ABSTRACT

Introduction: This study aims to investigate the risk factors in elderly type-2 diabetes mellitus (T2DM) patients with cerebral infarction.

Materials and methods: Among the patients admitted at the First People's Hospital of Lanzhou from June 2012 to May 2014, 162 elderly T2DM patients with cerebral infarction (group A), 98 elderly T2DM patients without cerebral infarction (group B), and 112 elderly cerebral infarction patients without diabetes (group C) were enrolled into the present study. All patients were measured for fasting blood glucose, glycosylated hemoglobin, fasting insulin, blood lipid, blood pressure, body mass index, leptin, adiponectin and neutrophil.

Results: Blood glucose, glycated hemoglobin, fasting insulin, blood lipid, blood pressure, body mass index, leptin and neutrophil were significantly higher in group A, than in group B and C (P<0.05). Furthermore, adiponectin was significantly lower in group A, than in group B and C (P<0.05). The stepwise logistic regression analysis revealed that blood glucose, glycosylated hemoglobin, fasting insulin, blood lipid, blood pressure, body mass index, leptin, adiponectin and neutrophil were significantly correlated with cerebral infarction.

Conclusion: Hyperglycemia, hyperlipidemia, hypertension, high body mass index, hyperleptinemia, hypoadiponectinemia and high neutrophil are important risk factors for T2DM with cerebral infarction.

Keywords: Leptin, Low adiponectin, Type-2 diabetes mellitus, Cerebral infarction, Risk.

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Introduction

At present, the incidence of diabetes is rapidly increasing worldwide(1), especially in developing countries. The latest statistics revealed that in China, the prevalence of diabetes in a population of over 65 years old is 11.6%, the prevalence of prediabetes is 50.1%, and the population with prediabetes in China has reached 490 million(2). The prevalence of cardiovascular and cerebrovascular events in diabetic patients is 2-4 times of that in non-diabetic patients(3), and 3.6-6.2% of diabetic patients have cerebral infarction(4). Diabetes mellitus complicated with cerebral infarction is a cerebrovascular disease caused by cerebral ischemia induced by cerebral vascular occlusion(5,7). Cerebral infarction is one of the main causes of death and disability in elderly patients with type-2 diabetes mellitus (T2DM). Furthermore, it easily relapses, and often leads to hemiplegia, aphasia and dysphagia, which seriously affects the health and quality of life of patients, bringing a heavy burden to patients and their families. Thus, it is particularly important in clinic to compare, study and discuss these various factors between elderly diabetic patients with cerebral infarction and patients without cerebral infarction, and actively provide comprehensive intervention, in order to reduce the incidence of cerebral infarction. In the present study, changes in blood glucose, glycated hemoglobin, fasting insulin, blood lipid, blood pressure, body mass index, leptin, adiponectin and neutrophils in elderly T2DM patients with cerebral infarction were studied to summarize the risk factors of elderly T2DM patients with cerebral
infection, especially the fatality of leptin and adiponectin in elderly T2DM patients with cerebral infarction. The details are reported, as follows.

Materials and methods

*General information*

From June 2012 to May 2014, the following patients, who were admitted in our hospital, were included into the present study: 162 T2DM patients with cerebral infarction (group A), 98 T2DM patients without cerebral infarction (group B), and 112 cerebral infarction patients without diabetes (group C). In group A, the age of these patients ranged within 65-73 years old, with a median age of 68 years old. Among these patients, 88 patients were male, and 74 patients were female, and the male-to-female ratio was 1.2:1.0. In group B, the age of these patients ranged within 65-83 years old, with a median age of 70 years old. Among these patients, 53 patients were male, and 45 patients were female, and the male-to-female ratio was 1.2:1.0. In group C, the age of these patients ranged within 65-85 years old, with a median age of 72 years old. Among these patients, 60 patients were male, and 52 patients were female, and the male-to-female ratio was 1.2:1.0. T2DM was diagnosed according to the 1999 World Health Organization (WHO) diagnostic criteria. All patients with cerebral infarction were confirmed by brain computed tomography (CT) or magnetic resonance imaging (MRI), and the diagnostic criteria were based on the resolution of the Fourth Academic Conference of National Cerebral Vascular Disease in 1995. The diagnostic criteria for hypertension were as follows: the patient was presently treated with antihypertensive drugs, or had a blood pressure higher than 140/90 mmHg in two measurements.

*Exclusion criteria:*

- patients with acute stage of cerebral infarction;
- patients with gout, and hepatic and renal vascular diseases;
- patients with a history of oral diuretic drugs.

**Methods**

**Determination of biochemical indexes**

An automatic biochemical analyzer was adopted to detect fasting blood glucose, fasting insulin, triglyceride, and glycosylated hemoglobin. A fully automatic hematology analyzer was adopted to determine the leukocyte count, and the percentage and absolute value of neutrophils. Body mass index = body weight (kg)/ the square of height (m).

**Determination of serum leptin and adiponectin**

The human leptin kit was purchased from Technological Development Company Affiliated to Chinese People's Liberation Army General Hospital, and the minimum measurable concentration was 0.05 mg/ml. Inter-batch coefficient of variance (CV) was >4.9%, while intra-batch CV was <4.5%. The adiponectin kit was purchased from Linco (USA), and the sensitivity of the kit was 0.001 μg/L. Intra-batch CV was <6.21%, while inter-batch CV was <9.25%. Enzyme-linked immunosorbent assay (ELISA) was used for the determination.

**Statistical analysis**

Measurement data were expressed as mean ± standard deviation (x ± SD). Inter-group comparison was conducted using t-test. All data were statistically analyzed using SPSS 11.0 software package. P<0.05 was considered statistically significant. The correlation analysis was conducted using stepwise logistic regression analysis.

**Results**

Comparison of the clinical data of T2DM patients between the two groups (Table 1).

<table>
<thead>
<tr>
<th>Index</th>
<th>A group</th>
<th>B group</th>
<th>C group</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI(kg/m²)</td>
<td>28.2±4.7</td>
<td>25.1±3.6</td>
<td>26.2±2.8</td>
</tr>
<tr>
<td>FBG(mmol/L)</td>
<td>9.7±3.3</td>
<td>6.9±2.9</td>
<td>8.5±1.6</td>
</tr>
<tr>
<td>HbA1C(%)</td>
<td>9.2±1.7</td>
<td>5.2±2.6</td>
<td>9.0±1.3</td>
</tr>
<tr>
<td>FINS(μ/L)</td>
<td>10.2±3.8</td>
<td>7.3±3.6</td>
<td>9.8±5.2</td>
</tr>
<tr>
<td>ΔSBP(mmHg)</td>
<td>146.2±19.4</td>
<td>138.4±14.7</td>
<td>145.3±3.6</td>
</tr>
<tr>
<td>ΔDBP (mmHg)</td>
<td>86.2±9.5</td>
<td>84.4±8.8</td>
<td>75.6±9.0</td>
</tr>
<tr>
<td>TG(mmol/L)</td>
<td>2.35±0.93</td>
<td>2.17±0.81</td>
<td>2.7±1.3</td>
</tr>
<tr>
<td>PMN(x10⁹/L)</td>
<td>7.22±3.06</td>
<td>3.22±1.40</td>
<td>3.4±2.0</td>
</tr>
</tbody>
</table>

Table 1: Comparison of clinical and biochemical indexes among groups.

Note: BMI, Body Mass Index; FBG, Fasting Blood Glucose; HbA1c, glycated hemoglobin/hemoglobin A1c; FINS, fasting serum lisulin; SBP, systolic blood pressure; DBP, diastolic blood pressure; TG, Triglyceride; PMN, polymorphonuclear; Compared with A group, * P<0.05, ΔP<0.05.

Fasting blood glucose, systolic blood pressure, blood lipid, fasting insulin, glycosylated he-
moglobin and neutrophil count were significantly higher in group A than in group B, and the differences were statistically significant (P<0.01). Furthermore, age, body mass index and diastolic blood pressure did not significantly change, and the differences were not statistically significant (P>0.05).

Comparison of leptin and adiponectin levels among groups (Table 2)

<table>
<thead>
<tr>
<th>Index</th>
<th>A group</th>
<th>B group</th>
<th>C group</th>
</tr>
</thead>
<tbody>
<tr>
<td>LEP(μg/L)</td>
<td>12.2±5.2</td>
<td>7.8±3.4*</td>
<td>8.3±4.7*</td>
</tr>
<tr>
<td>ADPN(mg/L)</td>
<td>12.4±4.8</td>
<td>19.8±5.2*</td>
<td>15.1±6.7*</td>
</tr>
</tbody>
</table>

Table 2: Comparison of leptin and adiponectin levels among groups.
Note: LEP, Leptin; ADPN, Adiponectin; Compared with A group, *P<0.05.

Leptin levels were significantly higher and adiponectin levels were significantly lower in group A, when compared with groups B and C, and the differences were statistically significant (P<0.05).

The main risk factors of diabetes mellitus combined with cerebral infarction are presented in Table 3.

Table 3: Logistic regression analysis of major risk factors for T2DM combined with cerebral infarction.
Note: T2DM, type-2 diabetes mellitus; SE, Standard error; OR, odds ratio; BMI, Body Mass Index; SBP, systolic blood pressure; DBP, diastolic blood pressure; TG, Triglyceride; FBG, Fasting Blood Glucose; HbA1c, glycated hemoglobin/hemoglobin A1c; FINS, fasting serum insulin; LEP, leptin; ADPN, Adiponectin.

Discussion

With the increase in age and the improvement of living standards, the incidence of T2DM in China continuously increases year by year(8). T2DM is also a major risk factor for cerebrovascular diseases, such as cerebral infarction. Its disability rate and medical cost are high, and its prognosis is poor, making it extremely easily to cause serious social and economic burdens. Hyperglycemia is a risk factor for diabetic cerebrovascular complications. The "European Diabetes diagnostic criteria cooperation group" points out that postprandial blood glucose is closely correlated to macrovascular complications, and it was also found that the incidence of macrovascular atherosclerosis in diabetics significantly increased in the stage of impaired glucose tolerance(9,10).

In addition, under the state of high glucose in the long term, plasma fibrinogen level is elevated and blood viscosity is increased(11). Furthermore, in the hyperglycemia state, the number of aging red blood cells is increased, aggregation and fragility are increased, circulatory blood flow is slowed down, and red blood cells accumulate and rupture(12), making it easy to cause cerebral infarction. In T2DM, with the increase in blood glucose, blood viscosity increases, and subsequently causes damage to arterial vascular endothelial cells. Hence, the visible components of blood, such as platelets, adhere and gather on the damaged vascular endothelial cells, allowing blood to flow through the narrowed cerebral artery more slowly. This finally leads to the formation of thrombus, causing ischemic stroke(13-15). In the present study, the mean fasting blood glucose was 9.7 ± 3.3 mmol/L in group A and 6.9 ± 2.9 mmol/L in group B, and the difference was statistically significant (P<0.05).

Diabetic patients often have lipid metabolic disturbance, which mainly manifests as an increase in triglyceride level. This increase in triglyceride promotes the transformation of low density lipoprotein (LDL) from the A type with larger particles to the B type with smaller particles, and also affects the metabolism of high density lipoprotein (HDL). The results of the present study revealed that the difference in the increase in systolic blood pressure among groups was statistically significant. The reason may be that diabetic patients mostly have insulin resistance and hyperinsulinemia. Hyperinsulinemia can increase sympathetic nervous system excitability, stimulate the proliferation of vascular
smooth muscle cells, and reduce endothelium-dependent diastolic function, while hyperglycemia can increase plasma osmotic pressure and increase the re-absorption of renal tubules to sodium ions, thereby increasing blood volume, and causing the increase in blood pressure. The prevalence of hypertension is four times or more in diabetic patients than in the general population(16,17). A large number of epidemiological studies have also confirmed that hypertension is an independent and important risk factor for cerebral infarction. In particular, the increase in systolic blood pressure can increase the risk of cerebral infarction in diabetes(18).

In recent years, the spontaneous activation of leukocytes has become a hot research spot. The leukocyte count serves as one of prognostic indicators of diabetic cerebrovascular disease(19,20). Furthermore, the present study also revealed that the leukocyte count was higher in group A than in group B, and the difference was statistically significant. Moreover, the present study also revealed that with the increase in the number of leukocytes, the absolute value and percentage of neutrophils increase, and the risk of cerebral infarction in T2DM patients also increases, and the difference was statistically significant (P<0.05).

A literature confirmed that(21) high serum leptin level is an important risk factor for cerebrovascular diseases in both men and women. The results of the present study revealed that for the risk factors for cerebral infarction in T2DM, leptin is also an independent risk factor, in addition to hypertension, hyperlipidemia and increased body mass index. Cell experiments have revealed that(22,23) leptin could bind to ob-Rb on macrophages, increase its hormone-sensitive lipase activity, reduce the degradation of cholesteryl ester, and increase foam cell formation in obese and diabetic patients, which is one of the mechanisms that lead to thrombosis. Nakata et al. revealed that(24) the long form of the leptin receptor is expressed, and after binding to the receptor, leptin phosphorylates tyrosine residues. This further increases platelet aggregation induced by adenosine diphosphate, and it works in a concentration-dependent manner. High concentration of leptin promotes platelet aggregation, and leads to thrombosis. This suggests that hyperleptinemia is one of the risk factors for thrombosis in obese people.

Experimental results at home and abroad have revealed that plasma adiponectin levels are significantly decreased in patients with coronary heart diseases(25,26). Hypoadiponectinemia is an independent predictor of coronary heart disease and an important indicator of the severity of coronary atherosclerosis. The results of a study suggested that adiponectin played an important role in inhibiting inflammatory reactions and anti-atherosclerosis. Some scholars have revealed that(27) plasma adiponectin levels were lower in T2DM patients with cardiovascular and cerebrovascular diseases than in T2DM patients without cardiovascular and cerebrovascular diseases. The reason may be that adiponectin, which accumulates in atherosclerotic arterial walls, shortens its half-life to decrease its concentration. When the barrier of endothelial cells is damaged, adiponectin easily deposits on the vascular wall to regulate the inflammatory response of endothelial cells through the interaction between cyclic adenosine monophosphate-dependent protein kinase and the nuclear factor signaling pathway(28). Adiponectin bridges adipose tissues and arteries, which indicates that hypoadiponectinemia promotes the occurrence and development of atherosclerosis.

References


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