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ORIGINAL ARTICLE

Study on the Protective Effect of Edaravone on Myocardial Ischemia Reperfusion Injury

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ABSTRACT **Objective:** Discussion the role of edaravone as a free radical scavenger in protective effect of thrombolysis in acute myocardial ischemia reperfusion injury. Besides compared with the control group and analyze the possible mechanism which is widely used in clinical setting. **Method:** 80 patients hospitalized within year 2012–2013 with acute myocardial infarction (AMI) were treated with intravenous thrombolytic therapy, and were divided into treatment group (n = 41) and control group (n = 39). Edaravone injection 30 mg + 0.9% normal saline solution 100 mL with intravenous drip, BID for 14 days was given to the treatment group before and after thrombolytic treatment. Whereas, control group was treated with intravenous drip of placebo. Both groups were monitored by echocardiography and hemodynamic monitoring, and the myocardium was measured by echocardiography. Coronary artery CT was used to determine the degree of obstruction. **Results:** Compared with the control group, pain and reperfusion arrhythmia in treatment group was reduced. The area of myocardial wall movement disorder was significantly decreased ($p < 0.05$), the difference was statistically significant. CT result comparing treatment group and control group and show that rate of coronary recanalization increases 1.7 times ($p < 0.01$), the differences were statistically significant. **Conclusion:** For acute myocardial ischemia injection of edaravone before reperfusion and combine with pharmacological treatment can alleviate myocardial ischemia reperfusion injury, effectively scavenge oxygen free radicals and improve the ability of antioxidant. Both improve the thrombolytic treatment and protective effect for acute myocardial ischemia were significant. Hence, edaravone can is a kind of new milestone in the clinical cardiovascular drugs.

KEYWORDS

Ischemia reperfusion injury

Edaravone

Free radical scavenger

1. Introduction

Acute myocardial infarction is the heart disease that have complicated treatment, high mortality rate, and poor prognosis. Previous treatment mainly target on the specific symptoms, treatment for the primary disease and application of anticoagulant, however the therapeutic effect was less effective. Acute myocardial infarction (AMI) drug reperfusion therapy has been used in clinical practice, so that the prognosis of patients with ST segment elevation acute myocardial infarction (STEMI) has improved significantly. Thrombolytic therapy aimed at the opening the lumen of blood vessels to save the necrotic myocardium in the treatment of myocardial infarction and was achieved good results. It not only significantly reduce the mortality of patients, but also greatly improve the quality of life of patients. But it is a hot topic in clinical research to reduce the injury of ischemia and reperfusion injury. Edaravone is a new hydroxy free radical scavenger, during animal testing of myocardial ischemia and perfusion experiments the drug prove that can reduce the ischemia-reperfusion injury [1]. The theory of edaravone has great potential for myocardial ischemia-reperfusion protection. In September 2012 to September 2013, author studied on patient that hospitalized due to myocardial infarction and treated by combined ultra-early urokinase and intravenous injection of edaravone treatment of acute myocardial infarction had

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obtain better curative effect.

2. Materials and methods

2.1. Clinical data

This group of patients with myocardial infarction hospitalized from September 2012 to September 2013. Standard criteria: (1) Age is more than or equal to 18 years old, (2) Symptoms of myocardial ischemia continued more than or equal to 30 min, (3) AMI symptoms (chest pain) onset within 6 hours, (4) Two or more than two limb lead ST segment elevation is equal to or more than 0.1 mV or two or more adjacent precordial ST segment elevation is equal to or larger than 0.2 mV; (5) Required to sign the informed consent. Treatment group consist of 41 cases (male 35 cases, female 6 cases), aged 42 to 73 years old and average age was 54.2 years old. Control group consist of 39 cases (31 males and 8 females), aged from 39 to 69 years, with an average age of 52.2 years.

2.2. Treatment method

Patients after clinically diagnosed and do the appropriate checks, to comply with thrombolysis time and signed the indications and surgical agreement. After that, immediately infusion of diluted urokinase with 20,000 U/kg for less than 30 min. Subsequently, after the end of thrombolysis patient subjected underwent ECG, for determine the effect of thrombolysis. After diagnosed, patients in the treatment group administrated with edaravone 30 mg (Jiangsu Simcere Pharmaceutical Co., Ltd.) +0.9% normal saline solution 100 mL by intravenous infusion. After thrombolytic therapy with intravenous infusion, same dose of edaravone was administrated for 14 days. The control group was treated with intravenous drip of placebo. 24 h after thrombolysis both group were given low molecular weight heparin sodium 5000 U subcutaneous injection, QD, for 7 d, and control blood pressure [2,4].

2.3. Efficacy evaluation criteria

ECG and hemodynamic monitoring were performed in all groups, and the occurrence of reperfusion arrhythmia was observed. The coronary CT was determined by the blood vessel and the case fatality rate.

2.4. Statistical processing

Data mean + standard deviation said, using the SPSS 11.0 statistical software, using t test, $p < 0.05$ significant, $p < 0.01$ is extremely significant.

3. Results

Observed and compared the standard of both groups, from there ST segment elevation for both group, and the condition of arrhythmia and infarction angina pectoris was recorded in the results.

ST segment elevation type myocardial infarction after thrombolytic therapy of edaravone in treatment group reperfusion rate was 65.5%, besides, data of after reperfusion group and no reperfusion group in ST segment elevation, arrhythmia and infarction angina occurred rate was compared. Difference was statistically significant ($p < 0.01$).

The comparison of two groups of arrhythmia shown that in treatment group, having frequent ventricular premature beat, compared to the control group. There was no significant difference ($p > 0.05$) in the acceleration of ventricular arrhythmia, ventricular tachycardia, sinus arrest and ventricular fibrillation, the difference was statistically significant ($p < 0.01$).

In the both groups, the rate of blood vessel and the mortality of 4 weeks, the rate of vascular retreated by CT was significantly improved, and the difference was statistically significant [3].

4. Discussion

Myocardial infarction is refer to acute, persistent ischemia, hypoxia (coronary insufficiency) which caused by myocardial necrosis. Because of the non-regeneration of myocardial cells, the effective and timely opening of blood vessels are to achieve reperfusion to save the ischemic myocardium is very important. Only the adequate reperfusion, able to rescue the condition, where function of severe ischemia myocardial cell able to quickly restore, and provide an effective treatment. But not all patients with reperfusion can have a good clinical effect. Many cases of reperfusion injury will cause AMI extended or severe arrhythmia, and resulting in death.

Among all the mechanisms that cause ischemia reperfusion injury, free radical chain reaction [5–7] is considered to be one of the important mechanisms in the pathogenesis of myocardial tissue damage which caused by ischemia reperfusion. Due to an abnormality of the blood supply, through the mitochondria of myocardial cells, xanthine oxidase in vascular endothelial cells, neutrophil respiratory burst and catecholamine oxidation pathway, these process produces a large number of free radicals, which enable the biofilm structure damaged, and cause the generation of lipid peroxidation, in further releasing large amounts of intracellular enzyme, that cause swelling of mitochondria, and resulting in dysfunction of myocardial cell. Moreover, it resulting in reperfusion arrhythmia, myocardial stunning suppression, apoptosis and necrosis of tissues, and microvascular injury. Eventually, cause severe myocardial cell necrosis. Cardiac arrhythmia is easy to occur during reperfusion, and the occurrence rate is very high. The ECG of reperfusion myocardial injury was more than that of ST segment after reperfusion, and the elevation of myocardial injury was greater. Multiple manifestations of ventricular premature contractions in the short-array of ventricular tachycardia, acceleration of ventricular arrhythmia and late diastolic phase. The emergence of reperfusion arrhythmia is a sensitive indicator of the end stage to save the reversible injury of myocardium. Successful reperfusion can

occur with fatal reperfusion arrhythmia, which must be attached great importance in the process of thrombolysis. In patients with chest pain, the blood pressure decreased and arrhythmia, which indicated that reperfusion injury was obvious, and the ischemic injury of myocardium was lead to irreversible damage. The new injury of reperfusion injury and the extent of the injury, make the myocardial injury become more serious, and affect the improvement of myocardial ischemia, hence it should be paid attention to. A large number of experiments and clinical data confirmed that inhibition of free radical production and scavenging free radical provide protective effect to ischemia reperfusion injury [8–11].

Edaravone is currently the only effective clinical use free radical scavenger, the research shows that it scavenging harmful hydroxyl radical (OH) and other toxic free radicals produced after reperfusion and provide excellent protection effect in the treatment of acute myocardial infarction, at the same time improve the prognosis effect. This study found that urokinase thrombolysis combined with edaravone can decrease free radical chain reaction after urokinase thrombolysis reperfusion of blood flow and promote the timely removal of free radicals and rescue ischemic myocardium. Besides, it reduce serious malignant reperfusion arrhythmia, increased coronary recanalization rate, and reduce mortality in patients [12–14]. This suggests that importance of timely removal of the free radicals in myocardial ischemia and early reperfusion. The combined use of Edaravone and urokinase treatment of myocardial infarction might have synergistic effect, safe and effective, and worthy of promotion.

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