The Relationship between Plasma Type B Brain Natriuretic Peptide Precursor, CTN-I, Platelet Activation Factor and Prognosis in Elderly Patients with Advanced Cerebral Infarction

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Abstract: To study the effect of plasma levels of Plasma type B brain natriuretic peptide precursor, Cardiac troponin I, Platelet alpha - granular membrane protein and Platelet aggregation rate on the prognosis of elderly patients with advanced cerebral infarction. Methods: There were included 86 cases of elderly patients with advanced cerebral infarction admitted to our hospital from March 2016 to March 2019 .The concentrations of NT-proBNP, CTN-I, GMP-140 and PAgT were detected in all patients within 24 hours of onset. The patients were divided into three groups, and It were observed the levels of NT-proBNP, CTN-I, GMP-140 and PAgT in patients with different cerebral infarction according to NHISS and BI scores on admission. Patients were followed up for 6 months, 6 of whom died within 3 months. The patients were followed up for 6 months, 6 of whom died within 3 months. The difference value of NIHSS scores is greater than four is considered good prognosis, while NIHSS score is less than considered poor prognosis according to the difference value of two NIHSS scores. To compare the levels of related indicators, which NT-proBNP, CTN-I, GMP-140 and PAgT, in the survival and death cases, the good prognosis group and the poor prognosis group. Conclusion: It was significantly increased that the level of NT-proBNP, CTN-I, GMP-140 and PAgT in patients with progressive cerebral infarction, and the prognosis was worse. It can be used as clinical indicators to observe the prognosis of senile patients with advanced cerebral infarction.

Keywords: Cerebral infarction; NT-proBNP; CTN-I; GMP -140; PAgT

1. Introduction

Progressive cerebral infarction is a major disease endangering the life and health of the elderly and it has a high fatality rate and disability rate, which is a type of neurological impairment gradually or progressively aggravated within 6 hours to 2 weeks after onset, until more serious neurological impairment occurs. The elderly are more prone to infection, cardiac dysfunction, renal insufficiency and other important organ dysfunction and coagulation dysfunction, leading to poor prognosis. This study explore the related factors affecting the short-term prognosis of acute cerebral infarction integrated the medical history and serological indexes.

2. Data and methods

2.1. subjects

Cerebral infarction patients hospitalized in the department of neurology in our hospital from March 2016 to March 2019, meeting the following criteria: (1) age ≥60 years; (2) the patient was admitted within 72h after onset, meeting the diagnostic criteria formulated by the fourth national conference on cerebrovascular diseases of the Chinese medical association; The head was confirmed by CT or MR, but cerebral hemorrhage was excluded. The neurological dysfunction symptoms gradually worsened after medical intervention within 2 weeks after onset. Exclusion criteria: previous history of coronary heart disease, heart failure, chest tightness and chest pain, history of cardiac surgery, existence of emboli such as atrial fibrillation.

2.2. Methods

Prospective studies were used to continuously enroll all patients meeting the inclusion criteria.
The national institutes of health neurofunctional impairment scale (NIHSS) score was used to determine the degree of neurofunctional impairment, and the daily living

ability (BI) score and modified Rankin scale (mRS) score were used to evaluate the prognosis on admission. During hospitalization, standardized treatment was conducted according to the 2011 guidelines for the prevention and treatment of cerebrovascular diseases in China, and it was completed that ultrasound examination of head M R l, M R A, CTA and carotid and vertebral arteries

Severity of cerebral infarction was assessed by NIHSS grading [1]. Mild neurological dysfunction: NIHSS<4 points; moderate neurological dysfunction: NIHSS score 4 ~ 15; severe neurological dysfunction: NIHSS>15. Patients in the observation group were divided into three groups according to the degree of neurological dysfunction: mild, moderate and severe. It was compared among the three groups that levels of NT-proBNP, CTN-I, GMP-140 and PAgT. It was respectively measured that NIHSS scores of patients in the observation group at admission and discharge at 1 month, 3 months and 6 months. It is considered good prognosis that two NIHSS score differences greater than four, while it is considered poor prognosis that NIHSS score differences less than four [2]. The good prognosis, poor prognosis and mortality were compared among the three groups.

Biochemical test indicators platelet activation indicators: plasma mp-140 content determination kit provided by Shanghai sun biotechnology company, using the ELESA method detection, in strict accordance with the operation instructions. Platelet aggregation rate (PAgT): after blood collection, it was separated platelet-rich plasma and platelet-poor plasma. it was strictly in accordance that ADP was used as the inducer and the operation with the instructions. The method was measured on FYXN 9125 intelligent blood aggregation instrument. The normal group received one test during physical examination. Patients in the two groups were tested before and 3 months after treatment. All patients in two groups were received 4mL venous blood on an empty stomach on the morning after admission for examination: it was extracted from the subjects that blood BNP index detection 2mL venous blood from elbow, BNP was detected by MAGLuMI chemiluminescence detector using chemiluminescence sandwich method. Instrument: production and production automatic light measuring instrument of us B E C K M A N - C O U I T E R company, test agent: B E C K M A N - C O U L T E R company production original assembly test agent.

2.3. Follow-up and final events

Divided into good prognosis group and poor prognosis group according to NIHSS, ADL and mRS scores were reexamined at 1 month, 3 months and 6 months after onset. Prognosis: good group: BI>60 points; Poor prognosis group: BI score was 0-60.

2.4. Statistical treatment

SPSS20.0 software was used for statistical analysis. Measurement data of normal distribution were expressed as mean ± standard deviation (X±s), and T-test was used for comparison between groups. The counting data were expressed as a percentage (%), and X test was used for comparison between groups. Multivariate Logistic regression analysis was used to determine the short-term prognostic factors of elderly patients with acute cerebral infarction, and ROC curve was developed to calculate the optimal critical value, sensitivity, specificity, positive predictive value and negative predictive value. P<0.05 was considered statistically significant.

3. Results

It were collected 86 elderly patients with acute cerebral infarction in this study, six of whom died within 3 months. Among them, they were aged from 60 to 89 years in 46 males and 34 females. with an average age of （75.27±10.69） years.

3.1. Demographic characteristics and clinical data analysis:

57 cases in the good prognosis group and 24 cases in the poor prognosis group. elderly, female, and previous cerebral infarction in the group with poor prognosis. The difference was statistically significant compared with the group with good prognosis (P<0.05 or P<0.01).

Table 1. The prognosis of different groups of clinical data and the analysis of serological indexes

Items	Good prognosis group	Poor prognosis group
NHISS (point)	3.46±2.8	14.21±6.7
NHISS (point)	3.46±2.8	14.21±6.7
BI (point)	76.24±18.5	21.54±23.25
MRs (point)	1.84±0.86	4.25±0.84
NT-proBNP (pg/ml)	462.7±366.5	2816.4+1680.2
CNT-I (ug/L)	2.21±0.16	5.49±2.37
GMP-140 (ng/L)	10.8±5.23	20.4±9.46
PAgT (%)	42.1±12.5	70.2±+18.7

3.2. It was performed that logistic regression analysis of related factors with poor prognosis ultifactorial logistic regression analysis for the above statistically significant indicators

Results showed that NIHSS score (OR=1.537, 95% CI: 1.167～2.063), BNP (OR= 1.342, 95% CI: 1.103 ～ 1.944) and ctn-I (OR= 1.268, 95% CI: 1.051 ～1.732) at admission were correlated with poor prognosis.

3.3. The ROC curve was drawn for the related factors of poor prognosis

The ROC curve was drawn for the above four factors. The optimal critical value of N IH SS score at admission was 7 points, the sensitivity was 78.2%, the specificity was 91.8%, and the positive predictive value was 86. The area under the R O C curve was 0.82. It was 568pg/ml that optimal critical value of serum BNP, the sensitivity was 100%, the specificity was 91.8%, the positive predictive value was 85.1%, the negative predictive value was 100%, and the area under ROC curve was 0.98. It was 254 ng/ml that optimal critical value of ctn-I in blood serum, the sensitivity was 84.7%, the specificity was 71.1%, the positive predictive value was 56.1%, the negative predictive value was 85.4%, and the area under ROC curve was 0.77.It was 15ng/ml that optimal critical value of GMP-140, and the sensitivity was 82.4%, with a specificity of 71.2%, positive predictive value 59. The negative predictive value was 88.7%. The area under the ROC curve is 0. 85.

Table 1. 2.4 Nt-proBNP, CNT-I, GMP-140 and PAgT level of patients with varying degrees of nerve damage

	Cases	NT-proBNP (pg/ml)	CNT-I (ug/L)	GMP-140 (ng/mL)	PAgT (%)
Mild	28	233.7±321.4*	0.23±0.03*	8.21± 3.1*	30.5±8.2*
Moderate	29	576.4±601.3▲	1.85± 0.21▲	11.7±4.12▲	54.1±12.5▲
Severe	29	4871.5±3482.9△	7.24± 0.62△	25.9± 8.14△	83.2± 19.1△

Note: * comparison between mild group and severe group, ▲ comparison between mild group and moderate group, and △ comparison between moderate group and severe group, all P <0.05

4. Discussion

Progressive cerebral infarction, which is a common and severe clinical subtype of acute cerebral infarction, is accounting for 26% - 43% of all cerebral infarction and it usually occurs on the basis of atherosclerosis. Platelet is the initial factor of atherosclerosis and the core link of thrombosis. As is known to all, it is the two major physiological functions displayed by activated platelets that platelet adhesion energy and aggregation energy , which are the guarantees for further activation of blood plaque, participation in hemostasis, and promotion of blood coagulation, as well as the important basis for thrombosis. Platelets are highly activated in the body during the onset of cerebral infarction, and directly involved in the occurrence, development and outcome of ischemic brain injury through various effects, which is an important risk factor for the occurrence of ACI.GMP-140 is a glycoprotein mainly found in platelet particles and endothelial cells in wechsler's small body, which is the product of activating platelets. This egg white component is expressed on the cell surface and released into plasma when endothelial cells are damaged and platelets are activated, resulting in increased plasma GMP-140 levels. Therefore, the content of G M P140 will also increase when vascular lesions occur. Changes in GMP 140 concentration are a specific marker of platelet activation and release.

This study showed that the poor prognosis group was significantly higher than the good prognosis group, and there was a significant difference between the two groups. Platelet aggregation rate and gmp-140 were risk factors for poor prognosis in elderly patients with cerebral infarction.

The measurement of platelet aggregation rate is the performance of platelet activation and release response and platelet membrane protein receptor comprehensive factors, as well as the basis of platelet function detection. Therefore, the detection of platelet aggregation function is of great significance for the mechanism and prognosis of cerebral infarction.

N-terminal brain natriuretic peptide precursor is the amino terminal fragment left in the process of brain natriuretic peptide precursor cracking into brain natriuretic peptide. The secretion of BNP and n-brain natriuretic peptide precursors increased correspondingly when intracavity pressure increased and cardiac function was impaired [3]. The N-terminal brain natriuretic peptide precursor was released in proportion to brain natriuretic peptide, and the half-life was 6 times that of BNP [4]. It is well used in clinical practice because serum nt-pro-BNP is easier to detect.BNP is a neuroendocrine hormone secreted and stored by the heart. Studies have shown that there are specific BNP receptors in brain tissue, so the change of plasma BNP concentration has a certain impact on brain function. It plays an important role in the regulation of peripheral biological effects, which can reduce the sympathetic excitability of brain stem, reduce the secretion of arginine vasopressin and a drenocorticotropin in the hypothalamus, and reduce the desire to drink salt and water caused by the third ventricle although the concentration of brain secretion synthesis BNP is very low. Foreign scholars believed that BNP is cerebral infarction and transient ischemic attack predict death after strong indicators, in order to further study the BNP can for.

Prediction of in-hospital death risk in the process of biological indicators, it is found that the BNP in hospitalized

death group was obviously higher than the survival group, which showed that blood BNP levels can predict the prognosis of patients with this part serves as an important role [5]. Jensen JK et al. concluded similarly that plasma BNP levels were a strong independent predictor of mortality at 6 months after cerebral infarction [6]. It is not clear that the mechanism of elevated concentrations of cardiac markers after acute stroke, but one idea is that cardiogenic elevation, which is caused by previous or concomitant coronary artery disease. Currently, more scholars tend to another view, That is increased neurogenesis: stroke leads to autonomic nervous dysfunction followed by heart injury. Patients with acute ischemic stroke are often complicated with cardiovascular events, including myocardial ischemia, myocardial infarction and arrhythmia [7-9], which increases the mortality and affects the prognosis of patients. In our study, the case group with normal ctn-i had a case fatality rate of 3.76 %, while the case group with increased ctn-i had a case fatality rate of 18.42 %, with a statistically significant difference ($P < 0.05$). Therefore, the prognosis of patients with elevated troponin is worse than that of patients with normal troponin, and the mortality of hospitalized patients is significantly increased. This suggests that the serum ctn-i concentration at admission is an indicator to determine the prognosis of hospitalized patients with acute ischemic stroke.

This study showed that It were correlated with prognosis which BNP and CNT-I levels at the early stage of cerebral infarction .It showed poor prognosis that Serum BNP>576pg/ml and CNT-I >1.85ug/L, which together could be used as prognostic indicators. The deficiency of this study is that the sample size is small, which is only the data of our study. In the future, we should expand the sample size and carry out multi-center joint studies to reduce the selection bias of patients among medical institutions. In addition, the follow-up time can be extended to compare the difference between short-term prognosis and long-term prognostic risk factors, which is conducive to more timely adjustment and treatment, and better improve the patients' pre-treatment.

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