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Acute Ischemic Stroke in Patients with Endocrine Disorders

Key words*: ischemic stroke, endocrine disorders, diabetes, hypothyroidism.*

Annotation: *The prevalence of endocrine disorders among patients with ischemic stroke, clinical features of acute stroke in patients with comorbid endocrine pathology, and the impact of diabetes and hypothyroidism on stroke case fatality is studied. Type 2 diabetes significantly increased the risk of case fatality in patients with ischemic stroke and it was associated with increased stroke severity of deep functional deficit.*

Introduction. Endocrine disorders are among significant risk factors for cerebrovascular diseases and stroke (2). Recent studies suggest that endocrine pathology not only increases the risk of stroke, but also contributes to worsening of neurological deficit and disease outcome in stroke patients (3).

The most prevalent type of endocrine pathology among population is thyroid disease (5). Both hyperfunction and hypofunction of thyroid gland are associated with the worse cardiovascular risk profile and progression of cerebrovascular disorders. Thus, hypothyroidism is associated with cardiogenic embolism in consequence of atrial fibrillation, antiphospholipid syndrome, cerebral vasculitis, internal carotid artery compression with enlarged thyroid gland (10). Hypothyroidism leads to progression of atherosclerosis of large and small vessels through increase of low-density lipoprotein cholesterol (4), endothelial dysfunction, elevation of diastolic blood pressure, and hyperhomocysteinemia (9).

Diabetes mellitus is an independent risk factor for stroke that also influences stroke outcome (8). Diabetes potentiates atherogenesis, leads to development of diabetic cardiomyopathy and changes in blood rheology, in particular elevation of fibrinogen level, factor V and factor VII, activation of platelet adhesion and aggregation, inhibition of fibrinolysis (6). Type 2 diabetes is one of the most significant factors of acute decompensation of cerebral circulation. It has been shown that diabetes is associated with severe neurological deficit n stroke patients (8) and high risk of infectious complications of acute stroke (13).

Primary hyperaldosteronism can become the underlying condition for ischemic or hemorrhagic stroke, as it causes hypertension, myocardial infarction, atrial fibrillation and metabolic syndrome. Besides it has been shown that hypokalemic type of hyperaldosteronism is associated with high cardiovascular mortality (6).

Hypercortisolism facilitates occurrence of ischemic (atherothrombotic) stroke indirectly through hyperglycemia, obesity, dyslipidemia, and hypertension. Increased cortisol level potentiates vasoconstrictive effects of catecholamines and leads to insulin resistance (6).

Thus, endocrine disorders directly or indirectly increase the risk of acute cerebrovascular pathology and have a valuable impact on stroke severity and outcome, as they modify the background state of cerebral metabolism, as well as energy needs of the brain and reactivity of neuroimmunoendocrine system. So the aim of our research was the study of the prevalence of endocrine diseases among patients with ischemic stroke, assessment of clinical presentation of stroke in patients with comorbid endocrine pathology, and determination of association between endocrine pathology and stroke case fatality.

Materials and methods. A total of 421 patients hospitalized with acute ischemic stroke were examined. Among them 232 were women and 189 were men. Mean age of the patients was 69.4±0.9 years (67.5±0.8 years in men and 72.2±0.8 in women).

Stroke was diagnosed according to WHO recommendations based on standard criteria (11). Differential diagnosis of stroke subtype was based on clinical data, neuroimaging results (computed and magnetic resonance imaging, carotid ultrasonography), cerebrospinal fluid examination, and autopsy in fatal cases. Ischemic stroke was diagnosed in case of focal impairment of neurological functions that develops acutely (minutes, hours), lasts more than 24 hours and is accompanied (or not accompanied) by characteristic changes on brain tomograms.

The level of consciousness was assessed with Glasgow Coma Scale (GCS, G. Teasdale, B. Jennet, 1974). For the quantification of initial stroke severity the National Institute's of Health Stroke Scale (NIHSS; T. Brott et al., 1989) was used. Neurological evaluation was performed during the first 24 hours after hospitalization. Comorbid endocrine diseases (ICD-10 codes E00-E35) were registered according to specialists' records in patients' medical documentation. The study data were assessed statistically with Student's t-test for the differences between two samples, Fisher's exact test for the analysis of contingency tables. For measurement of association between an exposure and an outcome odds ratio (OR) and its 95% confidence interval (CI) was calculated.

Results. Among all stroke patients 26.6% had comorbid endocrine pathology. The most prevalent was type 2 diabetes which was diagnosed in 21.1±2.0% of patients (23.3±2.8% in women and 18.5±2.8% in men). Duration of diabetes in 34.8% patients exceeded 10 years, in 22 patients (24.7%) – from 6 to 10 years, in 25 cases (25.8%) – less than 5 years. At the same time 11 patients (12.3%) were first diagnosed with diabetes. In two cases duration of diabetes was not determined.

Distribution of patients according to diabetes severity was the following: 51 patients (57.3%) had moderate form, 14 (15.7%) – severe, and 24 (26.9%) – mild form of diabetes. For a constant control of glycemia 82.0% patients regularly used hypoglycemic drugs, while 18.0% patients received insulin therapy.

Thyroid diseases were registered in 20 patients. Acquired primary hypothyroidism as a result of chronic autoimmune thyroiditis, iodine deficiency was recorded from 18 stroke patients, so its frequency comprised 6.0% among women and 2.1% among men. These percentages significantly exceed the levels of prevalence of hypothyroidism in general

population – 1.4-2% in women and 0.2% in men, which is probably related to the age of stroke patients. Most of patients received replacement therapy with synthetic derivatives of L-thyroxine in prestroke period, but 3 patients were first diagnosed with hypothyroidism during their current hospital stay in neurology department.

Thyroid hyperfunction was found in 2 women with ischemic stroke (0.48% of all patients). One case was presented with diffuse toxic goiter, while the other – with autoimmune thyroiditis in thyrotoxic phase. Both patients received thiourea derivatives therapy in prestroke period.

Exogenous Cushing syndrome resulting from continuous glucocorticoid therapy was diagnosed in one female with stroke.

For a comparative analysis of clinical presentation and course of acute ischemic stroke all patients were divided into three groups: 1 – stroke + diabetes (n=89), 2 – stroke + hypothyroidism (n=18), and 3 – 309 patients without clinical evidence of endocrine pathology. All patients received basic and differentiated stroke therapy according to internationally recognized standards that excludes the effect of drug treatment on the study group.

The results of clinical assessment have shown that 249 patients (59.9%) had normal level of consciousness (GCS score 15). 167 patients were found to have altered level of consciousness from mild to severe; mean GSC score was 12.8±0.16.

The distribution of the severity of neurological deficit was the following: mild neurological deficit with NHSS score 0-4 was found in 63 patients (15.1%); moderate stroke was diagnosed in 218 patients (52.4%) with NHSS score ranging from 5 to 14; moderate to severe stroke – 88 patients (21.2%) with NHSS score 15-20; severe stroke with a score 21-40 was diagnosed in 47 patients (11.2%). Mean score of all stroke patients was 12.5±0.41.
Of all stroke cases 71 were fatal. Thus, the overall level of 28-day case fatality in ischemic stroke comprised 17.1±1.79%.

The comparative analysis of acute phase of ischemic stroke in different study groups has shown that patients with type 2 diabetes had more severe clinical presentation of stroke. Mean GCS score in this group of patients 11.9±0.34 was significantly lower in comparison to patients without comorbid endocrine pathology – 13.8±0.17 (p=0.002) which indicated deeper consciousness impairment. The severity of neurological deficit according to NIHSS assessment was also significantly higher in patients with diabetes than in group without endocrine pathology – 13.7±0.93 vs. 10.3±0.40 (p=0.009). Accordingly this group of patients has shown higher level of 28-day case fatality – 24.1±4.59% vs. 13.8±1.99 (p=0.041).

In the group of patients with hypothyroidism the severity of consciousness disturbance and neurological deficit was generally higher than in patients without comorbid endocrine pathology, but these differences were not statistically significant: GCS scores 12.9±1.23 vs. 13.8 ±0.17 (p=0.820), NIHSS 12.2±1.61 vs. 10.3±0.40 (p=0.300). Similar results were obtained regarding stroke case fatality: 15.9±8.91% and 13.8±1.99% (p=0.999). It is likely that this is due to small sample size and a relatively small proportion of patients with clinically significant thyroid hypofunction in the population.

Defining an association of type 2 diabetes and hypothyroidism with ischemic stroke case fatality with OR has shown that diabetes increases the probability of death in acute

period 2.24-fold (95% CI 1.18-3.91). Association in hypothyroidism was not statistically significant (OR 1.63 with 95% CI 0.47-5.21).

The results of previous studies suggest that type 2 diabetes increases the severity of acute stroke period and stroke outcome either directly or potentiating the main stroke risk factors – hypertension, dyslipidemia, coronary heart disease, peripheral artery disease (12). Diabetes is associated with increased frequency of complications after stroke, such as urinary tract infections, multiple organ dysfunction syndrome, deterioration of neurological deficit, recurrent stroke, and enlargement of ischemic brain lesion (7). Stroke case fatality in patients with diabetes depends on increase in blood glucose that leads to brain edema and changes of cerebral vascular reactivity (12). At the same time the other studies failed to find connection between comorbid diabetes and stroke severity on admission to hospital, mortality, duration of hospital stay and ischemic stroke outcome (7).

Some of the studies give evidence that severe neurological presentation of stroke in patients with hypothyroidism can occur due to unfavorable somatic comorbidity such as multiple organ dysfunction caused by deficiency of thyroid hormones. The leading signs of hypothyroidism are cardiovascular disorders, in particular hypertension with significant elevation of diastolic pressure, arrhythmias, dyslipidemia, hypercoagulation, coronary heart disease, and congestive heart failure. The risk of neurological deterioration in the first 48 hours after stroke onset in patients with congestive heart failure is 2.5 times higher, and the risk o fatal stroke is 2.6 times higher than in patients without this cardiac pathology (1).

Thereby comorbid endocrine pathology, particularly type 2 diabetes increases the risk of fatal stroke and the risk of unfavorable outcome with severe general and focal signs that leads to deep functional deficit. Therefore, timely therapeutic compensation of diabetes can reduce disability and mortality in stroke patients. The data regarding association of the other endocrine diseases with stroke severity and outcome require further investigation.

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