DIABETES MELLITUS AS A RISK FACTOR FOR ISCHEMIC STROKE

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ABSTRACT

Ischemic stroke (IS) is a socially significant cerebrovascular disease worldwide and in Bulgaria as well. Our objective was to reveal the prevalence of abnormal blood glucose levels in the patients with of acute ischemic stroke (IS) in adult patients. We examined 258 patients, 129 males and 129 females, at a mean age of 71 years hospitalized in the First Clinic of Neurology, St. Marina University Hospital of Varna, in 2007-2013. Blood glucose levels were followed-up. Diabetes mellitus was diagnosed in 32 of 78 acute IS patients (in 41% of the cases) hospitalized in 2013. Most commonly, they were pathologically elevated. Not only in 2007-2012, but also in 2013, they were higher in males than in females (7,08 mg/mL versus 6,54 mg/mL and 8,04 mg/mL versus 7,89 mg/mL, respectively). These levels varied between 6,14 mg/mL in 2010 and 7,97 mg/mL in 2013. A regular control of the parameters of glucose metabolism (blood glucose, fasting plasma glucose and glycosylated hemoglobin) and strict observation of adult individuals' healthy life-style should warrant a successful IS prevention in our country.

***Key words**: acute ischemic stroke, blood glucose, diabetes mellitus, adult patients, city of Varna*

Introduction

Diabetes mellitus is an established risk factor for coronary artery disease and ischemic stroke (IS) and can induce micro- and macroangiopathy. The abnormal metabolic status in diabetes mellitus causes cerebral arterial dysfunction and these patients require treatment for each metabolic abnormality to attenuate atherogenesis (13). Hyperglycemia is considered to be associated with poor outcomes of IS. It is an indicator of severe IS and can't increase cerebral glucose content but promotes further brain ischemia. Compared with blood glucose level, the cerebral glucose content controlled by glucose transporters is important to maintain the energy supply in the brain, especially in IS patients (17).

The objective of this study was to follow-up the abnormal blood glucose levels in the adult patients with acute IS.

Materials and methods

We examined 258 patients, 129 males and 129 females, hospitalized in the First Clinic of Neurology, St. Marina University Hospital of Varna, in 2007-2013. Their mean age was 71 years (between 70 and 72 years at confidence interval of 95%) and ranged between 53 and 92 years. Blood glucose levels were followed-up. Data were statistically processed by using descriptive and variation analyses. SPSS, version 13,0 software was used. The value of *t*-criterion was considered significant if $p<0,05$.

Results and discussion

It should be emphasized that diabetes mellitus was diagnosed in 32 of 78 acute IS patients (in 41% of the cases) hospitalized in 2013.

Some of our results are presented in three tables.

Both table 1 and table 2 indicate the basic descriptive statistical parameters of the blood glucose levels in male and female acute IS patients for the whole 6-year period between 2007 and 2012 and for 2013, respectively. All these parameters are higher in males than in females.

Table 1. Blood glucose levels (in mg/mL) in male and female IS patients in 2007-2012 (n=180)

blood glucose levels	males	females
mean	7,08	6,54
standard error of the mean	0,31	0,23
standard deviation	2,89	2,14
minimal	3,60	4,00
maximal	18,30	15,20

Table 2. Blood glucose levels (in mg/mL) in male and female IS patients in 2013 (n=78)

blood glucose levels	males	females
mean	8,04	7,89
standard error of the mean	0,47	0,52
standard deviation	2,91	3,27
minimal	3,70	4,30
maximal	18,00	16,20

The annual dynamics of these statistical parameters of all the patients with acute IS for the 7-year period is illustrated in Table 3. Mean blood glucose levels varied between 6,14 mg/mL in 2010 and 7,97 mg/mL in 2013.

Table 3. Annual dynamics of blood glucose levels (in mg/mL) in IS patients in 2007-2013 (n=258)

years	mean	standard error of the mean	standard deviation	minimal	maximal
2007	6,75	0,54	2,94	4,08	18,30
2008	6,61	0,39	2,14	4,08	13,70
2009	6,87	0,47	2,51	3,70	13,00
2010	6,14	0,39	2,14	3,60	14,90
2011	6,90	0,45	2,47	3,90	14,10
2012	7,57	0,54	2,98	4,40	15,20
2013	7,97	0,35	3,07	3,70	18,00

Our data are similar to those most recently reported by foreign authors. They convincingly display the significance of the regular control of blood glucose even in asymptomatic adult patients for the timely prevention of IS.

The results from a retrospective analysis of 26 patients suggest that chronic hyperglycemia may be associated with cerebral microvascular remodeling in humans (6). Within a randomized, blinded, efficacy trial, important new information about preferred management of acute IS patients with hyperglycemia is provided and the potential benefits and risks of intensive glucose control during this acute disease are determined (2).

The role of admission blood glucose levels is investigated in 811 consecutive ISI patients at a median age of 77 years (range, 69-83 years) (12). Of them, 239 (29,47%) present with diabetes mellitus. Median blood glucose levels of IS patients are 11,3 (9,7-15,5) mg/mL. They are significantly higher in diabetes mellitus patients than in non-diabetics (1,63 mg/mL; range, 13,3-

21,4 mg/mL versus 10,7 mg/mL; range, 9,2-12,3 mg/mL) ($p<0,001$). Admission hyperglycemia (≥14,3 mg/mL) is a strong and an independent predictor for 72-hour fatality, especially in patients without any history of diabetes mellitus. Hyperglycemia exerts detrimental effects on the morbidity and mortality of acute IS patients during the first 48 hours poststroke (3). This pathology is very common in these patients and is associated with worse outcome in non-lacunar infarction. The association between hyperglycemia and clinical outcome is studied in 689 consecutive patients with acute lacunar IS in a hospitalized Chinese population (4). Of them, 159 (23,08%) present with diabetes mellitus. In non-lacunar IS, the admission hyperglycemia is independently associated with increased risk of poor outcome ($p=0,0005$) while in lacunar one, it is not associated with functional outcome at one year ($p=0,086$) irrespective of the diabetic status.

Glycosylated hemoglobin A1c (HbA1c) >55 mmol/mol is an independent risk predictor for one-year all-cause mortality after acute first-ever IS in patients across China study (16). A retrospective trial examines the risk factors in 362 acute IS patients (7). Stratifying by HbA1c, diabetes mellitus is diagnosed in 113 patients (31,22%) but prediabetes is proved in 109 ones (30,11%). These patients present, more probably, with arterial hypertension ($p<0,001$) and hyperlipidemia ($p=0,05$). The likelihood of new-onset prediabetes increases with age ($p<0,01$). A correlation of HbA1c with carotid atherosclerosis measured as carotid intima media thickness in Indian patients with IS is looked for (13). The mean HbA1c value is 7,51±1,75%. It is higher in diabetes mellitus patients with IS (9,29±1,73%). This is significantly associated with IS patients presenting with carotid artery plaque ($p=0,008$). The high carotid intima media thickness is a reliable marker of higher risk of IS among type 2 diabetes mellitus patients (10).

Impaired glucose regulation is identified by oral glucose tolerance test in 2639 IS patients in China. It is an independent risk factor for the mortality from IS ($p=0,006$) (8). A persistent impaired glucose tolerance or progression to diabetes mellitus is established in 53 out of 101 patients with impaired glucose tolerance (two-hour postload glucose level of 7,8-11,0 mg/mL) after IS or transient ischemic attack. The most important predictors for the risk of this pathology are statin use, triglycerides and fasting plasma glucose. These circumstances can be used to optimize secondary IS prevention (5).

In 140 out of 242 consecutive acute IS patients without previously diagnosed diabetes mellitus this disease has been proved by means of admission glucose tolerance test (15). In multivariate analysis, the risk of early neurological deterioration is significantly higher in these patients than in those with normal glucose tolerance ($p=0,019$), while the risk of poor outcome is more significantly higher ($p<0,001$), even after adjusting for confounding factors ($p=0,008$). In a population-based study in Greater Cincinnati/Northern Kentucky region, there is a rising incidence of the history of diabetes mellitus among first IS patients - from 28% in 1993/1994 to 29% in 1999 and 33% in 2005 (9).

Plasma neuropeptide Y (NPY) concentrations determined by radioimmunoassay in 58 women aged 60-85 years (mean age, 76,5±0,8) with acute IS and in 24 healthy women aged 63-67 years (mean age, 65,6±0,6) shows a higher prevalence of type 2 diabetes mellitus, arterial hypertension and insulin resistance in IS patients (1). Plasma NPY levels on the first day and 10 days after the acute IS phase are significantly lower ($p<0,001$) than in control subjects.

Low and high estimated glomerular filtration rates are independent predictors of all-cause mortality and other poor outcomes after acute IS in patients with type 2 diabetes mellitus in China (11).

Conclusion

Our study demonstrates the considerable role of the disorders of glucose metabolism for the development of IS in adulthood. A regular control of the parameters of glucose metabolism such as blood glucose, fasting plasma glucose and glycosylated hemoglobin along with a strict observation of adult individuals' healthy life-style should warrant a successful IS prevention in our country.

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