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CLINICAL RESEAPCH

Study on the Level Changes and Diagnostic Values of FIB, Hcy and UA in Type 2 Diabetes Mellitus Patients with Cerebral Infarction

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Keywords

Fibrinogen, Homocysteine, Uric acid, Type 2 diabetes mellitus, Cerebral infarction

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Abstract

Objective To investigate the level changes and diagnostic values of fibrinogen (FIB), homocysteine (Hcy) and uric acid (UA) levels in type 2 diabetes mellitus (T2DM) patients with cerebral infarction. **Methods** A total of 60 T2DM patients with cerebral infarction treated in our hospital from Jan. 2018 to Dec. 2019 were selected as the observation group, and they were divided into the mild group (n=22), moderate group (n=19) and severe group (n=19) according to the severity of cerebral infarction, and 60 cases of healthy people who accepted physical examination for the same period were selected as control group. The levels of FIB, Hcy and UA were compared among groups, and the diagnostic values of the FIB, Hcy and UA levels alone and in combination in T2DM with cerebral infarction were evaluated using receiver operating characteristic curve (ROC), and the correlation between the levels of FIB, Hcy and UA and the severity of T2DM patients with cerebral infarction was analyzed by Spearman correlation analysis. **Results** The levels of FIB, Hcy and UA in the observation group were significantly higher than those in the control group; The AUC value of the combined detection of FIB, Hcy and UA levels was significantly higher than that of single detection for each index; The levels of FIB and Hcy in the moderate and severe groups were significantly higher than those in the mild group, there was no significant difference in UA level between the moderate group and mild group, the UA level in the severe group was significantly higher than that in the mild group, and the level of Hcy in the severe group was significantly higher than that in the moderate group, there were no significant difference in FIB and UA levels between the moderate group and severe group; after Spearman correlation analysis, the levels of FIB, Hcy and UA were positively correlated with the severity of T2DM with cerebral infarction (r=0.490, 0.730, 0.439, P<0.01). **Conclusion** The levels of FIB, Hcy and UA were elevated with the increase of the severity of T2DM patients with cerebral infarction, and the combined detection of FIB, Hcy and UA levels is of great value in the diagnosis of T2DM with cerebral infarction.

Introduction

Diabetes mellitus (DM) is one of the chronic diseases affecting human life and health, among which type 2 DM (T2DM) accounts for more than 90% of the incidence of DM, and it is increasing year by year with extremely high rates of disability and lethality; cerebral infarction , one of the common vascular complications in DM patients, is a key factor in the lethality and disability of T2DM patientswith high recurrence rate, which seriously affects the survival quality of patients [1]. Therefore, it is necessary to have a deep understanding of the risk factors that cause T2DM with cerebral infarction, and take active intervention and treatment to help patients to return to their normal lives. Several studies have shown [2-3] that fibrinogen (FIB), homocysteine (Hcy) and uric acid (UA) levels can change abnormally in T2DM patients with cerebral infarction and are potential risk factors for triggering cardiovascular and cerebrovascular diseases, therefore detecting the levels of FIB, Hcy and UA is of great significance for the diagnosis and treatment of patients. The aim of this study is to investigate the changes of FIB, Hcy and UA levels in T2DM patients with cerebral infarction and their diagnostic values, and the results were reported as below.

Materials and methods

Clinical data

General data

The study subjects consisted of 60 T2DM patients with cerebral infarction (observation group) and 60 healthy people (control group) who accepted physical examination in our hospital during the same period from January 2018 to December 2019, and according to the severity of cerebral infarction, the patients in the observation group were divided into the mild (n = 22), moderate (n = 19) and severe (n = 19) groups. Observation group: 36 males and 24 females, aged 40-75 years, with a mean age of 54.42 ± 8.71 years, weighted 52-80 kg, with a mean body weight of 60.57 ± 8.26 kg. Control group: 34 males and 26 females, aged 38-75 years, with a mean age of 54.06 ± 9.82 years, weighted 54-78 kg, with a mean body weight of 62.02 ± 8.61 kg. The general data of study subjects in each group were not significantly different (P>0.05) and comparable. This study was performed with the approval of the ethics committee of our hospital, and all study subjects gave written informed consent.

Inclusion and exclusion criteria

Inclusion criteria: met the diagnostic criteria for DM developed by the World Health Organization (WHO) and the American Diabetes Association (ADA) and the diagnostic criteria for cerebral infarction in the *Diagnostic essentials of various cerebrovascular diseases* developed by the fourth national cerebrovascular conference; and confirmed by pathological examination, MRI and CT. Exclusion criteria: Patients with tumor, other renal system diseases and blood system diseases; patients with trauma and intracranial vascular malformation; patients taking vitamins, immunosuppressants, hormones and other drugs that affect the test results.

Methods

5 ml of fasting venous blood was collected from study subjects in each group, serum and plasma were separated for the detection of each index. Hcy and UA levels were detected by automatic biochemical analyzer; FIB levels were detected by automatic hemagglutination analyzer.

Statistical analysis

SPSS 20.0 was used for statistical analysis, and the count data were compared using the $\chi 2$ test, and the measurement data were expressed as the mean ± standard deviation ($\bar{x}\pm s$), and the t test was used for comparison between two groups, analysis of variance was used for comparison among multiple groups, and the correlation was analyzed using Spearman correlation analysis. The area under the curve (AUC) of receiver operating characteristic (ROC) was plotted to analyze the diagnostic value of FIB, Hcy and UA levels detected individually and jointly: the AUC value of 0.5-0.7 was of low value, the AUC value of 0.7-0.9 was of medium value, and the AUC value of above 0.9 was of high value, the higher the AUC, the

greater the diagnostic value, the AUC comparison was made using z-test, and P<0.05 was taken as the difference for statistical significance.

Results

Comparison of FIB, Hcy and UA levels between the two groups

The levels of FIB, Hcy and UA in the observation group were significantly higher than those in the control group (P<0.05), as shown in Table 1.

Table 1 Comparison of FIB, Hcy and UA levels between the two groups

Group	Cases	FIB（g/L）	Hcy（umol/L）	UA（umol/L）
Observation group	60	3.86±1.28	21.47±5.38	375.25±57.80
Control group	60	2.35±0.87	12.16±2.53	186.14±49.22
t		7.557	12.130	19.295
P		0.000	0.000	0.000

Diagnostic values of FIB, Hcy, and UA levels alone and in combination in T2DM patients with cerebral infarction

The AUC values of the detection of FIB, Hcy and UA levels alone and in combination for the diagnosis of T2DM with cerebral infarction were 0.807, 0.853, 0.827 and 0.944, respectively; the AUC value of the combined detection of FIB, Hcy and UA levels was significantly higher than those AUC values of the single test of each index (*P*<0.05), see Table 2 and Figure 1.

Correlation between FIB, Hcy, and UA levels and severity in T2DM patients with cerebral infarction

The levels of FIB and Hcy in the moderate and severe groups were significantly higher than those in the mild group (*P*<0.05), and there was no significant difference in UA level between the moderate group and mild group (*P*>0.05), but the level of UA in the severe group was significantly higher than that in the mild group (*P*<0.05). And the level of Hcy in the severe group was significantly higher than that in the moderate group (*P*<0.05). Moreover, there was no significant difference in FIB and UA levels between the severe group and moderate group (*P*>0.05). Spearman correlation analysis showed that FIB, Hcy and UA levels were significantly positively correlated with the severity of T2DM patients with cerebral infarction (*r*=0.490, 0.730, 0.439, *P*<0.01), as shown in Table 3 and Figure 2.

Table 2 Diagnostic value of FIB, Hcy, and UA levels alone and in combination in T2DM patients with cerebral infarction

Item	AUC	SE	95% *CI*	Sensitivity （%）	Specificity （%）
FIB	0.807[a]	0.0405	0.725 to 0.873	66.7	85.0
Hcy	0.853[a]	0.0349	0.777 to 0.911	81.7	80.0
UA	0.827[a]	0.0375	0.747 to 0.890	83.3	71.7
Combined detection	0.944	0.0198	0.886 to 0.978	80.0	93.3

Note: compared with the combined detection, [a]*P*<0.05.

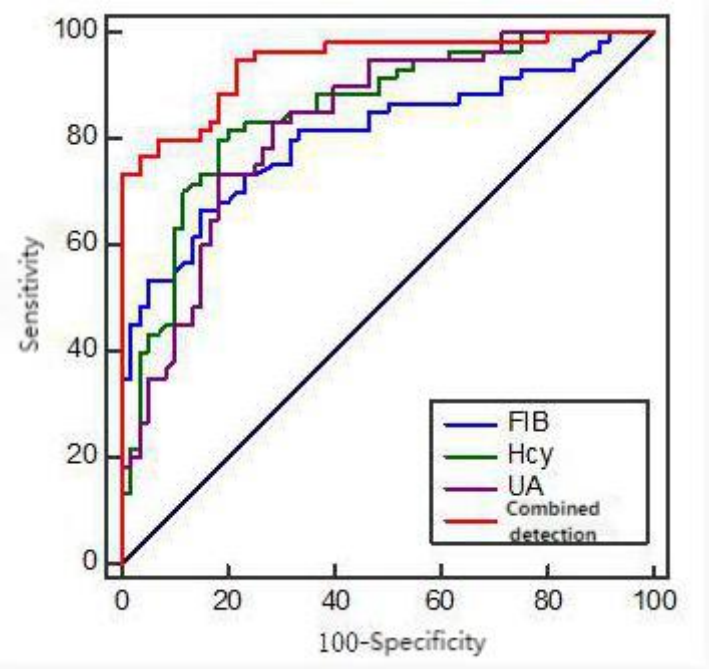

Figure 1 ROC curves of FIB, Hcy, and UA levels alone and in combination in T2DM patients with cerebral infarction

Table 3 Correlation between FIB, Hcy, and UA levels and severity in T2DM patients with cerebral infarction

Group	Cases	FIB（g/L）	Hcy（umol/L）	UA（umol/L）
Mild group	22	3.05±0.93	18.95±3.88	343.42±51.20
Moderate group	19	3.74±1.12[a]	22.28±4.61[a]	375.25±57.80
Severe group	19	4.22±1.36[a]	31.24±5.74[ab]	411.67±66.08[a]
F		9.439	33.949	6.826
P		0.000	0.000	0.002

Note: compared with the mild group, [a]*P*<0.05; compared with the moderate group, [b]*P*<0.05.

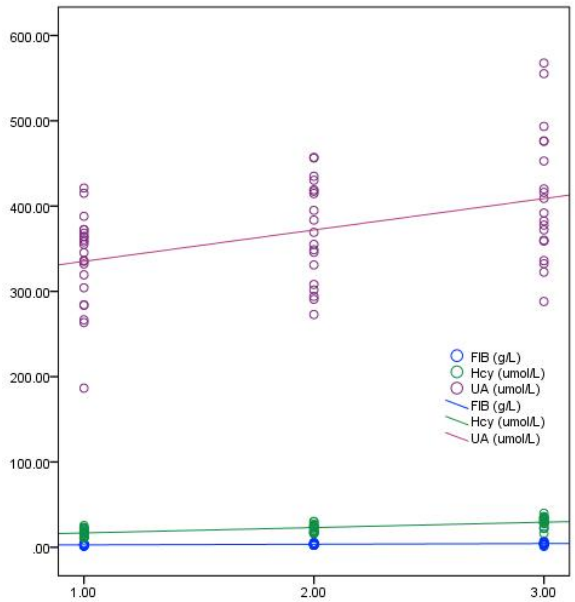

Figure 2 Spearman analysis of the correlation between the severity of T2DM patients with cerebral infarction and FIB, Hcy, UA levels

(Note: 1 is mild group, 2 is moderate group, 3 is severe group)

Discussion

The reason why DM patients are prone to cerebral infarction is related to the hyperglycemia environment in patients, hyperglycemia will damage vascular endothelial cells, induce lipid metabolism disorder, and then cause atherosclerosis, while atherosclerosis will cause vascular thickening, lumen stenosis and occlusion, and then lead to cerebral tissue ischemia, which triggers the local brain damage or necrosis, affecting the life safety of patients [4]. The levels of FIB, Hcy and UA in the body are closely related to the occurrence and development of cerebrovascular diseases. Therefore, the detection of these three indicators has certain significance for the diagnosis of cerebral infarction. However, researches on FIB, Hcy and UA levels mainly focus on DM with coronary heart disease and other related diseases, and lack of in-depth research on T2DM with cerebral infarction. In view of this, this study detected the levels of FIB, Hcy and UA in T2DM patients with cerebral infarction, explored the correlation between the levels of FIB, Hcy and UA and the severity of T2DM patients with cerebral infarction, and their diagnostic values in T2DM patients with cerebral infarction, so as to provide more comprehensive diagnostic basis for clinical diagnosis and treatment.

Studies have found that high levels of FIB can promote the occurrence and development of cardiovascular and cerebrovascular diseases in patients with DM [5]. Compared with normal people, the level of Hcy in patients with T2DM is significantly higher, and it is considered that high level of Hcy is one of the risk factors of chronic complications in DM patients [6]. In T2DM patients with acute cerebral infarction, the level of UA is significantly increased, it is believed that high UA level is one of the risk factors of cardiovascular and cerebrovascular diseases, which will lead to increased morbidity and lethality in patients with cerebral infarction [7]. The results of this study showed that the levels of FIB, Hcy and UA in the observation group were significantly higher than those in the control group, indicating that the levels of FIB, Hcy and UA in T2DM patients with cerebral infarction were significantly higher than those in healthy people, and the levels of FIB, Hcy and UA can be used as diagnostic indicators for predicting T2DM patients with cerebral infarction.

In this study, the AUC values for the diagnostic value of FIB, Hcy and UA levels detected individually in T2DM with cerebral infarction were 0.807, 0.853, and 0.827, respectively, which had moderate diagnostic efficacy, and the AUC value for the diagnostic values of FIB, Hcy and UA levels detected jointly in T2DM with cerebral infarction was up to 0.944, which had high diagnostic efficacy, indicating that the FIB, Hcy, and UA levels could all be used as diagnostic markers for the diagnosis of T2DM with cerebral infarction, and that the combined detection of FIB, Hcy and UA levels had important value in the early diagnosis of T2DM with cerebral infarction.

FIB is a coagulation factor that is synthesized and secreted by hepatocytes and plays an important role in the development and progression of platelet aggregation and atherosclerosis, and the deposition of FIB can cause changes in vascular endothelial permeability, prompting the aggregation of low-density lipoproteins under the vascular endothelium, stimulating the proliferation and migration of vascular smooth muscle cells to the vascular intima, and forming atherosclerotic plaques [8]. Hcy is a potentially toxic metabolite produced during methionine metabolism, and high level of Hcy is involved in the progression of cerebral infarction in DM patients, which can lead to vascular endothelial damage, stimulate the binding of platelet and vascular intima, cause arterial vascular inflammatory responses, and promote atherosclerosis [9]. UA is the end product of purine metabolism in the nucleic acid metabolism pathway in the body, and the daily

production and excretion of UA in the human body approximately balance, while DM patients have abnormal blood glucose metabolism, leading to the occurrence of insulin resistance and glomerular vasoconstriction and the reduction of the excretion of UA .As the UA is deposited in the renal interstitium ,it leads to damage of the renal tubules, causing renal function decline. At the same time, it will induce the formation of a large number of oxygen free radicals, causing vascular inflammation and neuronal cell damage, triggering platelet aggregation and thrombus formation, accelerating atherogenesis [10]. And atherosclerosis is the root cause of the occurrence and development of cerebral infarction. In this study, the levels of FIB, Hcy and UA in patients with moderate and severe cerebral infarction were higher than those in patients with mild cerebral infarction, and the levels of FIB, Hcy and UA in patients with severe cerebral infarction were higher than those in patients with moderate cerebral infarction, indicating that the levels of FIB, Hcy and UA in patients with cerebral infarction were elevated with the increase of the severity of cerebral infarction, and may directly participate in the occurrence and development of T2DM with cerebral infarction. Meanwhile, this study found that FIB, Hcy and UA levels were positively correlated with the severity of T2DM patients with cerebral infarction, it suggested that FIB, Hcy and UA levels were gradually increased with the aggravation of T2DM patients with cerebral infarction.

In conclusion, the levels of FIB, Hcy, and UA are closely related to T2DM with cerebral infarction, and with the aggravation of T2DM patients with cerebral infarction, FIB, Hcy and UA levels show an upward trend, and FIB, Hcy and UA levels alone and in combination can be used as diagnostic indicators of T2DM patients with cerebral infarction, which has important significance for early diagnosis and prevention of T2DM patients with cerebral infarction.

Declaration of conflict-of-interest

The authors declare no conflict-of –interest.

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