ISCHEMIC STROKE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

Sayitov Sunnatillo Hayit o'g'li
City Clinical Hospital No. 7, Neurologist
Tashkent, Uzbekistan
Nurilloyeva Sitorabonu Alisher qizi
Tashkent State Medical University, Clinical Resident
Tashkent, Uzbekistan

Abstract: Type 2 diabetes mellitus adversely affects the course of ischemic stroke, aggravating its clinical manifestations and increasing the likelihood of a fatal outcome. The main pathogenetic mechanism underlying the development of stroke in the setting of diabetes mellitus is primarily related to the effects of a pathologically altered vascular wall on hemorheology and the processes of hemostasis and fibrinolysis. In the present study, a correlation was established between blood glucose level and the severity of neurological deficit on days 1 and 21: the higher the glucose level, the more pronounced the neurological deficit. Therefore, more thorough history taking is required in patients with stroke, with timely assessment of glycemia and appropriate treatment.

Keywords: ischemic stroke, type 2 diabetes mellitus, glycemia, lacunar infarction, European Stroke Scale.

Type 2 diabetes mellitus in the medical history is associated with increased severity of stroke manifestations, an increased probability of recurrent stroke during the subsequent 10 years, and higher mortality in the setting of acute cerebrovascular events (20–40%) [1]. The pathogenetic mechanism underlying the development of ischemic stroke in the setting of diabetes mellitus is primarily related to the effects of a pathologically altered vascular wall on hemorheology, hemostasis, and fibrinolysis. Diabetes mellitus contributes to the development of ischemic stroke. Hyperglycemia causes excessive uptake and accumulation of glucose within cells; primarily affected are retinal endothelial cells, renal glomerular mesangial cells, and endothelial cells of the peripheral nerves. Alternative metabolic pathways are activated, resulting in the formation of glycation products and reactive oxygen species. The resulting free radicals activate lipid peroxidation, leading to destruction of cell membranes and DNA damage [2]. Interaction of free radicals with nitric oxide (NO) results in the formation of peroxynitrite, which reduces NO-dependent vasodilation. This contributes to the development of endothelial dysfunction. In diabetes mellitus, the oxygen-transport function of hemoglobin deteriorates as a consequence of glycation,

subsequently resulting in tissue hypoxia. Reduced erythrocyte deformability and increased erythrocyte aggregability impair blood flow in the microcirculatory bed and contribute to vascular wall injury [3]. Dysfunction of the hemostatic system is manifested by increased fibrinogen levels, increased activity of coagulation factors VII and VIII, and decreased levels of antithrombin III and thrombomodulin.

Non-enzymatic glycation under conditions of hyperglycemia reduces the clearance of atherogenic lipoprotein fractions and prolongs their circulation time, while also enhancing low-density lipoprotein (LDL) oxidation. These metabolic processes create conditions conducive to vascular atherogenesis. Plaque development leads to narrowing of the arterial lumen and is one of the causes of cerebral hypoxia. In patients with diabetes mellitus, morphological changes in the vascular wall and impaired glucose utilization result in insufficient oxygenation of neurons, leading to hypoxia of brain tissue. Metabolic disturbances that develop, as in stress reactions—lactic acidosis, oxidative stress, and potentiation of glutamate–calcium excitotoxicity—under conditions of cerebral hypoxia lead to further expansion of the infarct area. Based on these findings, a more severe course of ischemic stroke and a poorer prognosis may be expected in patients with diabetes mellitus.

During the hyperacute phase of stroke, hyperglycemia may have a positive role. Excess glucose within cells becomes a substrate for anaerobic glycolysis and thus serves as an additional energy source under conditions of insufficient neuronal oxygenation. This fact may explain the occurrence of hyperglycemia during the first 24 hours of ischemic stroke in patients without a history of diabetes mellitus. A high glycemic profile in patients with diabetes mellitus during the first day of stroke leads to pronounced or moderate impairments of vital functions. The dynamics of changes in vascular-platelet hemostasis demonstrate increased platelet aggregatory activity in these patients; ADP levels are also elevated up to day 21. von Willebrand factor, the principal marker of endothelial alterations, is most markedly elevated in patients with type 2 diabetes mellitus; its level increases during the first three weeks and decreases by the third month. An increased number of damaged erythrocyte forms is also detected, with elevated levels persisting until day 21. Regarding changes in the lipid profile, against a background of a marked decrease in HDL cholesterol and increases in total cholesterol and LDL cholesterol, significant increases in triglycerides and the atherogenic index are observed only in patients with type 2 diabetes mellitus [4].

A study was conducted with the primary objective of establishing a correlation between blood glucose level and the characteristics of ischemic stroke development. The study included 50 patients aged 45 to 75 years with acute ischemic stroke. The main inclusion criteria were ischemic stroke confirmed by computed tomography (CT), hospitalization within no more than 24 hours from stroke onset, absence of

traumatic or inflammatory lesions of the brain parenchyma and brain neoplasms, and a history of diabetes mellitus or its detection on the basis of laboratory findings, defined as fasting glycemia above 7 mmol/L throughout the observation period. The severity of the neurological deficit was assessed using the European Stroke Scale on days 1, 5, and 21 after stroke onset. The nature, localization, and size of the ischemic stroke lesion were determined by CT according to OSCP criteria. Venous plasma glucose concentration was measured in the fasting state on days 1, 3, and 5 after stroke onset. The obtained results were statistically processed using SPSS 13.0. Differences were considered statistically significant at $p<0.05$.

Results demonstrated an association between serum glucose concentration during the first 24 hours and the severity of neurological deficit on days 1 and 21. The lowest scores on the European Stroke Scale were observed in patients with the highest glucose concentrations. A more pronounced neurological deficit on day 21 was recorded in patients with higher glucose levels on day 1 ($p<0.05$).

The relationship between glucose concentration on days 3 and 5 after ischemic stroke and the severity of neurological deficit on days 1 and 21 was not statistically significant. Among deceased patients, glucose concentration on day 1 was higher than in survivors (9.3±0.8 mmol/L and 5.4±0.6 mmol/L; $p<0.01$); glucose concentration was also higher among deceased patients on day 3 (8.7±0.6 mmol/L and 5.1±0.5 mmol/L; $p<0.05$) and day 5 of stroke (9.3±0.5 mmol/L and 5.0±0.4 mmol/L; $p<0.01$). An association was identified between glycemia level and fatal outcome ($p<0.01$). Lacunar ischemic strokes were more frequent among patients with type 2 diabetes mellitus (37.8% and 20.2%; $p<0.01$).

Thus, an association was identified between disorders of carbohydrate metabolism and the mechanisms underlying the development of ischemic stroke. The presence of type 2 diabetes mellitus was significantly associated with a higher frequency of lacunar infarctions. Therefore, more thorough history taking, timely detection of glycemic abnormalities, and appropriate treatment of glycemia are necessary in patients with ischemic stroke.

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