ORIGINAL ARTICLE
https://doi.org/10.1590/1806-9282.20210693

Relationship of uric acid, C-reactive protein, and N-terminal pro-B-type natriuretic peptide with acute cerebral infarction

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SUMMARY

OBJECTIVE: The objective was to study the relationship of serum uric acid, C-reactive protein, and N-terminal pro-B-type natriuretic peptide levels with acute cerebral infarction.

METHODS: A total of 96 acute cerebral infarction patients were divided into small, middle, and large infarct size groups based on the size of infarct focus and mild, moderate, and severe infarction groups based on the evaluation criteria of nerve defect degree. In addition, 75 healthy people were selected as the control group. The serum uric acid, C-reactive protein, and N-terminal pro-B-type natriuretic peptide levels of all subjects were detected.

RESULTS: The serum uric acid, C-reactive protein, and N-terminal pro-B-type natriuretic peptide levels in the acute cerebral infarction group were significantly higher than the control group ($p<0.05$). Compared with the small infarct size group, each index in middle and large infarct size groups was significantly increased ($p<0.05$). Compared with the middle infarct size group, each index in the large infarct size group was significantly increased ($p<0.05$). The serum uric acid, C-reactive protein, and N-terminal pro-B-type natriuretic peptide levels in moderate and severe infarction groups were significantly higher than the mild infarction group ($p<0.05$). Compared with the moderate infarction group, each index in the severe infarction group was significantly increased ($p<0.05$). The serum uric acid, C-reactive protein, and N-terminal pro-B-type natriuretic peptide levels were positively correlated with the infarct size and nerve defect degree ($p<0.05$).

CONCLUSIONS: The serum uric acid, C-reactive protein, and N-terminal pro-B-type natriuretic peptide levels are closely correlated with the occurrence and development of acute cerebral infarction. The detection of these indexes has significance for understanding the severity of acute cerebral infarction, guiding the individual treatment scheme, and evaluating the prognosis.

KEYWORDS: Cerebral infarction. Uric acid. C-reactive protein. N-terminal pro-BNP

INTRODUCTION

Acute cerebral infarction (ACI) mainly refers to brain tissue necrosis due to brain blood circulation disorders caused by tissue ischemia, hypoxia, and other factors[1]. ACI patients often have varying degrees of dizziness, unclear speech, numbness, and other symptoms, and severe ACI patients may have a disability, or even death[2]. Therefore, the reasonable and effective evaluation of ACI condition is very critical. It is a hot topic to search for serum markers related to the diagnosis and prediction of ACI. Uric acid (UA) is a purine metabolite, which is excreted by kidney and intestine. The high serum UA level is closely associated with cardiovascular and cerebrovascular diseases[3]. C-reactive protein (CRP) is a reactive protein produced with tissue damage or inflammation. It is also a major inflammatory factor involved in atherosclerotic disease[4]. B-type natriuretic peptide (BNP) is a kind of hormone

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Conflicts of interest: the authors declare there are no conflicts of interest. Funding: none.
Received on August 11, 2021. Accepted on August 14, 2021.

substance existing in various tissues of the body, especially in brain tissue and heart muscle. It can antagonize the renin-angiotensin-aldosterone system and has the diuretic, sodium excreting, and vasodilating effects[5]. N-terminal pro-B-type natriuretic peptide (NT-proBNP) is the cleavage product of BNP, which has the homology with BNP[6]. In view of this, this study explored the relationship of serum UA, CRP, and NT-proBNP levels in patients with ACI, so as to provide the effective guidance and scientific basis for the clinical diagnosis and treatment of ACI.

METHODS

Subjects

A total of 96 ACI patients treated in the Affiliated Hospital of Zunyi Medical College from March 2018 to May 2020 were enrolled in this study. There were 55 males and 35 females. The age of patients was 46–74 years old, with an average age of 60.45±11.45 years. The time from disease onset to admission was 8–24 h, with an average time of 16.56±6.44 h. Based on the size of infarct focus, the patients were divided into small infarct size group (infarct diameter ≤3 cm; 48 cases), middle infarct size group (3 cm < infarct diameter ≤5 cm; 30 cases), and large infarct size group (infarct diameter >5 cm; 12 cases). Based on the evaluation criteria of nerve defect degree issued by the National Institutes of Health Stroke Scale (NIHSS), the patients were divided into mild infarction group (NIHSS score ≤4 points; 45 cases), moderate infarction group (4 points < NIHSS score ≤15 points; 35 cases), and severe infarction group (NIHSS score >15 points; 10 cases). In addition, 75 healthy people receiving physical examination in our hospital in the same period were selected as the control group. There were 50 males and 25 females. Their age was 45–74 years, with an average age of 62.16±10.18 years. There was no significant difference in gender or age between the two groups ($p>0.05$). This study has been approved by the Ethics Committee of the Affiliated Hospital of Zunyi Medical College. All the subjects had signed the informed consent to this study.

Inclusion and exclusion criteria

The inclusive criteria were as follows:

(i) the age was 30–75 years;
(ii) the ACI was diagnosed by computed tomography or magnetic resonance imaging;
(iii) the ACI was the first onset;
(iv) the time from disease onset to admission was <24 h; and
(v) the patients had not received surgical treatment recently.

The exclusion criteria were as follows:

(i) the patients had incomplete clinical data;
(ii) the patients had severe diseases of lung, liver, kidney, or other organs;
(iii) the patients had blood diseases or diabetes;
(iv) the patients had a history of brain diseases; and
(v) the patients were pregnant or lactating women.

Study method

In the ACI group, 5 mL of venous blood was collected in the morning after admission. In the control group, 5 mL of venous blood was taken in the morning of the day of physical examination. The blood was centrifuged at 3000 r/min for 10 min. The serum was obtained and was stored at -80°C for detection. The UA was detected by the peroxidase method. The CRP was detected by immunoturbidimetry. The NT-proBNP was detected by quantum dots-based immunofluorescence chromatography. The detection operations were in strict accordance with the instruction of the kits. The comparisons of serum UA, CRP, and NT-proBNP levels between ACI and control groups, among small, middle, and large infarct groups, and among mild, moderate, and severe infarction groups were performed. The correlations of UA, CRP, and NT-proBNP with infarct size and the correlations of UA, CRP, and NT-proBNP with NIHSS score were analyzed.

Statistical analysis

Data were analyzed by SPSS 20.0 software (SPSS Inc., Chicago, IL, USA). The enumeration data were expressed as a percentage (%), and the comparison was conducted using the χ^2 test. The measurement data were expressed by mean±standard deviation. The comparison between two groups was conducted by the t-test, and that among multiple groups was conducted by the analysis of variance with the SNK-q test. Spearman's correlation analysis was used for the correlations of each serum index with infarct size and each serum index with NIHSS score. $p<0.05$ was considered statistically significant.

RESULTS

Comparison of serum uric acid, C-reactive protein, and N-terminal pro-B-type natriuretic peptide levels between control and acute cerebral infarction groups

As shown in Table 1, the serum UA, CRP, and NT-proBNP levels in the ACI group were significantly higher than those in the control group ($p<0.05$).

Comparison of serum uric acid, C-reactive protein, and N-terminal pro-B-type natriuretic peptide levels among small infarct, middle infarct, and large infarct size groups

Compared with the small infarct size group, the serum UA, CRP, and NT-proBNP levels in middle and large infarct size groups were significantly increased ($p<0.05$). Compared with the middle infarct size group, the serum UA, CRP, and NT-proBNP levels in the large infarct size group were significantly increased ($p<0.05$) (Table 2).

Comparison of serum uric acid, C-reactive protein, and N-terminal pro-B-type natriuretic peptide levels among mild infarction, moderate infarction, and severe infarction groups

Table 3 showed that the serum UA, CRP, and NT-proBNP levels in moderate and severe infarction groups were significantly higher than those in the mild infarction group ($p<0.05$). Compared with the moderate infarction group, the serum UA, CRP, and NT-proBNP levels in the severe infarction group were significantly increased ($p<0.05$).

Table 1. Comparison of serum uric acid, C-reactive protein, and N-terminal pro-B-type natriuretic peptide levels between control and acute cerebral infarction groups.

	n	UA (nmoL/mL)	CRP (μg/mL)	NT-pro BNP (pg/mL)
Control	90	266.61±45.29	1.08±0.26	52.04±11.08
ACI	75	403.32±88.02	7.16±1.53	336.60±84.37
t		12.840	37.084	31.690
p-value		<0.001	<0.001	<0.001

ACI: acute cerebral infarction; t: statistic value; UA: uric acid; CRP: C-reactive protein; NT-pro BNP: N-terminal pro-B-type natriuretic peptide.

Table 2. Comparison of serum uric acid, C-reactive protein, and N-terminal pro-B-type natriuretic peptide levels among small infarct, middle infarct, and large infarct size groups.

	n	UA (nmoL/mL)	CRP (μg/mL)	NT-proBNP (pg/mL)
Small infarct size	48	305.84±62.09	5.38±0.78	245.07±52.05
Middle infarct size	30	473.13±55.45*	6.81±0.93*	383.25±60.27*
Large infarct size	12	543.90±67.37*#	9.54±1.34*#	463.72±72.91*#
F		112.797	102.657	95.228
p-value		<0.001	<0.001	<0.001

UA: uric acid; CRP: C-reactive protein; NT-proBNP: N-terminal pro-B-type natriuretic peptide; F: statistic value. *p<0.05 compared with small infarct size group; #p<0.05 compared with middle infarct size group.

Table 3. Comparison of serum uric acid, C-reactive protein, and N-terminal pro-B-type natriuretic peptide levels among mild, moderate, and severe infarction groups.

	n	UA (nmoL/mL)	CRP (μg/mL)	NT-proBNP (pg/mL)
Mild infarction	45	316.45±45.62	5.65±1.34	276.27±34.07
Moderate infarction	35	466.12±78.17*	7.32±1.13*	376.82±54.30*
Severe infarction	10	565.06±72.04*#	10.16±1.01*#	441.04±72.71*#
F		92.914	60.117	70.765
p-value		<0.001	<0.001	<0.001

UA: uric acid; CRP: C-reactive protein; NT-proBNP: N-terminal pro-B-type natriuretic peptide; F: statistic value. *p<0.05 compared with mild infarction group; #p<0.05 compared with moderate infarction group.

Correlation of uric acid, C-reactive protein, and N-terminal pro-B-type natriuretic peptide with infarct size and nerve defect degree

Spearman's correlation analysis showed that, in 90 ACI patients, the serum UA, CRP, and NT-proBNP levels were positively correlated with the infarct size (UA with infarct size: r=0.683, p<0.001; CRP with infarct size: r=0.698, p<0.001; NT-proBNP with infarct size: r=0.564, p<0.001). The serum UA, CRP, and NT-proBNP levels were also positively correlated with the nerve defect degree (UA with nerve defect degree: r=0.401, p<0.001; CRP with nerve defect degree: r=0.389, p<0.001; NT-proBNP with nerve defect degree: r=0.523, p<0.001).

DISCUSSION

ACI is a common and high-incidence cerebrovascular disease. It is commonly found in the middle-aged and elderly population. It has a high disability rate, recurrence rate, and mortality rate. Studies have shown that the most common cause of ACI is atherosclerosis[7]. When atherosclerosis-caused brain ischemia or hypoxia occurs, it will cause a series of local inflammatory reactions, leading to the damage to brain tissue[8]. Therefore, the key to the treatment of ACI is to improve the oxygen supply of brain tissue for promoting the recovery of nerve tissue.

With the continuous development of medical technology, the research on the mechanism of ACI is becoming more and more mature. Study[9] has shown that hyperuricemia is an important risk factor for cerebral infarction. The mechanism may be that the high level of UA damages the vascular endothelial function by inhibiting oxidative reaction and affects the arterial capillary wall remodeling. This promotes thrombosis and participates in the inflammatory reaction[10]. CRP is mainly synthesized by hepatocytes, and the mononuclear phagocytes and fibroblasts can also produce a small amount of CRP. It is found that the content of CRP in the blood is increased sharply when the acute inflammatory reaction occurred[11]. In addition, CRP participates in the pathological process of thrombosis and arteriosclerosis, which is one of the risk factors of stroke[12]. NT-proBNP plays an important role in the progress of the cerebrovascular disease, which is closely related to the location and size of ACI lesion[13]. The increase in NT-proBNP level can reduce brain edema and protect brain tissue through diuretic and natriuretic effects[14].

This study explored the changes and clinical significance of serum UA, CRP, and NT-proBNP levels in patients with ACI. Results showed that the serum UA, CRP, and NT-proBNP levels in the ACI group were significantly higher than those in the control group. In addition, with the increase of infarct size and nerve defect degree, the serum UA, CRP, and NT-proBNP levels in ACI patients obviously increased. Spearman's correlation analysis showed that the serum UA, CRP, and NT-proBNP levels were positively correlated with the infarct size and nerve defect degree. This indicates that the serum UA, CRP, and NT-proBNP levels are closely correlated with the occurrence and development of ACI. The high level of UA promotes the platelet adhesion and aggregation, weakens the chemotaxis of red blood cells, and aggravates cerebral ischemia and hypoxia, worsening the progress of ACI[15]. CRP can activate the complement system and can form many terminal proteins and complexes, which causes the damage of vascular intima resulting in ACI[16]. After ACI, the brain tissue ischemia and necrosis causes the abnormal hypothalamus-pituitary secretion, resulting in increased NT-proBNP level[17], so the NT-proBNP level is closely related to ACI.

CONCLUSIONS

The serum UA, CRP, and NT-proBNP levels are closely correlated with the occurrence and development of ACI. The detection of these indexes has significance for understanding the severity of ACI, guiding the individual treatment scheme, and evaluating the prognosis. The limitation of this study is that the sample size is relatively small. In our subsequent studies, a larger sample size will make the results more convincing.

AUTHORS' CONTRIBUTIONS

SY: Conceptualization, Writing – review & editing. **GL:** Data curation. **CH:** Formal analysis. XX: Writing – original draft.

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