

Influence of Cinepazide Maleate on Vascular Endothelial Function of Patients with Acute Myocardial Infarction

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ABSTRACT Objective: To study influence of cinepazide maleate on vascular endothelial function of patients with acute myocardial infarction. **Methods:** 150 cases of patients with acute myocardial infarction were divided into the observation group and the control group, two groups were treated by conventional therapy about acute myocardial infarction, the observation group added 5%GS250 mL + cinepazide maleate 160 mg IV drip q.d, the control group added 5%GS250 mL IV drip q.d, the treatment course were 3 weeks, changes of vascular endothelial function and the blood serum no level before and after treatment were detected. **Result:** vascular endothelial function after treatment in observation group were obviously improved than that before treatment ($\rho = 0.03$), blood serum no level was obviously increased ($\rho < 0.05$); about 3 weeks after treatment, vascular endothelial function in the observation group was obviously better than that of the control group ($\rho = 0.04$), the blood serum no level of the observation group was obviously higher than that of the control group ($\rho < 0.05$). **Conclusion:** Cinepazide maleate remarkably improves vascular endothelial function of patients with acute myocardial infarction.

KEYWORDS

Acute myocardial infarction
Vascular endothelial function
Cinepazide maleate

1. Introduction

Cinepazide maleate is a novel substituted piperazines, has a variety of pharmacological effects such as endogenous adenosine to improve efficiency, calcium channel blockers, phosphodiesterase inhibition, etc. There are more clinical study on vasorelaxation action while less reports on effect of vascular endothelial function. In this paper, intravenous infusion of cinepazide maleate was administrated to patients

with acute myocardial infarction by the randomized, control design method, to observe the changes of endothelial function.

2. Materials and methods

2.1. Study subjects

150 patients with acute myocardial infarction treated in our hospital from March 2010 to December 2011 were selected as the study subjects. Inclusion criteria: (1) meet the diagnostic criteria of acute myocardial infarction [1–2]; (2) any vascular disease has not occurred; (3) excluding liver, gallbladder, pancreas, thyroid and kidney disorders; (4) have regular eating habits and a certain amount of activity; (5) non-diabetic patients; (6) hypertension. 150 patients were randomly divided into two groups, the observation group was 78 cases and the control group was 72 cases. The control group and observation group were roughly

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matched in age, gender, smoking, taking drugs, alcohol consumption, and body mass index, etc.

General information of the subjects (Table 1) displays there was no significant difference in gender, age, smoking, taking drugs, alcohol consumption, and body mass index and so on.

Table 1. General information.

	The observation group	The control group
Case(male/female)	78 (40/38)	72 (37/35)
Age(years)	55.4 ± 10.8	54.8 ± 9.5
Smoking(number)	10	8
Alcohol consumption(number)	15	12
Body mass index(kg/m ²)	25.1 ± 0.7	24.9 ± 0.6
ACEI/ARB	45	41
Ca channel antagonists	29	26
B receptor blocker	21	23

2.2. Methods

On the basis of routine treatment of myocardial infarction, the observation group added 5%GS250 mL + Cinepazide maleate 160 mg IV drip q.d, the control group added 5%GS250 mL iv drip q.d, the treatment course were 3 weeks.

2.3. Specimen collection and testing

Three mL elbow venous blood was taken from all the subjects after fasting for 12 hours in the morning of selection and 3 weeks after treatment. Immediately centrifuge for 25 minutes with high speed at room temperature (3000 rpm/min), separated serum was stored in the refrigerator under -70 °C to be measured, uniform determination of NO in serum was made.

2.4. Determination of vascular endothelial function

Non-invasive detection of vascular endothelial function is made before and 3 weeks after treatment respectively. Determination of vascular endothelial function: use the hpsonos 5500 color doppler ultrasound system (Hewlett-Packard Development Company), transducer frequency is 10 mhz, synchronously record the ECG. The subjects take a break for 10 min before testing, stay in supine position, right upper arm outreach for 15 degrees. Selected 2~15 cm range of brachial artery in the cubital fossa as the target artery, 4 cm depth, freeze after getting satisfactory long axis image of the brachial artery. At the top of the R wave in ECG, measure ventricular end-diastolic diameter of brachial artery, take the average of 3 cycles as a basis inner diameter of brachial artery (D0), mark on the skin of the test location for repeated operations. Bind cuff blood pressure monitor to the right forearm and inflate until blood pressure monitor readings reach to 300 mmHg, maintain for 5 min, quickly deflate, measure

ventricular end-diastolic diameter of brachial artery (D1) of original marked position again within 90 s. The patient rest for more than 10 min, give sublingual nitroglycerin 0.5 mg, 5 min later the brachial artery diameter (D2) is measured. Consider the brachial artery diameter change percentages before and after reactive hyperemia and taking nitroglycerin as endothelium-dependent vasodilation (Flow-mediated dilation, FMD) and non-endothelial dependent relaxation (endothelium-independent dilatation, EID). Calculated as: FMD = (D1 - D0) / D0 × 100%; EID = (D2 - D0) / D0 × 100%.

2.5. Statistics analysis

Using the SPSS 11.0 statistical software for statistical analysis: measurement data is represented as ($\bar{x} \pm s$); comparison between groups and within group is made by *t* test and analysis of variance, respectively; *p* < 0.05 is considered to be statistically significant difference.

3. Results

3.1. the FMD, EID changes of brachial artery in each group before and after 3 weeks (see table 2).

Table 2. The FMD, EID changes of brachial artery in each group before and after 3 weeks.

	The control group		the observation group	
	3 weeks ago	after 3 weeks	3 weeks ago	after 3 weeks
FMD (%)	8.9 ± 0.4	9.9 ± 1.4	9.0 ± 0.4	14.1 ± 1.2 *
EID (%)	14.6 ± 4.5	18.5 ± 5.9	17.7 ± 4.2	18.5 ± 4.0

FMD: flow-mediated vasodilation, EID: nitroglycerin-mediated vasodilation

*: comparison of before and after 3 weeks, the observation group FMD improved significantly (*p* = 0.03); 3 weeks after treatment, the FMD of observation group improved more significantly than the control group (*p* = 0.04);

3.2. Serum NO changes of each group before and after 3 weeks

Serum NO changes: serum NO level in observation group and control group has no significant difference 3 weeks ago; after 3 weeks, the serum NO level of observation group increases significantly (*p* < 0.05) while the control group has no significant difference, the serum NO level of observation group is significantly higher than the control group (*p* < 0.05) (Table 3).

Table 3. Serum NO changes of each group before and after 3 weeks.

NO (μ mol/l)	The control group		The observation group	
	3 weeks ago	After 3 weeks	3 weeks ago	After 3 weeks
	41.0 ± 5.1	42.3 ± 4.3	39.2 ± 3.8	61.0 ± 7.5*

NO: nitric oxide

*means the significant change in serum NO of observe group 3 weeks later compared with 3 weeks ago (*p* < 0.05); means serum NO level in

observation group is significantly higher than the control group after 3 weeks ($p < 0.05$);

3. Discussion

Cinepazide maleate is a novel substituted piperazines, has a variety of pharmacological effects such as endogenous adenosine to improve efficiency, calcium channel blockers, phosphodiesterase inhibition, etc. [3]. Cinepazide maleate has weak inhibitory effect of calcium ion, it also has good spasmolysis and expansion on coronary artery, cerebral arteries and peripheral vessels [4]. Cinepazide has a unique synergy of adenosine. It blocks adenosine inactivation process by blocking the reabsorption of adenosine and inhibition of adenosine deaminase activity, delay the metabolism of adenosine, thereby increasing the lesion local concentration of endogenous adenosine, regulating peripheral artery and coronary artery diastolic function [5]. Through using cinepazide maleate for 3 weeks on the basis of conventional therapy in patients with acute myocardial infarction, the study shows that cinepazide maleate has effect on improving vascular endothelial function, vascular active substance NO which associated with the vascular endothelial dilatation function is significantly increased.

Xiaoqi zhou [6], Lijing zhao [6] and others have made a study on unstable angina application patients who using cinepazide maleate. The results shows application of cinepazide maleate injection on the conventional treatment in UAP treatment can obviously improve the clinical curative effect, clinical symptoms and exercise tolerance, reduce whole blood low shear viscosity, whole blood high shear viscosity, plasma viscosity, platelet aggregation, platelet adhesion rate, improve ECG manifestations, reduce acute myocardial infarction, arrhythmia and other severe cardiovascular complications. The study by Huapin wang, et al [8] found that use of cinepazide maleate combined with xuesaitong in the treatment of UAP has synergy in improving the hemorheology and atherosclerosis inflammatory reaction. Xiaohua Luo, et al [9] found that cinepazide maleate combined with irbesartan can effectively control blood pressure, obviously improve clinical symptoms and ECG curative effect of angina pectoris patients, reduce the frequency of angina attacks, improve myocardial ischemia and enhance heart function. Chengjun shi, et al [10] found combination of sodium tanshinone IIA sulfonate and cinepazide maleate in the treatment of angina pectoris of coronary heart disease can improve clinical syndrome and the electrocardiogram in patients with coronary heart disease. Musheng Yu, et al [11] shows that after intravenous infusion of cinepazide maleate, diabetic patients artery FMD improves significantly, indicating improving vascular endothelial function. The above study shows cinepazide maleate can significantly improves vasodilation function and adenosine synergies, expand blood vessels, has good spasmolysis and expansion on coronary artery, cerebral arteries and peripheral vessels,

also can inhibit platelet aggregation, reduce the production of oxygen free radicals, reduce neutrophil chemotactic effects on vascular endothelial cells, increase the toughness and deformation capacity of cells and decrease blood viscosity, thereby improving the microcirculation perfusion. This study suggests that cinepazide maleate can significantly improve vascular endothelial function, increased endothelial-derived relaxing factor NO, it's mechanism need further research.

Conflicts of interest

These authors have no conflicts of interest to declare.

Authors' contributions

These authors contributed equally to this work.

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