofibrillary glomeruli and the accumulation of amyloid in individuals with this genotype, as well as the role of diabetes mellitus as a risk factor for Alzheimer's disease and mixed dementia [16]. However, not all studies support a role for type 2 diabetes as a risk factor for nonvascular dementia. Thus, a 5-year follow-up of 5574 individuals who initially had no cognitive impairment made it possible to establish that the existing type 2 diabetes was significantly associated with vascular dementia, as well as mild cognitive impairments that did not reach the degree of dementia. At the same time, no connection was established between disorders of carbohydrate metabolism and the development of Alzheimer's disease and the onset of mixed dementia [7]. Similar data on the relatively low risk of Alzheimer's disease in patients with type 2 diabetes were obtained as a result of 4-year follow-up of 1262 members of the multiethnic population of the elderly [1].

In patients with type 2 diabetes, an increase in the frequency and severity of cognitive impairments caused by vascular brain damage was found. The combination of type 2 diabetes and arterial hypertension is especially unfavorable. Interestingly, according to the results of the NHANES III study, in persons under the age of 60 who have not previously suffered a cerebral stroke, neither type 2 diabetes nor hypertension alone lead to significant impairments of higher cerebral functions. The combination of these two diseases is accompanied by a noticeable decrease in cognitive functions [9]. The mortality rate among these patients is 2.4 times higher than among persons of comparable age in the population.

Many large multicenter placebo-controlled studies have been devoted to the correction of hemostasis disorders for the purpose of secondary prevention of strokes and myocardial infarctions [11], which showed a greater efficacy of aspirin in combination with clopidogrel compared with aspirin monotherapy. The American Diabetes Association in 2001 [12] recommended the use of aspirin for primary prevention in diabetic patients with a high risk of macrovascular complications. However, acetylsalicylic acid blocks only one of the pathways of platelet activation and does not affect others, does not block the primary adhesion of platelets to the damaged





endothelium, or the attachment of fibrinogen to its receptors on the surface. The high mortality rates due to CCD, including in patients with diabetes, raise the question of the need to search for active measures for the diagnosis, treatment and prevention of strokes in this category of patients. The peculiarities of the state of carbohydrate metabolism in patients with T2DM and CVD, their relationship with pathogenetic subtypes, the severity and prognosis of stroke, the hemostasis system and the state of the vascular wall of the brachiocephalic arteries in patients with ischemic CCD remain insufficiently clarified.

Conclusion

In conclusion, it can be stated that medicine has a wide range of knowledge about the risk factors for cerebrovascular diseases in type 2 diabetes and a wide diagnostic potential for their detection. Only a strategy aimed at maximizing correction of all existing risk factors can be recognized as effective.

Literature

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