CHANGES AND RELATIONSHIP OF PLASMA HCY LEVELS AND COAGULATION AND FIBRINOLYSIS INDEXES IN PATIENTS WITH ACUTE CEREBRAL INFARCTION OF DIFFERENT SEVERITY AND ETIOLOGY

Zhihua Cheng, Cong Luo, Zhilin Guo*
Department of Neurosurgery, Shanghai Ninth People's Hospital, Shanghai Jiao Tong University, School of Medicine, Shanghai, PR China

ABSTRACT

Objective*: To explore the changes of plasma homocysteine (HCY) level and coagulation and fibrinolysis indexes in patients with acute cerebral infarction of different severity and etiology.*

Methods: *Ninety-four patients with acute cerebral infarction (ACI) hospitalized in the neurology department of our hospital from May 2016 to January 2018 were randomly selected as the experimental group. The patients were divided into mild ACI group, moderate ACI group and severe ACI group according to the severity of the disease. They were further divided into large artery atherosclerosis (LAA) group, cardiogenic embolism (CE) group, small artery occlusion (SAO) group, and SOE + SUE group with unknown etiology. Fifty healthy adults who underwent physical examination in our hospital during the same period were selected as the control group. The levels of HCY, activated partial thromboplastin time (APTT), plasma thrombin time (TT), plasma prothrombin time (PT), plasma fibrinogen degradation products (FDP), plasma fibrinogen (Fg) and plasma D-dimer (DD) were compared between the experimental and control groups, and the relationship between plasma HCY levels and coagulation and fibrinolysis indexes was further analyzed.*

Results: *The levels of HCY and Fg in the experimental group were significantly higher than those in the control group (P<0.05), while levels of APTT and DD were significantly lower than those in the control group (P<0.05). There was no significant difference in the levels of PT, TT and FDP between the two groups (P>0.05). HCY levels in mild ACI group, moderate ACI group and severe ACI group were significantly higher than those in the control group (P<0.05), and HCY levels in severe ACI group and moderate ACI group were significantly higher than those in mild ACI group (P<0.05). APTT levels in mild ACI group, moderate ACI group and severe ACI group were significantly lower than those in the control group (P<0.05), and APTT levels in moderate ACI group and severe ACI group were significantly lower than those in mild ACI group (P<0.05). Fg levels in moderate ACI group and severe ACI group were significantly higher than those in mild ACI group (P<0.05). There was no significant difference in TT and FDP levels among groups (P>0.05). DD levels in moderate ACI group and severe ACI group were significantly higher than those in mild ACI group and the control group (P<0.05). HCY levels in CE group, SAO group and other groups were significantly lower than those in LAA group (P<0.05). APTT levels in CE group, SAO group and other groups were significantly higher than those in LAA group (P<0.05). There was no significant difference between the other two groups (P>0.05). HCY was negatively correlated with APTT and positively correlated with Fg and DD. There was no significant correlation with PT, TT and FDP.*

Conclusion: *There is a significant correlation between plasma HCY and APTT, Fg and DD in patients with acute cerebral infarction, and the more severe the disease, the higher the level of HCY, and the worse the stability of coagulation and fibrinolysis system. Meanwhile, plasma HCY may be more correlated with LAA-ACI.*

Keywords: *Acute cerebral infarction, HCY level, coagulation and fibrinolysis indexes.*

DOI: 10.19193/0393-6384_2021_1_11

Received *November 30, 2019;* ***Accepted*** *January 20, 2020*

Introduction

Cerebral apoplexy is divided into ischemic stroke and hemorrhagic stroke. Ischemic stroke is the most common type of stroke[1]. A World Health Organization (WHO) survey shows that stroke poses a serious threat to people's life and health, and at the same time brings a heavy burden to the families of patients. The incidence of stroke in China is increasing each year[2]. Therefore, early prevention and treatment of stroke has become one of the urgent public health issues in China. Many studies have confirmed that homocysteine (HCY) is closely related to the occurrence and prognosis of cerebral

infarction, and its elevated level can be used as one of the independent risk factors for cerebrovascular diseases[3]. The relationship between metabolic imbalance of HCY and various pathologies is not yet fully understood, but the relationship between HCY and vascular diseases has been confirmed[4].

Clinical studies have shown that patients with HCY urine have vascular lesions. HCY plays an important role in the occurrence and development of cerebral infarction through vascular endothelial injury and vascular endothelial injury[5]. Some scholars have suggested that elevated levels of HCY are related to different subtypes of TOAST in patients with cerebral infarction to some extent. Large artery atherosclerosis (LAA) has the strongest correlation with HCY levels, followed by small artery occlusion (SAO), but with cardiogenic embolism (CE) and others. Type type is independent[6].

There are few reports on the correlation between plasma HCY levels and coagulation and fibrinolysis indexes in patients with acute cerebral infarction. Therefore, this study examines the levels of plasma HCY and coagulation and fibrinolysis indexes in patients with acute cerebral infarction of different severity and etiology, and further explores the correlation between the levels of HCY and coagulation and fibrinolysis indexes.

Materials and methods

General information

Ninety-four patients with acute cerebral infarction (ACI) hospitalized in the neurology department of our hospital from May 2016 to January 2018 were randomly selected as the experimental group. According to the severity of the disease, the patients were divided into mild ACI group, moderate ACI group and severe ACI group. They were further divided into large artery atherosclerosis (LAA) group, cardiogenic embolism (CE) group, small artery occlusion (SAO) group, and other (SOE + SUE) group. Another 50 healthy adults who underwent physical examination in our hospital during the same period were selected as the control group.

Inclusion criteria:

All patients met the diagnostic criteria of ACI in the Guidelines for the Diagnosis and Treatment of Acute Ischemic Stroke in China (2014);

• The onset time was less than two weeks;

• The symptoms of patients lasted more than several hours;

• Patients provided informed consent;

• Patients were approved by the Hospital Ethics Committee.

Exclusive criteria:

• Cerebral hemorrhage and other pathological changes;

• Poor mental state and compliance;

• Lactating and pregnant women;

• Patients with malignant tumors and autoimmune diseases;

• Patients with cardiac insufficiency, hyperthyroidism or hypothyroidism, and severe anemia.

There were 50 males and 44 females in the experimental group, with an average age of (63.45±4.91) years, while there were 30 males and 20 females in the control group, with an average age of (64.01±4.53) years. There was no significant difference in general data among the experimental groups ($P<0.05$).

Methods

On the second day of admission, 5 ml fasting venous blood was taken from the patients in the experimental group, and 5 ml fasting venous blood was centrifuged in anticoagulant tube in the morning of the physical examination in the control group. HCY levels were measured by enzyme-linked immunosorbent assay (ELISA) and activated partial thromboplastin time (APTT) of coagulation and fibrinolysis indices were measured by automatic coagulation analyzer. The plasma thrombin time (TT), prothrombin time (PT), fibrinogen degradation product (FDP) and fibrinogen (Fg) were measured by immunoturbidimetric assay. The plasma D-dimer (DD) level was measured.

Statistical methods

SPSS 23.0 software was used to process the data. The counting data were expressed by (n/(%)) and χ^2 test; the measurement data were expressed by ($\bar{x}\pm s$) and t test; the comparison among groups was expressed by single-factor analysis of variance (ANOVA); and the correlation analysis was expressed by Pearson analysis. $P<0.05$ as the difference has statistical significance.

Results

Comparison of HCY, coagulation and fibrinolysis in two groups

The levels of HCY and Fg in the experimental group were significantly higher than those in the control group ($P<0.05$), while levels of APTT and DD were significantly lower than those in the control

group (P<0.05). There was no significant difference in the levels of PT, TT and FDP between the two groups (P>0.05). See Table 1.

Index	Control group	Experimental group	*t*	*P*
HCY (umol/L)	14.50±11.96	25.28±10.75	5.329	<0.001
PT (sec)	13.07±1.59	13.48±1.81	1.403	0.163
APTT (sec)	31.08±4.64	25.35±4.98	6.877	<0.001
Fg (g/L)	3.08±0.96	4.14±1.25	5.665	<0.001
TT (sec)	16.08±3.25	16.23±2.26	0.325	0.746
FDP (mg/L)	2.27±2.16	2.95±2.37	1.738	0.084
DD (mg/L)	1.81±0.85	0.58±0.46	9.508	<0.001

Table 1: Comparison of HCY, coagulation and fibrinolysis in two groups ($\bar{x}\pm s$).

Comparison of HCY, coagulation and fibrinolysis in ACI group with different severity

HCY levels in mild ACI group, moderate ACI group and severe ACI group were significantly higher than those in the control group (P<0.05), and HCY levels in severe ACI group and moderate ACI group were significantly higher than those in mild ACI group (P<0.05).

APTT levels in mild ACI group, moderate ACI group and severe ACI group were significantly lower than those in the control group (P<0.05), and APTT levels in moderate ACI group and severe ACI group were significantly lower than those in mild ACI group (P<0.05). Fg levels in moderate ACI group and severe ACI group were significantly higher than those in mild ACI group (P<0.05). There was no significant difference in TT and FDP levels among groups (P>0.05). DD levels in moderate ACI group and severe ACI group were significantly higher than those in mild ACI group and the control group (P<0.05). See Table 2.

Index	Control group	Mild ACI group	Moderate ACI group	Severe ACI group
HCY (umol/L)	12.52±17.43	13.63±9.62[a]	24.60±10.75[ab]	29.65±20.75[ab]
PT (sec)	12.84±5.43	13.64±8.85[a]	14.48±1.81[ab]	13.89±2.74[ab]
APTT (sec)	35.96±6.41	31.75±6.37[a]	30.08±5.98[ab]	25.57±6.02[ab]
Fg (g/L)	2.44±1.54	2.68±3.32	2.72±1.25[ab]	2.93±2.26[ab]
TT (sec)	16.56±7.57	14.76±8.50	19.23±2.26	17.64±5.47
FDP (mg/L)	2.45±4.32	2.47±2.86	3.92±11.01	3.47±8.45
DD (mg/L)	0.09±0.57	0.21±1.54[a]	0.46±0.58[ab]	0.71±1.43[ab]

Table 2: Comparison of HCY, coagulation and fibrinolysis in ACI group with different severity ($\bar{x}\pm s$).
Note: Compared with the control group, [a]P<0.05; compared with mild ACI group, [b]P<0.05.

Comparison of HCY, coagulation and fibrinolysis in ACI patients with different etiology

HCY levels in CE group, SAO group and other groups were significantly lower than those in LAA group (P<0.05). APTT levels in CE group, SAO group and other groups were significantly higher than those in LAA group (P<0.05). There was no significant difference between the other two groups (P>0.05). See Table 3.

Index	LAA group	CE group	SAO group	Other group
HCY (umol/L)	25.29±6.84	21.54±3.37[a]	20.64±4.48[a]	19.50±5.31[a]
PT (sec)	13.74±4.63	12.68±3.72	14.39±2.60	13.65±1.47
APTT (sec)	25.35±4.47	33.87±5.39[a]	36.67±4.78[a]	32.85±5.37[a]
Fg (g/L)	2.78±1.45	2.76±0.34	3.25±1.65	2.97±0.74
TT (sec)	15.73±5.75	14.47±4.84	16.46±6.47	15.46±2.01
FDP (mg/L)	3.36±6.85	2.76±3.21	3.37±4.32	2.28±2.04
DD (mg/L)	0.45±0.58	0.46±2.54	0.40±1.82	0.46±0.38

Table 3: Comparison of HCY, coagulation and fibrinolysis in ACI group with different etiologies ($\bar{x}\pm s$).
Compared with group LAA, [a]P<0.05.

Analysis of correlation between HCY levels and coagulation and fibrinolysis indexes

HCY was negatively correlated with APTT and positively correlated with Fg and DD.

There was no significant correlation with PT, TT and FDP. See Table 4.

Index	HCY	
	r	*P*
PT	0.129	0.092
APTT	-0.325	0.003
Fg	0.413	0.028
TT	0.077	0.471
FDP	0.045	0.106
DD	0.203	0.044

Table 4: Analysis of correlation between HCY levels and coagulation and fibrinolysis indexes.

Discussion

HCY, as a non-essential sulfur-containing non-protein amino acid, can be produced in almost all tissues. It primarily comes from methionine ingested in diet. It is detoxified mainly through liver, kidney, small intestine, pancreas and lens[7]. Acute cerebral infarction is a common ischemic cerebrovascular disease. The relationship between HCY and acute cerebral infarction is currently a focus point for clinical researchers. Several studies have shown that the plasma HCY levels in patients with acute

cerebral infarction is significantly higher than that in healthy people. Elevated HCY levels can therefore be used as an independent risk factor for the onset of acute cerebral infarction, and is closely related to the severity of the disease and the prognosis of patients[8]. Domestic research has shown that HCY levels are positively correlated with the severity of acute cerebral infarction.

Recent studies have shown that HCY levels are strongly correlated with neurological diseases, osteoporosis, tumors and other diseases[9]. PT prolongation is mainly seen in congenital coagulation factor deficiency and acquired coagulation factor deficiency; APTT shortening is mainly seen in prethrombotic state and thrombotic disease[10]; Fg is an independent risk factor for predicting cardiovascular and cerebrovascular diseases, synthesized by the liver, and its elevation is mainly seen in diabetes, acute infectious diseases, pre-thrombotic state and other diseases[11]; TT prolongation is mainly seen in abnormal fibrinogenemia. FDP was mainly found in primary fibrinolysis and secondary hyperfibrinolysis; DD was mainly found in deep vein thrombosis and pulmonary thromboembolism, which was one of the important indicators reflecting secondary fibrinolysis and thrombosis[12].

The results showed that the levels of HCY and Fg in the experimental group were significantly higher than those in the control group (P<0.05), while levels of APTT and DD were significantly lower than those in the control group (P<0.05). There was no significant difference in the levels of PT, TT and FDP between the two groups (P>0.05). HCY was negatively correlated with APTT and positively correlated with Fg and DD; there was no significant correlation with PT, TT and FDP. The results of this study showed that HCY was significantly correlated with the changes of some coagulation and fibrinolysis indexes in patients with acute cerebral infarction.

In the course of treating acute cerebral infarction, some scholars have found that the increase of HCY levels can lead to the increase of patients' score within 48 hours (based on the National Institutes of Health Stroke Scale (NIHSS)). It is suggested that elevated HCY levels may increase the risk of adverse prognosis in patients with acute cerebral infarction[13]. Another study found that 30 days after the onset of acute cerebral infarction, the NIHSS score of patients with high HCY levels was significantly higher than that of patients with normal HCY levels, suggesting that the increase of HCY levels can affect the recovery of neurological function and daily living ability of patients with acute cerebral infarction[14]. The elevated levels of HCY impairs the structure and function of vascular endothelial cells on the basis of aggravating local inflammatory response, oxidative stress activating endoplasmic reticulum, immune response and other mechanisms, and then causes vulnerable plaques, while plaque rupture and exfoliation can lead to acute cerebral infarction[15]. HCY, coagulation and fibrinolysis in patients with acute cerebral infarction of different severity and degree were detected. The results showed that HCY levels in mild ACI group, moderate ACI group and severe ACI group were significantly higher than those in the control group (P<0.05), and HCY levels in severe ACI group and moderate ACI group were significantly higher than those in mild ACI group (P<0.05). APTT levels in mild ACI group, moderate ACI group and severe ACI group were significantly lower than those in the control group (P<0.05), and APTT levels in moderate ACI group and severe ACI group were significantly lower than those in mild ACI group (P<0.05). Fg levels in moderate ACI group and severe ACI group were significantly higher than those in mild ACI group (P<0.05). There was no significant difference in TT and FDP levels among groups (P>0.05). DD levels in moderate ACI group and severe ACI group were significantly higher than those in mild ACI group and the control group (P<0.05). HCY levels in CE group, SAO group and other groups were significantly lower than those in LAA group (P<0.05). APTT levels in CE group, SAO group and other groups were significantly higher than those in LAA group (P<0.05). There was no significant difference between the other two groups (P>0.05).

In conclusion, plasma HCY is significantly correlated with APTT, Fg and DD in patients with acute cerebral infarction; and the higher the severity of the disease, the higher the level of HCY, and the worse the stability of coagulation and fibrinolysis system; at the same time, plasma HCY may be more correlated with LAA-ACI.

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Corresponding Author:
Zhilin Guo
Email: mtwyg0@163.com
(China)