Original Article
Changes in soL-CXCL16 and NT-proBNP levels in patients with acute myocardial infarction before and after percutaneous coronary intervention

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Abstract: Objective: To investigate the changes in the serum soluble chemokine 16 (soL-CXCL16) and N-terminal prohormone of brain natriuretic peptide (NT-proBNP) levels and their therapeutic effects in patients with acute myocardial infarction (AMI) after percutaneous coronary invention (PCI). Methods: A total of 100 AMI patients undergoing PCI were included in the experimental group, and other 50 patients without coronary heart disease (CHD) as demonstrated by coronary angiography were included in the control group in the same period. The enzyme linked immunosorbent assay (ELISA) was used for detection of the serum NT-proBNP and soL-CXCL16 levels before surgery, and at 1 day, 1 week, and 4 weeks after surgery in patients of the two groups. The correlations among the serum NT-proBNP and soL-CXCL16 levels, postoperative cardiovascular adverse events and myocardial ischemia (cTnT) levels were analyzed. Results: There were significant differences in the serum soL-CXCL16 and NT-proBNP levels in the experimental group at different time points before and after PCI ($P<0.05$). The serum soL-CXCL16 and NT-proBNP levels at different time points before and after surgery were significantly higher in the experimental group than in the control group ($P<0.05$). As compared with that before surgery, the serumsoL-CXCL16 levels increased significantly in the experimental group at 1 day after surgery, but strikingly dropped at 1 week, 4 weeks after surgery, respectively ($P<0.05$). In addition, the serum NT-proBNP level in the experimental group was significantly lower than that before operation. Pearson correlation analysis showed that there were positive correlations among the serum soL-CXCL16 and NT-proBNP levels and cTnT, and the incidence of cardiovascular adverse events was correlated to the serum soL-CXCL16 and NT-proBNP levels at 1 week after surgery. Conclusion: The serum soL-CXCL16 and NT-proBNP levels in patients with AMI were significantly reduced after PCI, and may play certain role in the prognosis of patients with AMI after PCI.

Keywords: Percutaneous coronary invention, acute myocardial infarction, soL-CXCL16, NT-proBNP

Introduction

The incidence and mortality of acute myocardial infarction (AMI) are increasing on a yearly basis. AMI brings increasing harmto men. It becomes a major threat to our health and lives. Percutaneous coronary coronary intervention (PCI) is a main method for the treatment of myocardial infarction, which can establish rapidand effective coronary artery evascularisation, and improve the prognosis of patients with coronary artery disease [1, 2]. Inflammation plays a crucial role in the development of coronary heart disease (CHD), and coronary artery inflammation remains after PCI [3]. Moreover, the rate of postoperative cardiovascular ad-

verse events is still high. Therefore, it is of great practical and theoretical significance to find an effective inflammatory marker which can evaluate the prognosis of patients with AMI after PCI.

Chemokines play a decisive role in inflammatory response by mediating inflammatory cells to the site of injury or inflammation. Soluble chemokine 16 (sol-CXCL16), a small molecule inflammatory cytokine, is a member of CXC chemokine family [4, 5]. It has been reported that elevated soL-CXCL16 concentration is an independent risk factor for myocardial infarction (MI) [6]. SoL-CXCL16 functions as a chemokine in the pathogenesis of coronary atherosclerosis and plays a crucial role in the presence and pro-

gression of acute coronary syndrome. However, the changes in expression levels and functions of soL-CXCL16 after PCI remains unknown. The N-terminal prohormone of brain natriuretic peptide (NT-proBNP), composed of 76 amino acids, is a common marker for clinical evaluation of heart failure [7, 8]. One study has demonstrated that NT-proBNP is of significance in assessing the prognosis of patients with acute ST-segment elevation myocardial infarction [9]. Transient myocardial ischemia induced by balloon dilation in PCI has reported to contribute to rapid elevevation in NT-proBNP levels [10]. Currently, however, there are no large-scale reports on the changes in NT-proBNP levels after coronary artery stent implantation. Therefore, the purpose of our study was to detect soL-CXCL16 and NT-proBNP levels in the patients with AMI after PCI, so as to investigate the dynamic changes and effects of soL-CXCL16 and NT-proBNP in patients with AMI in the perioperative period.

Materials and methods

General data

A total of 100 patients who confirmed as having AMI in our hospital from January 2014 to December 2016 were enrolled in the study. All patients successfully completed PCI procedures. The patients were included if they met the diagnostic criteria of AMI, showed PCI indications, and provided written informed consents signed by themselves and their families. The patients were excluded if they had PCI, infective endocarditis, heptic and renal dysfunction, rheumatic heart disease, intra-aortic balloon pump (IABP)-assisted patients, cardiac function at Grade IV, malignancy and autoimmune diseases. The patients treated in the hospital in the same period, who did not have CHD as demonstrated by coronary angiography, were included in the control group (n=50). This study was approved by the Hospital Ethics Committee of our hospital.

Coronary artery stent implantation

All the AMI patients underwent PCI via the radial or femoral artery access as done in coronary artery stent implantation [11]. Firstly, all the patients were examined by routine coronary angiography. Then rapamycin drug-eluting stents were implanted into their bodies by senior surgeons, who adjusted the length of the stents in accordance with the coronary lesions of each patient, making the stents long enough to completely cover the overall coronary lesions and the balloon-induced damages. The criteria for a successful PCI include complete coronary artery revascularization by PCI, blood flow restored to Grade TIMI3 immediately after PCI, and the lumen residual stenosis less than 20%.

Detection of soL-CXCL16, NT-proBNP and cardiac troponin T (cTNT)

Venous blood (5 ml) was extracted from all patients before surgery, and at 1 day, 1 week and 4 weeks after surgery, respectively, and then treated with heparin anticoagulation. After centrifugation at 3000 r/min for 10 min, plasma was stored in the refridge at -20°C for use. The serum soL-CXCL16 and NT-proBNP levels were detected by enzyme-linked immunosorbent assay (ELISA) before PCI. Determination of serum bsoL-CXCL16 and NT-proBNP levels in the patients before and after surgery was strictly carried out according to the instructions on the kit (Sigma, USA). The cTNT levels were measured using double anti-photoelectrochemy before surgery and at 1 day after PCI. A C51-type electrochemiluminescence analyzer was purchased from Roche Company in Germany.

Follow-ups

Patients were followed up for 1 year, through telephone or outpatient clinic visits once a month. The follow-up included recurrent MI or angina, severe arrhythmia, heart failure and death as well as other cardiovascular adverse events, and explored the association of the adverse events with the soL-CXCL16 and NT-proBNP levels.

Statistical analysis

Data analysis was performed using SPSS software, version 19.0. All quantitative data were expressed as mean ± standard deviation (mean ± SD). Comparison between the two groups was made with the use of the student's t test, whereas comparisons among more than two groups were performed using one-way analysis of variance (ANOVA). Companions of soL-CXCL16 and NT-proBNP levels before and after PCI were carried out using repeated measures ANOVA. The correlations among soL-CXCL16

Table 1. Comparison of baseline characteristics of the patients between both groups

Variable	Control (n=50)	Experiemntal (n=100)	P
Gender (male/female)	29/21	55/45	0.344
Age (year)	61.55±8.51	62.73±8.69	0.532
BMI (Kg/m^2)	25.15±2.35	24.87±2.09	0.652
Hypertension (n, %)	36 (72%)	75 (75%)	0.482
Hyperlipidemia (n, %)	33 (66%)	68 (68%)	0.519
DM (n, %)	32 (64%)	66 (66%)	0.472
Smoking	25 (50%	48 (48%)	0.538
FHOCHD (n, %)	16 (32%)	33 (33%)	0.621

Note: DM denotes Diabetes mellitus and FHOCHD family history of coronary heart disease.
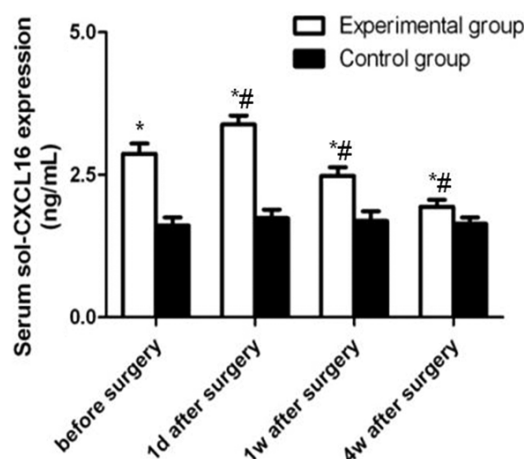
Figure 1. Comparison of serum soL-CXCL16 levels between the two groups. As compared with the control group, *P<0.05; as compared with preoperative levels, #P<0.05.
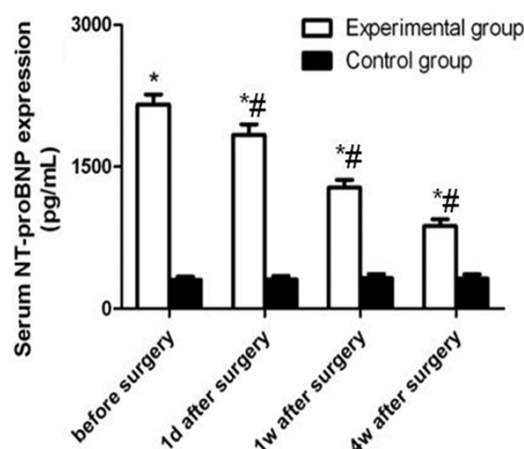
Figure 2. Comparison of the serum NT-proBNP levels between the two groups. As compared with the control group, *P<0.05; as compared with preoperative levels, #P<0.05.

and NT-proBNP levels and cTNT were evaluated using Pearson correlation analysis. Multivariate correlation was assessed by logistics regression analysis. By contrast, the count data were expressed as percentages or rates, and the chi-square test was used to compare the differences between groups. P<0.05 was considered statistically significant.

Results

Comparison of baseline characteristics of the patients between both groups

There was no significant difference in gender, age, medical and family history of the disease between the two groups (P>0.05), indicating thatthe two groups were comparable (**Table 1**).

Changes in serum soL-CXCL16 and NT-proBNP levels before and after PCI

The serum soL-CXCL16 levels was not significantly different before and after coronary angiography in the control group (P>0.05). However, the serum levels before surgery, and at 1 day, 1 week and 4 weeks after surgery, respectively were significantly higher in the experimental group than in the control group (P<0.05, **Figure 1**). In the experimental group, compared with that before surgery, the level at 1 day after PCI increased significantly (P<0.05). Nevertheless, the levels at 1 week or 4 weeks after surgery significantly reducedas compared with those before surgery (P<0.05).

The serum of NT-proBNP levels showed no significant difference among patients in the control group before and after coronary angiography (P>0.05). Before surgery, and at 1 day, 1 week and 4 weeks after surgery, respectively, the serum levels in the experimental group were significantly higher than those in the control group (P<0.05). However, after surgery, the levels in the experimental group decreased gradually, which was strikingly lower than those before surgery (P<0.05, **Figure 2**).

Association of cardiovascular adverse events with serum soL-CXCL16 and NT-proBNP levels

Of 100 PCI patients at 1 year postoperatively, seven had recurrent myocardial infarction, eight had severe arrhythmia, four had recurrent angina, four had heart failure and three died.

Table 2. Postoperative cardiovascular adverse events and serum soL-CXCL16 and NT-proBNP-levels at 1 week after PCI

Group	Case	soL-CXCL16 (ng/mL)	NT-proBNP (pg/mL)
Presence of CAE	26	3.17±0.19	1789.54±94.22
Absence of CAE	74	2.11±0.16	946.82±88.71

Note: CAE denotes cardiovascular adverse event.

Table 3. Correlation coefficients among soL-CXCL16 and NT-proBNP and cTNT

Marker	Correlation coefficient (r)	P
soL-CXCL16	0.361	0.002
NT-proBNP	0.456	0.003

The serum soL-CXCL16 and NT-proBNP levels at 1 week postoperatively showed significant differences between the patients with cardiovascular adverse events and those without (P<0.05, **Table 2**).

Multivariate Logistics regression analysis was performed with the absence or presence of adverse events as dependent variable, and gender, age, BMI, hypertension, hyperlipidemia, diabetes mellitus, a history of CHD, smoking, serum soL-CXCL16 and NT-proBNP levels as independent variables. The results show that the serum soL-CXCL16 (r=2.521, P=0.011) and NT-proBNP (r=1.452, P=0.021) levels are risk factors for adverse events.

Correlations among soL-CXCL16 and NT-proBNP levels and the cTNT level

The mean preoperative cTnT levels were (3.14± 1.02) ng/L, but reduced to (0.86±0.23) ng/L at 1 day after surgery among the patients in the experiment group. On Pearson correlation analysis, NT-proBNP level was positively correlated with cTnT level (r=0.361, P=0.002), and soL-CXCL16 level was also positively correlated with cTNT level (r=0.456, P=0.003), suggesting that there was certain correlation among NT-proBNP and soL-CXCL16 levels and cTNT level (**Table 3**).

Discussion

Thrombosis at the site of rupture of atherosclerotic plaque in a coronary artery is one of the decisive causes of AMI. It has been reported that the cytokines secreted by IL-8, TNF-α and other T cells play a major role in promoting the development and progression of coronary atherosclerosis and plaque instability [12, 13]. Ischemia reperfusion injury associated with PCI procedures may lead to subendothelial collagen exposure, plaque rupture, and platelet adhesion, production of adhesion molecules and monocyte chemokines, improvements in the infiltration of inflammatory cells and the release of various inflammatory cytokines, thereby increasing the local inflammatory reaction. In addition, the coronary stent as a foreign body itself can produce inflammatory response [14, 15]. Thus, coronary atherosclerosis is an inflammatory disease, and inflammation plays a decisive role in the occurrence and development of CHD.

SoL-CXCL16, a newly-discovered inflammatory marker of CHD, consists of 254 amino acids. It can activate T cells to secrete a variety of cytokines, promoting the proliferation of smooth muscle cells in the coronary artery and inducing inflammatory reaction [16]. SoL-CXCLI6, a potential factor in the development of coronary atheroslerosis, has the characteristics of scavenger receptor SR-PSOX, which mediates the intake of low-density lipoprotein and inflammatory chemotaxis. Previous studies have confirmed that statins can significantly reduce soL-CXCLI6 levels in patients with CHD, and their therapeutic effect on CHD are not associated with and reduction in blood lipids, suggesting that soL-CXCLI6 may be a new target for the treatment of acute coronary syndrome [17]. Therefore, we explored perioperative dynamic changes in soL-CXCLI6 levels of patients with AMI during the PCI procedures, and found that the serum soL-CXCL16 levels at 1 day, and 1 week and 4 weeks respectively after surgery in the experimental group were strikingly higher than those in the control group, with the serum soL-CXCL16 level at 1 day the highest, which is significantly higher than that before PCI (P<0.05). This demonstrates myocardial infarction can activate the inflammatory system, and inflammatory reaction can be further aggravated after PCI.

Brain natriuretic peptide (BNP) is a kind of neural polypeptide secreted by ventricular myocytes, and is one of the common biomarkers for prognosis of heart failure [18, 19]. In recent years, increasing attention has been attracted to NT-proBNP as a clinical diagnostic marker.

NT-proBNP is more stable and has a higher concentration in plasma than BNP. Studies have reported that there is a close correlation between the NT-ProBNP level and cardiac structure and functions in patients with CHD [20]. The purpose of our study was to investigate the changes in NT-ProBNP levels in patients with AMI after PCI. The results showed that the postoperative serum NT-proBNP levels in patients with AMI was significantly lower than those preoperatively. As compared with the control group, the serum NT-proBNP levels after surgery in the experimental group were significantly lower that that before surgery. This may be due to the fact that PCI led to the restoration of coronary blood flow, which effectively saved the dying cardiomyocytes, and then improved the cardiac functions and prevented the occurrence of cardiac remodeling. After PCI, the cardiac dilatation was inhibited; the tract pressure of cardiac muscle significantly reduced; the secretion and synthesis of NT-proBNP decreased gradually.

To further elucidate the roles of soL-CXCL16 and NT-proBNP levels in cardiovascular diseases, we concudcted the Pearson correlation analysis and found that there was a correlation among NT-proBNP and soL-CXCL16 levels and cTNT level, indicating that NT-proBNP and soL-CXCL16 were closely correlated to myocardial ischemia. Accoring to 1-year follow-up, the incidence of cardiovascular adverse events after PCI was associated with the serum soL-CXCL16 and NT-proBNP levels at 1 week after PCI. This might be the reasons that the regulation of lipid deposition by soL-CXCL16 promotes the proliferation of vascular endothelial cells and aggravation of inflammatory response, affecting the stability of atherosclerotic plaque, thereby resulting in cardiovascular adverse events. In addition, the cardic loading was constantly too heavy, plus the cardiac function did not improve markedly, leading to elevated NT-proBNP levels. It can be seen that the serum NT-proBNP and soL-CXCL16 levels can partly predict the cardiovascular adverse events after PCI.

In conclusion, close monitoring of serum soL-CXCL16 and NT-proBNP levels may have certainclinical implications for assessment on the perioperative coronary inflammation of patients with AMI during the PCI procedures and reductions in the incidence of cardiovascular adverse events and judgment of prognosis. However, the specific mechanism of serum soL-CXCL16 and NT-proBNP in the pathogenesis of CHD remains unclear, requiring further experimental validation.

Disclosure of conflict of interest

None.

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