Original Article
Clinical analysis of Han Chinese patients with acute coronary syndromes and complicated essential hypertension

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Abstract: Objective: To investigate the correlation between hypertension and clinical manifestations in patients with acute coronary syndromes through clinical feature analysis of Han Chinese patients with acute coronary syndromes (ACS) and complicated essential hypertension (EH). Methods: Six hundred and twenty-one cases of Han Chinese patients with acute coronary syndromes at our hospital, including 337 patients complicated by essential hypertension (the hypertension group) and 284 patients without essential hypertension (the non-hypertension group), were selected to participate in this study. All patients underwent coronary artery intervention. The number of diseased blood vessels and Gensini scores were calculated. Cytometric bead array was applied to test the EMP level in plasma of patients in two groups. Then gene chip technology and fluorescent quantitative PCR were applied to detect the genetic polymorphism of CYP2C19 in each patient. Optical turbidimetry was used to detect the platelet aggregation rate (PAR) of patients 7 days after patients took the medicine. Results: ages, and levels of hematuria acid and glycerol of patients in the hypertension group were significantly higher than patients in the non-hypertension group (P<0.05). Plasma EMP levels of patients in the hypertension group were significantly higher than patients in the non-hypertension group (P<0.05). The genetic polymorphism of CYP2C19 in the above two groups showed no significant differences (P>0.05). However, the platelet aggregation rate of patients in the hypertension group was significantly higher than that of patients in the non-hypertension group after anti-platelet treatment underwent for 1 week. The comparative analysis on coronary artery diseases showed that Gensini scores and the number of patients with three-vessel disease in the hypertension group were significantly higher than the non-hypertension group. In addition, there was a higher incidence of in-stent restenosis in the hypertension group (P<0.05). Conclusion: metabolic disorders are more likely to occur in patients with acute coronary syndrome and complicated essential hypertension. Vascular endothelial dysfunction is more serious in such patients. Pathological changes have a wider range and appear to be more severe. In addition, the incidence of in-stent restenosis is relatively high in those patients.

Keywords: Essential hypertension, acute coronary syndrome, clinical features

Introduction

Epidemiological studies have confirmed that hypertension and coronary heart diseases are closely related in etiology. Hypertension plays a very important role in the development of coronary heart diseases. Hypertension, one of the most important risk factors of the occurrence and development of coronary heart diseases, can accelerate the process of atherosclerosis in coronary artery diseases [1]. Acute coronary syndromes (ACS), a serious type of coronary heart disease, can cause arrhythmias, heart failure, and even death, seriously affecting

patients' quality of life and life expectancy. Through the analysis of clinical parameters in patients with acute coronary syndromes and complicated essential hypertension, this study investigates the correlation between hypertension and clinical manifestations in patients with acute coronary syndromes and provides a better basis for clinical practice.

Observer objects and methods

Observer objects

Six hundred and twenty-one cases of Han Chinese patients with acute coronary syndromes

who were treated at our hospital from January 2015 to December 2015 were selected to participate in this study. These cases included including 337 patients complicated by essential hypertension (the hypertension group) and 284 patients without essential hypertension (the non-hypertension group).

Diagnostic criteria: The inclusion criteria for hypertension: 2010 Chinese hypertension guideline [2]; that is, patients whose systolic blood pressure ≥140 mmHg and (or) diastolic blood pressure ≥90 mmHg without taking antihypertensive drugs are diagnosed with hypertension. In addition, for patients who have previous history of hypertension and take antihypertensive drugs currently, they should be diagnosed with hypertension even when their blood pressures do not reach the above levels.

The inclusion criteria for acute coronary syndrome: ACS includes unstable angina pectoris (UAP) and acute myocardial infarction (AMI). UAP refers to new-onset angina within 1 month and worsening angina pectoris within 1 month (the classification of angina increases at least one grade or reaches at least grade III in Canada cardiovascular society grading), in addition to angina pectoris occurring at rest with two adjacent lead new or dynamic changes of ST segment or T wave and normal level of cardiac troponin T (cTnT). AMI refers to myocardial infarction occurring within 24 hours. In addition, the chest pain lasts for more than 20 minutes, ECG shows at least two contiguous leads of ST segment elevation or depression and cTnT>0.1 µg/L.

Exclusion criteria: patients with secondary hypertension; patients with severe hepatic or renal insufficiency; patients with hematopoietic system diseases, infectious diseases, cancer and other wasting diseases.

Methods

Research methods: after treating in the hospital, 621 patients were given conventionally aspirin, clopidogrel, isosorbide mononitrate ester, rosuvastatin, and low molecular weight heparin calcium. The use and doses of benazepril and sustained-release metoprolol tablets increased or decreased according to the blood pressure, heart rates, medical history and other indicators of patients. Patients with dia-

betes continued to take insulin and/or oral hypoglycemic drugs to control blood sugar. On the second day after hospital admission, three venous samples of 5 ml were drawn from the elbow into three tubes, mixed with heparin sodium anticoagulation, sodium citrate anticoagulation, and EDTA. The first tube was sent to a testing center to test the levels of blood glucose, blood lipid, creactive protein and other biochemical indexes. The second tube was sent to the central laboratory. After two centrifugations, platelet-poor plasma was obtained. Specific antibody labeled samples, which were labeled with two fluoresceins CD31\CD42 provided by BD Company. US, were used. A FACSCalibur Flow Cytometry provided by BD Company. US was used to detect the plasma level of EMP. The result was marked as $CD31^+$/$CD42b^-$EMPs. The third tube was sent to cardiopulmonary laboratory. Gene chip technology and fluorescent quantitative PCR were applied to detect the genetic polymorphism of CYP2C19. On the seventh day after patients began to take clopidogrel in hospital, venous samples of 5 ml were drawn in tubes, mixed with sodium citrate as anticoagulant. The rate of platelet aggregation induced by 5 umol/L of adenosine diphosphate was detected. All patients underwent coronary artery intervention. Gensini scores were used to quantitatively calculate the degree of narrowing of each vessel and the severity of diseased vessels: the diseased vessels were divided into left main coronary arteries, left anterior descending coronary arteries, circumflex branch of left coronary arteries, and right coronary arteries; one score was given if the degree of narrowing is no more than 25%, two scores were given if the degree of narrowing was something between 26% and 50%, four scores were given if the degree of narrowing was something between 51% and 75%, eight scores were given if the degree of narrowing was something between 76% and 90%, sixteen scores were given if the degree of narrowing was something between 91% and 99% and thirty-two scores were given if the degree of narrowing was 100%. Scores of coronary arteries of different sections multiplied by corresponding coefficients were the accumulate scores for the coronary arteries. The corresponding coefficients of coronary arteries of different sections were listed as follows: the corresponding coefficient for diseased left main coronary arteries was 5, for proximal left anterior descending arteries was

Table 1. Comparison of baseline data of the two groups of patients

Values	The hypertension group (n=337)	The non-hypertension group (n=284)	t values	χ² values
General clinical data				
Ages (years)	64.7±10.5**	62.5±11.0	2.613	0.009
Males [cases (%)]	201 (59.6)	136 (47.9)	0.350	0.554
Smoking [cases (%)]	57 (16.9)	59 (20.8)	0.801	0.371
Diabetes [cases (%)]	94 (27.9)	62 (21.8)	3.011	0.083
AMI [cases (%)]	83 (24.6)	73 (25.7)	0.095	0.758
UAP [cases (%)]	254 (75.4)	211 (74.3)	0.095	0.758
Biochemical indexes				
G (mmol/L)	5.95±2.68	5.65±2.58	1.395	0.164
TC (mmol/L)	4.42±1.11	4.48±1.12	0.643	0.520
TG (mmol/L)	1.95±1.74**	1.69±1.32	2.095	0.037
HDL (mmol/L)	1.01±0.30	1.02±0.30	0.100	0.920
LDL (mmol/L)	2.44±0.85	2.51±0.92	0.802	0.423
CRP (mg/L)	4.83±7.61	4.27±5.86	1.026	0.305
UA (umol/L)	334.64±104.25**	314.58±97.45	2.461	0.014
Drug usage [cases (%)]				
Bayaspirin	337 (1)	284 (1)		
Clopidogrel	337 (1)	284 (1)		
Isosorbide dinitrate	337 (1)	284 (1)		
Rosuvastatin	337 (1)	284 (1)		
Low molecular weight heparin calcium	337 (1)	284 (1)		
Benazepril	284 (84.3)	239 (77.1)	0.002	0.968
Sustained-release metoprolol tablets	273 (81.0)	222 (78.2)	0.769	0.381
Oral hypoglycemic agents	63 (67.0)	39 (62.9)	0.280	0.597
Insulin	31 (33.0)	23 (37.1)	0.280	0.597

Note: hypertension group **P <0.05; G: fasting glucose, TC: cholesterol TG: triglycerides, HDL: high density lipoprotein cholesterol, LDL: low-density lipoprotein cholesterol, CRP: C-reactive protein, UA: UA.

Table 2. The comparison of plasma levels of CD31⁺/CD42b⁻EMPs in the two groups

Groups	Cases	CD31⁺/CD42b⁻EMPs (units/ul)*
The hypertension group	337	1253.96±230.35
The non-hypertension group	284	890.58±62.40
t values		18.697
P values		0.000

*Cytometric bead array was applied to test the EMP level in plasma of patients in two groups.

2.5, for the middle part of the left anterior descending arteries was 1.5 and for the distal part was 1; the corresponding coefficient for the first diagonal arteries was 1 and for the second diagonal arteries was 0.5; the corresponding coefficient for proximal left circumflex arteries was 2.5, for the distal part and descending posterior branch was 1, and for the posterolateral arteries was 0.5; all the corresponding coefficients for proximal right coronary arteries, the middle part of right coronary arteries, the distal part of right coronary arteries and the descending posterior branch of right coronary arteries were 1. The final accumulative score is the sum of accumulative scores of all the arteries. The accumulative scores were independently assessed by two skilled cardiologists. An average value was calculated.

Observation indexes: ① the medical history of patients and application of drugs which had effects on endothelial function were recorded; ② laboratory indicators: blood glucose, uric acid, triglycerides, cholesterol, c-reactive protein, and so on; ③ the plasma levels of CD31⁺/CD42b⁻EMPs in each patients; ④ the genetic polymorphism distribution feature of CYP2C19 in plasma of patients in the two groups; ⑤ the average value of platelet aggregation rates on the seventh day after patients

Table 3. Analysis of diseased coronary arteries of the hypertension group and non-hypertension group

Groups	Cases	Three-vessel diseases	Double vessel diseases	Single vessel diseases	Restenosis rates	Gensini scores
The hypertension group	337	163 (48.4)	107 (31.8)	67 (19.8)	29	37.77±27.01
The non-hypertension group	284	111 (39.1)	82 (28.9)	91 (32.0)	12	32.82±26.32
χ^2 values		5.387	0.368	12.015	4.795	
t values						2.303
P values		0.020	0.544	0.001	0.029	0.022

Table 4. CYP2C19 genetic polymorphism and Platelet aggregation rates in the two groups

Groups	Cases	Fast metabolizers	Medium metabolizers	Slow metabolizers	Platelet aggregation rates
The hypertension group	337	136 (40.4)	155 (46.0)	46 (13.6)	45.09±22.33
The non-hypertension group	284	135 (47.5)	118 (41.5)	31 (11.0)	40.98±22.67
χ^2 values		3.230	1.236	1.061	
t values					2.196
P values		0.072	0.266	0.303	0.028

took drugs were calculated; ⑥ numbers of diseased vessels in the two groups were analyzed and compared, Gensini scores were calculated and restenosis rates were calculated.

Statistical treatment

SPSS 17.0 software package was used for data processing. Measurement data was expressed as mean ± standard deviation (x±s); and the analysis of variance was conducted to make comparison between the two groups. The description of categorized data was expressed in the form of component ratio, and χ^2 tests were used for the comparison between two groups. The difference was statistically significant when P<0.05.

Results

Baseline data of the two groups of observed objects were compared (**Table 1**): the two groups of observed objects showed no significant difference in gender, smoking, complicated diabetes and baseline drug treatment for endothelial functions; the component ratios of AMI patients and UAP patients were similar; ages, blood uric acid levels and glycerol triester levels of patients in the hypertension group were higher than patients in the non-hypertension group while levels of cholesterol, high density lipoprotein, low density lipoprotein and C-reactive protein in the two groups had no meaningful differences.

The comparison of plasma levels of CD31⁺/CD42b⁻EMPs in the two groups of observed objects shows that levels of the hypertension group increased significantly compared with the non-hypertension group (**Table 2**).

The numbers of diseased coronary arteries in the two groups, Gensini scores and restenosis rates were calculated. The rate of three-vessel diseases, Gensini scores and restenosis rates of the hypertension group were all higher than the non-hypertension group whereas the rate of single vessel diseases was lower than the non-hypertension group (**Table 3**).

The genetic polymorphism of CYP2C19 in the two groups had no significant differences (P>0.05). However, in the first week of antiplatelet therapy the rate of platelet aggregation of the hypertension group was higher than the non-hypertension group (P<0.05) (**Table 4**).

Discussion

Coronary heart diseases have become one of the leading causes of death in the world. A large number of epidemiological studies in China and abroad have confirmed that hypertension is one of the most important risk factors of coronary heart disease [3]. Although the pathogenesis of both diseases has their own independence, they have promotion effects on each other. The process of atherosclerosis in patients with coronary heart diseases can be

significantly accelerated due to hypertension while reduce on coronary flow reserve caused by microangiopathy of hypertension can exacerbate coronary artery stenosis.

This study conducted analysis on vascular lesion results of 621 patients who received percutaneous coronary intervention. It found that three-vessel disease rates of patients with acute coronary syndromes and complicated essential hypertension were significantly higher than patients without essential hypertension, and that the incidence of in-stent restenosis was higher in the hypertension group. Gensini scores of diseased vessels showed that values in the hypertension group were higher. The study suggests that high blood pressure can lead to structure changes of coronary vessel walls, causing and accelerating the process of atherosclerosis, and that hypertension, along with other factors, leads to coronary artery lipid formation, luminal stenosis, coronary insufficiency and imbalances of myocardial oxygen supply, widening the range of pathological changes and aggravating pathological changes [4].

Studies have shown that endothelial injury, inflammation and plaque ruptures cause coronary thrombosis and acute coronary syndrome. Plasma endothelial microparticles (EMP) are small vesicles released at the apoptosis or activation of endothelial cells. The level of EMP is closely related to the endothelial function. In addition, EMP, an effective indicator of assessment of endothelial dysfunction, can reflect the level of endothelial inflammatory reaction and the extent of its damage [5, 6]. This study used antibody samples which were labeled by anti-CD31/CD42, two kinds of fluorescein, and detect plasma EMP levels in patients. Results showed that the level of CD31+/CD42- in the plasma were significantly higher in the hypertension group than the non-hypertension grouped. The result indicated that high blood pressure can cause consistent vascular endothelial damages and accelerate vascular endothelial dysfunction, thus speeding up the occurrence and development of coronary heart diseases, just as reported in the literature [7, 8].

Hypertension leads to systemic atherosclerosis easily. In addition, plaque ruptures subsequently occur and thrombosis forms. Platelet activation and inflammation play an important role in the thrombotic event. The platelet aggregation rate is currently widely used for determination of platelet activity as a classical method. In this study, platelet aggregation rates of all patients on the seventh days after patients took clopidogrel were detected. Results showed that in the situation where genetic polymorphism of CYP2C19 was similar in the two groups, the average value of the hypertension group was higher than that of the non- hypertension group (CYP2C19 is a gene which can reflect clopidogrel resistance). When the hypertension occurs, the abnormal haemorheology increases resistance to blood flow, and thus blood flow slows down, improving platelet aggregation and adhesion, so that the blood is in a hypercoagulable state. This state is conducive to thrombosis and contributes to the occurrence and development of atherosclerosis.

Studies have shown that hyperlipidemia is one of important independent risk factors for atherosclerosis and other cardiovascular and cerebrovascular diseases, especially when there is an obvious positive correlation between serum cholesterol levels and coronary heart disease as well as hypertension [9]. The results of this study show that blood triglyceride levels in hypertensive patients increased compared with non-hypertensive patients while cholesterol, low-density lipoprotein cholesterol and high-density lipoprotein cholesterol in the two groups had no significant differences, considering that this is because all patients were taking the statin cholesterol-lowering drugs and statin mainly targets at reducing cholesterol. This study also shows that the levels of blood uric acid in hypertensive patients were higher than non- hypertensive patients, indicating that metabolism disorders are more like to occur in patients with acute coronary syndromes and complicated essential hypertension, similar to the literature [10].

In conclusion, when we treat patients with acute coronary syndromes and complicated essential hypertension in clinical practice, we should comprehensively and effectively control metabolic disorders including blood lipid, uric acid, blood glucose, and strengthen the therapy of anti-platelet aggregation and improving endothelial function in addition to control of blood pressure. In this way cardio-cerebral vascular diseases will be prevented or delayed.

Disclosure of conflict of interest

None.

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