THE CHANGES OF SERUM HCY, CYSC, HS-CRP, ET-1 AND FIB IN PATIENTS WITH PRIMARY CEREBRAL INFARCTION

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ABSTRACT

Objective: *To investigate the changes of serum Hcy, CysC, hs-CRP, ET-1, and FIB levels in patients with primary cerebral infarction (CI) and their relationship with the occurrence and development of the disease.*

Methods: *78 cases with primary CI admitted to Department of Neurology in our hospital from June 2015 to October 2016 were selected as the observation group, and 80 healthy subjects of physical examination in the outpatient department of our hospital were selected as the control group in the same period. According to the results of cephalic CT, 78 patients with primary cerebral infarction were divided into three groups: there were 23 cases of small area cerebral infarction in group A, 28 cases of medium area cerebral infarction in group B, and 27 cases of large area cerebral infarction in group C. The concentrations of serum Hcy, CysC, hs-CRP, ET-1, and FIB in patients of group A, B and C were compared. At the same time, 78 patients with primary cerebral infarction were divided into three groups: mild neurological deficit (n=24), moderate neurological deficit (n=26) and severe neurological deficit (n = 28). The concentrations of serum Hcy, CysC, hs-CRP, ET-1, and FIB in the three groups were compared.*

Results: *Compared with the control group, the levels of serum Hcy, CysC, hsCRP, ET1, and FIB were significantly increased (P<0.05). There were significant differences in serum Hcy, CysC, hs-CRP, ET-1, and FIB concentrations after pairwise comparison of three groups of patients in group A, B and C (P<0.01), and the increase of the concentrations of plasma Hcy, CysC, hs-CRP, ET-1, and FIB in group C were more obvious (P<0.01). There was an increasing relationship of the concentrations of serum Hcy, CysC, hs-CRP, ET-1, and FIB among the three groups of mild, moderate and severe neurological deficit, and there was a significant difference among the three groups (P<0.01).*

Conclusion: *The levels of serum Hcy, CysC, hs-CRP, ET-1, and FIB in patients with primary cerebral infarction are closely related to the condition and prognosis of cerebral infarction and play an important role in the occurrence and development of cerebral infarction.*

Keywords: *Primary cerebral infarction, serum homocysteine (Hcy), cystatin (CysC), high sensitive C-reactive protein (hs-CRP), endothelin-1 (ET-1), fibrinogen (FIB).*

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Introduction

Cerebral stroke is the most common vascular lesion in the clinic. The incidence of cerebral stroke is 185/100000 in rural areas of China, and ischemic cerebral stroke accounts for 70 % of all cerebral stroke(1). Atherosclerosis is one of the main factors leading to the onset of cerebral infarction. The morbidity, disability rate, recurrence rate and death rate of cerebral infarction are high, which brings a heavy burden to patients and their families, so people are paying more and more attention to the prevention and treatment of cerebral infarction. The key to the treatment of this disease lies in early diagnosis and early treatment. Clinical studies have shown that serum homocysteine (Hcy), cystine (CysC), hypersensitive C-reactive protein (hs-CRP), endothelin-1 (ET-1) and fibrinogen (FIB) in patients with cerebral infarction are significantly higher than those in normal subjects(2). The serum concentration of these indicators plays an important role in the occurrence and process of cerebral infarction, but its relationship with the recurrence of cerebral infarction is not completely clear.

The purpose of this study was to investigate the changes of serum Hcy, CysC, hs-CRP, ET-1 and FIB levels in patients with primary cerebral infarction and to analyze their relationship with the occurrence and development of cerebral infarction. This study provides reference values for early diagnosis and treatment of cerebral infarction and observation of prognosis.

Clinical data and methods

General information

78 cases with primary CI admitted to Department of Neurology in our hospital from June 2015 to October 2016 were selected as the observation group. There were 53 males and 25 females in the observation group, aged 48 to 82 years old, with an average age of 61.8 years old. According to the results of cephalic CT, 78 patients with primary cerebral infarction were divided into three groups: there were 23 cases of small area cerebral infarction in group A, 28 cases of medium area cerebral infarction in group B, and 27 cases of large area cerebral infarction in group C. As shown in table 1, there was no significant difference in the basic data of the three groups of patients with cerebral infarction (P>0.05).

At the same time, the neurological deficit degree of 78 patients with primary cerebral infarction was evaluated according to the National Institutes of Health Stroke scale (NIHSS) (3) (mild: <4 points, moderate: 4 to 15 points, severe: ≥15 points). Among them, there were 24 cases of mild neurological deficit, 26 cases of moderate neurological deficit and 28 cases of severe neurological deficit. All the cases were in accordance with the diagnosis criteria with the combination of traditional Chinese and western medicine of cerebral infarction[4], and all the cases were diagnosed as the primary cerebral infarction by head CT or MRI.

Exclusion criteria:

- Previous history of cerebral infarction;
- Severe heart, liver, kidney, lung and other most important organ dysfunction;
- Endocrine, immune and blood system diseases;
- Malignant tumor;
- Patients with recent serious infections;
- Patients with recent use of diuretics, folic acid, vitamin B6, vitamin B1 and other drugs.

80 healthy subjects of physical examination in the outpatient department of our hospital were selected as the control group in the same period. There were 51 males and 29 females in the control group, aged 49 to 79 years old, with an average age of 60.3 years old. Statistical treatment indicated that there was no significant difference in sex and age between the two groups (P>0.05), suggesting comparability.

Groups	Cases	Male [n/(%)]	Female [n/(%)]	History of diabetes mellitus [n/(%)]	hyperlipemia [n/(%)]	Smoking history [n/(%)]	Age ($\bar{x}\pm s$)
A	23	16(69.56)	8(34.78)	13(56.52)	16(69.56)	8(34.78)	59.89±1.63
B	28	19(67.85)	9(32.14)	15(53.57)	18(64.28)	9(32.14)	61.33±2.03
C	27	18(66.67)	9(33.33)	15(55.56)	19(70.37)	11(40.74)	62.14±2.12
χ^2/F		0.15		0.64	0.83	0.53	0.03
P value		0.93		0.78	0.65	0.81	0.98

Table. 1: Clinical data and comparison of A, B, and C groups of patients with cerebral infarction.

Methods

Fasting peripheral venous blood was collected in all patients on the morning after admission. The concentrations of serum Hcy, CysC, ET-1, and FIB were determined by ELISA method, and the content of hs-CRP was measured by immunoturbidimetry. All reagents are provided by Beijing Jiuqiang companies, all operations are tested by the same inspector, and all tests are performed strictly in accordance with the instructions.

Statistical treatment

All the statistical data were analyzed by the SPSS18.0 system. The counting data were compared by the χ^2 test; the measured data were compared by t test and expressed as mean ± standard deviation ($\bar{x}\pm s$). P<0.05 indicated the difference was statistically significant.

Results

Comparison of plasma Hcy, CysC, hs-CRP, ET-1, and FIB concentrations between the two groups

Compared with the control group, the plasma Hcy, CysC, hs-CRP, and ET-1 concentration in the observation group was significantly increased compared to that in the control group (P<0.05), the concentration of FIB enhanced relatively obvious, and the difference was statistically significant.

Groups	Cases	Hcy (μmol/L)	CysC (mg/L)	hs-CRP (mg/L)	ET-1 (pg/ml)	FIB (mg/L)
Observation	78	30.23±9.14	1.89±0.35	21.03±0.48	71.36±6.36	3.73±0.46
Control	80	13.88±4.39	0.79±0.13	6.54±0.47	34.32±4.25	3.03±0.34
t		14.38	26.31	191.72	43.14	2.01
P		0.00	0.00	0.00	0.00	0.04

Table. 2: Comparison of plasma Hcy, CysC, hs-CRP, ET-1, and FIB concentrations between the two groups ($\bar{x}\pm s$).

Comparison of plasma Hcy, CysC, hs-CRP, ET-1, and FIB concentrations in group A, B, and C with cerebral infarction

There were significant differences in serum Hcy, CysC, hs-CRP, ET-1, and FIB concentrations after pairwise comparison of three groups of patients in group A, B and C (P<0.01), and the increase in concentrations plasma Hcy, CysC, hs-CRP, ET-1, and FIB in group C were more obvious (P<0.01), and the difference was statistically significant in all cases.

Groups	Cases	Hcy (μmol/L)	CysC (mg/L)	hs-CRP (mg/L)	ET-1 (pg/ml)	FIB (mg/L)
A	23	16.53±5.45	1.16±0.38	13.57±6.08	58.35±5.48	3.45±0.33
B	28	29.36±7.63*	1.54±0.36*	18.34±8.99*	60.83±6.36*	3.72±0.40*
C	27	32.36±8.92$^{*\#}$	2.16±0.47$^{*\#}$	25.68±11.39$^{*\#}$	80.34±6.35$^{*\#}$	3.93±0.42$^{*\#}$

Table. 3: Comparison of plasma Hcy, CysC, hs-CRP, ET-1, and FIB concentrations in group A, B, and C with cerebral infarction ($\bar{x}\pm s$).
Note: Compared with group A, $^{*}P<0.01$; compared with group B, $^{\#}P<0.01$.

Comparison of plasma Hcy, CysC, hs-CRP, ET-1 and FIB levels in patients with different neurological deficit

There were significant differences in plasma Hcy, CysC, hs-CRP, ET-1, and FIB levels after pairwise comparison of three groups of patients with a mild, moderate and severe neurological deficit (P<0.01). Moreover, the increase of levels of plasma Hcy, CysC, hs-CRP, ET-1, and FIB in patients with severe neurological deficit were more obvious (P<0.01).

Groups	Cases	Hcy (μmol/L)	CysC (mg/L)	hs-CRP (mg/L)	ET-1 (pg/ml)	FIB (mg/L)
Mild neurological deficit	24	20.32± 3.93	1.13± 0.36	13.62± 6.31	56.28± 4.39	3.38± 0.32
Moderate neurological deficit	26	28.93± 3.43*	1.46± 0.38*	16.32± 7.44*	60.14± 6.48*	3.46± 0.42*
Severe neurological deficit	28	33.24± 4.15$^{*\#}$	1.98± 0.4$^{*\#}$	24.57± 10.388$^{*\#}$	79.32± 6.05$^{*\#}$	3.84± 0.46$^{*\#}$

Table. 4: Comparison of plasma Hcy, CysC, hs-CRP, ET-1, and FIB levels in patients with different neurological deficit ($\bar{x}\pm s$).
Note: Compared with mild neurological deficit group, $^{*}P<0.01$; Compared with moderate neurological deficit group, $^{\#}P<0.01$.

Discussion

Cerebral infarction is a disease caused by a thrombus blocking an artery blood vessel. According to the size and severity of infarction, clinical manifestations show different degrees of limb numbness, limb dysfunction, limb weakness, language disorder, visual rotation, dizziness, vomiting, etc. With the continuous improvement of the standand of living in recent years, people's food has and diet have changed. In addition, poor eating habits lead to more and more people with hypertension, diabetes, and hyperlipidemia, which are important factors causing cerebral infarction. In fact, the occurrence and development of cerebral infarction are based on arteriosclerosis, and arteriosclerosis is closely related to inflammatory factors, vascular stenosis, vascular endothelial injury and ischemic hypoperfusion injury. An inflammatory reaction can cause vascular endothelial injury, mediate lipid deposition on the arterial wall, and induce atherosclerotic plaque rupture and thrombosis[5], which plays an important role in the ischemic injury of brain tissue. Some clinical studies have shown that the occurrence and development of cerebral infarction are closely related to laboratory biochemical indexes, which are objective and convenient to detect and can dynamically reflect the severity and development of cerebral infarction. Therefore, laboratory biochemical indexes can provide an objective basis for judging the condition and prognosis of patients.

Hcy is an important intermediate product in amino acid metabolism. It has been proved that high Hcy has direct cytotoxicity to vascular endothelial

cells, direct injury to blood vessels and nerves, and leads to arteriosclerosis, which is an independent risk factor for cardiovascular and cerebrovascular diseases[6-7]. The main effects of oxidation are as follows: leading to the dysfunction of vascular endothelial cells and damage of vascular endothelial cells, thus promoting the proliferation of vascular smooth muscle cells; causing abnormal coagulation and fibrinolysis; interfering with lipid metabolism; and promoting an inflammatory response. The oxidation form of Hcy is highly reactive, which can promote cell uptake and condensation of LDL, resulting in cholesterol deposition and aggravated vascular calcification. A large number of studies have shown that the higher the concentration of Hcy, the higher the severity and risk of cerebral infarction, and the greater the effect on neural function. In this experimental study, the level of Hcy in the observation group was significantly higher than that in the control group (P<0.01), and there was an increasing relationship among the levels of Hcy in groups A, B and C patients with cerebral infarction (P<0.01). Moreover, the level of Hcy in the three groups with mild, moderate and severe neurological deficit was also increased (P<0.01), which was consistent with the above point of view.

CysC has the function of regulating the activity of cysteine protease, promoting the metabolism of peptide and protein, hydrolyzing prohormone protein, and making hydrolysates act on target tissues to play a biological role. Some scholars have proved that CysC is involved in the pathophysiological process of cardiovascular diseases such as atherosclerosis[8]. It may be involved in vascular injury and inflammatory reaction and promote the formation of arteriosclerosis. The level of serum CysC increased in different degrees in the early stage of cerebral infarction, and the more serious the clinical symptoms of patients with cerebral infarction, the more significant the increase of CysC level[9]. Combined with the results of this study, the level of CysC in the observation group was significantly higher than that in the control group (P<0.01), and there was an increasing relationship among the levels of CysC in group A, B, C and the three groups of mild, moderate and severe neurological deficit (P<0.01), which also proved the hypothesis.

Hs-CRP, as a marker of an acute inflammatory reaction, is very low in the blood of healthy people, and the concentration hs-CRP is rapidly increased when the body is stimulated by related inflammatory factors. Atherosclerosis is a chronic inflammatory lesion of blood vessels. Some studies have shown that hs-CRP is closely related to the occurrence and development of arteriosclerosis[10]. Hs-CRP is a reactive protein produced by hepatocytes stimulated by cytokines secreted by activated giant cells. It can induce the production of MCP-1 and decrease the expression level of nitric oxide synthase at the same time, causing the dysfunction of vascular endothelial cells, the increase of plasma thrombin activating factor and the expression and activity of inhibitory factor, promote the imbalance of kinetic energy of coagulation and fibrinolysis system and accelerate thrombosis. The results of this study indicated that the level of hs-CRP in the observation group was significantly higher than that in the control group (P<0.01), and the levels of hs-CRP in group A, B and C were all increased (P<0.01). Moreover, with the aggravation of neurological deficit, the level of hs-CRP increased significantly (P<0.01), suggesting that the level of serum hs-CRP is positively correlated with the degree of cerebral infarction and the degree of neurological deficit.

The important pathophysiological changes of atherosclerosis are lipid deposition, inflammatory reaction and vascular endothelial injury. Vascular endothelial injury runs through the whole process of disease occurrence and development and plays a key role in arteriosclerosis and thrombosis. ET-1 is involved in the pathophysiological process of vascular endothelial injury. Some studies have shown that the concentration of serum ET-1 increases sharply in the case of vascular endothelial injury, so the level of ET-1 can reflect the condition of vascular endothelial injury, thus reflecting the occurrence and development of cerebral infarction[11-12]. The level of ET-1 in the observation group was significantly higher than that in the control group (P<0.01), and the concentration of ET-1 in groups B and C was significantly higher than that in group A. In addition, there was an increasing relationship of ET-1 levels among mild, medium and severe neurological deficit (P<0.01), which was consistent with the results of Liu Feng et al.[13].

FIB is closely related to atherosclerosis and cerebral infarction. The clinical epidemiological study found that the increase of FBI is an important risk factor leading to cardiovascular and cerebrovascular thrombotic diseases, which can change vascular endothelial permeability, increase LDL aggregation, stimulate smooth muscle cell proliferation, and migrate to the intima[14-15]. High-level FIB can seriously affect the coagulation and

fibrinolysis system, and the degradation product can directly damage the blood vessel wall. The results of this study showed that the FIB level in the observation group was significantly higher than that in the control group ($P<0.05$), and the FIB concentration was also increased with the increase of the area of cerebral infarction and the increase of the neurological deficit. Therefore, the FIB level can be used as one of the reliable indexes to evaluate the prognosis of cerebral infarction.

In conclusion, the levels of serum Hcy, CysC, hs-CRP, ET-1 and FIB in patients with primary cerebral infarction are closely related to the condition and prognosis of cerebral infarction and play an important role in the occurrence and development of cerebral infarction. With the increase of serum Hcy, CysC, hs-CRP, ET-1 and FIB levels, the cerebral infarction was more serious. Therefore, in the process of diagnosis and treatment of patients with primary cerebral infarction and prognosis, it is necessary to make good use of these laboratory biochemical indexes to provide a reliable basis for early diagnosis and treatment of cerebral infarction and prognosis.

References

1) Nannoni S, Sirimarco G, Cereda CW, Lambrou D, Strambo D, et al. Determining factors of better leptomeningeal collaterals: a study of 857 consecutive acute ischemic stroke patients. J Neurol 2019;266: 582-588.
2) Gao Y, Wang T. The application of combination detection of CysC, hs-CRP, Hcy, D-D in the diagnosis of acute cerebral infarction. Chin J Pract Nervous Dis 2018; 21: 1114-1118.
3) Griessenauer CJ, Medin C, Maingard J, Chandra RV, Ng W, et al. Endovascular Mechanical Thrombectomy in Large-Vessel Occlusion Ischemic Stroke Presenting with Low National Institutes of Health Stroke Scale: Systematic Review and Meta-Analysis. World Neurosurg 2018; 110: 263-269.
4) Romano DG, Cioni S, Vinci SL, Pero G, Comelli C, et al. Thromboaspiration technique as first approach for endovascular treatment of acute ischemic stroke: initial experience at nine Italian stroke centers. J Neurointerv Surg 2017; 9: 6-10.
5) Pan X, Hou R, Ma A, Wang T, Wu M, et al. Atorvastatin Upregulates the Expression of miR-126 in Apolipoprotein E-knockout Mice with Carotid Atherosclerotic Plaque. Cell Mol Neurobiol 2017; 37: 29-36.
6) Cui ZT, Liu JP, Yao JM. Antagonistic effects of endostatin-vascular endothelial growth inhibitor chimeric recombinant adenovirus on homocysteine-induced vascular endothelial cells injury in vitro and in vivo. Med 2016; 95: 5197.
7) Friedman AN, Rosenberg IH, Selhub J, Levey AS, Bostom AG, et al. Hyperhomocysteinemia in renal transplant recipients. Am J Transplant 2015; 2: 308-313.
8) He LY, Li J, Zhan JF, Yi FM, Fan XD, et al. The value of serum cystatin C in early evaluation of renal insufficiency in patients undergoing chemotherapy: a systematic review and meta-analysis. Cancer Chemother Pharmacol 2019; 83: 561-571.
9) Jiang YL, Wang SP, Zhang YQ. Effect and correlation of ischemic adaptation on NIHSS score and serum CysC level in patients with acute cerebral infarction. Chin J Gerontol 2016; 36: 849-850.
10) Cigliana G, Gulli F, Napodano C, Pocino K, De Santis E, et al. Serum free light chain quantitative assays: Dilemma of a biomarker. J Clin Lab Anal 2018; 32: 22243.
11) Wei P, Han B, Zhang WJ, Bai J, Jiang CY, et al. Effect of ticagrelor on the serum level of hs-CRP, ESM-1 and short-term prognosis of patients with acute STEMI. Exp Ther Med 2017; 13: 604-608.
12) Angus JA, Rja H, Wright CE. Distortion of KB estimates of endothelin-1 ETA and ETB receptor antagonists in pulmonary arteries: Possible role of an endothelin-1 clearance mechanism. Pharmacol Res Perspect 2017; 5: 374.
13) Liu F, Gao YJ. For the first time, gao min serum C-reactive protein in patients with cerebral infarction, endothelin-1, fibrinogen concentration and correlation of recurrent cerebral infarction. J Hunan Normal Univ (Med Sci) 2016; 13: 25-27.
14) Flint K, Kennedy K, Arnold SV, Dodson JA, Cresci S, et al. Slow Gait Speed and Cardiac Rehabilitation Participation in Older Adults After Acute Myocardial Infarction. J Am Heart Assoc 2018; 7: 8296.
15) Yu WC, Lin XG. Effects of dexmedetomidine on stress response and postoperative coagulation function in patients with radical gastrectomy. J Guangxi Med Univ 2019; 36: 84-88.

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