

## The value of ezetimibe in postoperative patients' blood lipids management after interventional therapy of acute coronary syndrome

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**Abstract: Objective** By observing the clinical efficacy and drug side effects of lipid-lowering treatment of ezetimibe combined with atorvastatin calcium, we evaluated the value of ezetimibe in postoperative patients' blood lipids management after interventional therapy of acute coronary syndrome. **Method** 160 abnormal plasma lipid patients with acute coronary syndrome who accepted coronary artery interventional therapy in our hospital, were randomly divided into two groups—the control group taking atorvastatin calcium tablets, the experimental group taking ezetimibe and atorvastatin calcium tablets, we compared the changes and side effects of low-density lipoprotein cholesterol (LDL-C) and total cholesterol (TC) after treatment for a month between the two groups. **Result** After 30 days, TC, TG (Triglycerides) and LDL-C in plasma of the experimental group are lower than the other group ( $p < 0.01$ ). **Conclusion** The clinical effect of ezetimibe combined with atorvastatin calcium tablets in treating hyperlipemia was obviously superior to taking atorvastatin calcium tablets alone, such as making the blood fat standardized earlier and without increasing side effects, which was particularly suitable for substandard plasma lipid patients after interventional treatment of acute coronary syndrome.

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**Key words:** ezetimibe; acute coronary syndrome; coronary artery interventional therapy; blood lipids; atorvastatin calcium

### Introduction

With the improvement of people's living standard, the quickening pace of life and the aging trend of social population, the number of patients with coronary heart disease (CHD) have increased year by year, and postoperative patients after interventional therapy of acute coronary syndrome (ACS) are also increasing significantly. Because of lipid-lowering therapy effectively improving the prognoses of patients with CHD, blood lipids management is very important to patients with CHD, especially the patients who had interventional therapy of ACS. During regular follow-up of patients with CHD after interventional therapy, we found many postoperative patients insisted on taking statins, but blood lipid still hadn't reached the intensive lipid-lowering standard. By observing and analyzing the curative effect of lipid-lowering therapy and side reactions of ezetimibe combined with atorvastatin calcium, this article evaluates their value in postoperative patients' blood lipids management after interventional therapy of ACS.

### Patients and Methods

#### I. Patients

A total of 160 patients including 86 males and 74 females, in the age range of 60 to 75 years, with an average of 68.2 years, received coronary angiography and interventional therapy from June

2010 to May 2012 in Henan Provincial People's hospital and plasma lipids of these patients weren't up to standard through one month of follow-up after surgery. The patient enrollment criteria: 1. Postoperative patients after interventional therapy of ACS. 2. The blood fat of patients taking lipitor 20 milligrams a day still hadn't reached the intensive lipid-lowering standard. 3. The intensive lipid-lowering standard: TC in serum below 4.68mmol / L, and/or LDL-C below 2.59 mmol / L, and LDL-C of extremely high risk patients (ACS or ischemic cardiovascular disease complicated with diabetes mellitus) below 2.00mmol / L or TG in serum below 1.70mmol / L. The exclusion criteria: 1. Active liver diseases or unexplained serum transaminase going up. 2. Hereditary diseases of abnormal lipid metabolism.

#### II. Methods

160 patients were allocated to 2 groups randomly, the control group (80 cases) taking a daily dose of 20 mg of atorvastatin calcium tablets (lipitor, 20mg of a pill, U.S. Pfizer Pharmaceuticals LLC) alone and the experimental group (80 cases) taking ezetimibe tablets (ezetimibe tablets, 10mg of a pill, U.S. Schering-Plough Corporation) in combination with atorvastatin calcium tablets (lipitor, 20mg of a pill, U.S. Pfizer Pharmaceuticals LLC). In the treatment period of 30 days, all cases continued taking medications such as platelet aggregation inhibitors,

vasodilator agents dilating coronary arteries and nutrition myocardial drugs, had a low cholesterol diet at the same level instead of high cholesterol food, like pork, salad dressings, fried food, etc. and ate fruits, vegetables or coarse food which are rich in more cellulose. They also adhered to aerobic exercise such as walking each day.

After 30 days, we respectively took fasting blood in 2 groups early in the morning, and separated the blood serum by centrifugation after 30 to 45 minutes at room temperature. For monitoring adverse drug reactions, we measured the contents of TC, TG, HDL-C, and LDL-C in serum, in addition to the levels of CK, AST, and ALT. we contrasted the gained results with the test results before treatment, watched the changes of each indicator, calculated and compared the qualification rates of these indicators about blood lipids after treatments in both groups, and observed drug side effects at different ages.

### III. Statistical Methods

Via using the statistical software SPSS (18.0), we statistically analyzed experimental data based on the content detection of TC, TG, HDL-C and LDL-C in serum in two groups before and after treatment. Measurement data through T-test were expressed in the form of ( $\bar{x} \pm s$ ); we counted the number of cases ( $n$ ) whose blood-lipid indexes were

up to standard in two groups of patients after treatment, calculated the qualification rates (%), and compared experimental data of two groups with the chi-square test. Taking  $p < 0.05$  for the difference was statistically significant.

## Results

### I. Comparison of blood lipids level of patients before and after treatment in two groups

The results of comparison, an average content of TC, TG, HDL-C and LDL-C in serum about two groups of patients before and after treatment, are shown in Figure 1. By comparison of the average content TC, TG, HDL-C and LDL-C in serum in two groups of patients before treatment, there is no statistically significant difference ( $P > 0.05$ ). After treatment, TC, TG, HDL-C and LDL-C levels of the experimental group are significantly lower than that of the control group ( $t=4.7625$ ,  $P < 0.01$ ;  $t=5.5613$ ,  $P < 0.01$ ;  $t=2.5412$ ,  $P < 0.05$ ). But the average contents of HDL - C are obviously higher than the control group ( $t=5.5165$ ,  $P < 0.01$ ). Results show that ezetimibe in combination with atorvastatin calcium tablets can more effectively improve blood lipids, so as to effectively achieve the goal of lipid reduction.

Table 1 Comparison of blood lipids level of patients before and after treatment in two groups ( $\bar{x} \pm s$ , mmol/L)

Groups	n	time	TC (mmol/L)	TG (mmol/L)	HDL -C (mmol/L)	LDL -C (mmol/L)
The experimental group	80	Before treatment	6.45±1.77	2.42±0.71	0.82±0.11	4.57±0.87
		After treatment	4.12±0.33	1.29±0.24	1.31±0.12	2.3±0.23
The Control group	80	Before treatment	6.32±1.81	2.38±0.66	0.82±0.09	4.52±0.96
		After treatment	5.65±0.41	2.21±0.16	0.97±0.09	3.87±0.73

### II. Comparison of the qualification rates of blood lipid indicators in two groups of patients after treatment

The qualification rates of testing TC, TG, and LDL-C are shown in table 2. The qualification rates of testing TC, TG, and LDL-C of the experimental group

are clearly higher than the other. The differences of two groups were statistically significant ( $P < 0.05$ ). It turns out that the clinical effect of ezetimibe and atorvastatin calcium tablets are better than atorvastatin calcium tablets.

Table 2 Comparison of the qualification rates of blood lipid indicators in two groups of patients after treatment [ $n$  (%)]

Groups	n	TC	TG	LDL-C
The experimental group	80	72 (90.00)	66 (82.50)	59 (73.75)
The Control group	80	53 (66.25)	47 (58.75)	40 (50.00)

### III. Adverse reactions

During the treatment of 30 days, none of two groups' patients had myalgia symptoms and withdrew from experiment without adverse reactions. At the end of treatment, there were 1 case what had diarrhea and

other gastrointestinal reactions, and an experimenter whose AST increased slightly but went back to normal after drug withdrawal for 2 weeks in the control group. In experimental group, 1 case had red swelling and itching on the skin which disappeared after stopping

the treatment, and a patient whose AST transiently elevated and returned to normal after taking half of dosage for a week. The incidence rate of adverse reactions was 5% and the differences of two groups were not statistically significant ( $P > 0.05$ ).

### Discussions

An important measure to preventing and treating atherosclerotic cardiovascular diseases (ASCVD) is to inhibit actively dyslipidemia, but the core is to lower the level of LDL-C and TC which is more significant for patients after CHD intervention therapy. The Latest European Dyslipidemia Management Guidelines explicitly shows that stable CHD and its equivalent diseases, type 2 diabetes mellitus, chronic renal disease, and especially carotid plaques out of ultrasonic testing are included in high-risk groups which emphasize more prognostic risk. Target values of extremely high-risk patients need to be controlled below the tendency of 1.8mmol / L (70 mg / dl); The target compared with the baseline should be reduced by over 50%<sup>[1]</sup> if it is difficult to achieve. Chinese Guidelines on Prevention and Treatment of Dyslipidemia in Adults also puts forward the idea that LDL - C is the main goal of blood lipid regulation, which means LDL-C<2.59mmol / L among high-risk patients(CHD and CHD risk equivalents) and LDL-C<2.00mmol / L<sup>[2]</sup> in most high-risk patients(ACS or ischemic cardio-vascular disease complicated with diabetes mellitus).

Although statins are most widely used due to powerful effect of lowering lipid and Anti-atherosclerosis, the qualification rates of LDL-C of most high-risk and extremely high-risk patients are lower than 42%<sup>[3]</sup>. At the moment there are three choices: 1. Add doses of statins. A large amount of clinical studies showed the role of reduplicated statins in reducing cholesterol is only up 6%, but the incidence rate of adverse reactions (especially hepatotoxicity and muscle toxicity) has significantly increased, which brings about the result that some patients cannot tolerate larger dosage of statins<sup>[4,5]</sup>. 2. Take more effective statins. Under regular doses, the degree of all kinds of statins lowering LDL-L is 30% to 40%, therefore when a kind of statin treatment can't reach the standard, regular doses of the other could be difficult to significantly improve efficacy of therapy. 3. Combine with other cholesterol-lowering drugs (fibrates and nicotinic acids drugs, etc.). This method is helpful to further lower the level of TC and LDL-C, but it remains to be proved whether it is safe and what kind of impact it will have on the long term prognosis of patients. So statins combined with ezetimibe provides a new thought.

Ezetimibe, as the only selective cholesterol absorption inhibitor<sup>[6]</sup> in the world, mainly blocks the way of exogenous absorption of cholesterol. After the rapid absorption of oral administration, it is combined into ezetimibe-glucuronide which works on the brush border of small intestinal cells, selectively inhibits cholesterol in meals and bile across small intestinal wall being transported into hepar by inhibiting the activity of NPCIL transporters, and dishoards cholesterol in hepar that results in increasing LDL receptor syntheses of the liver, boosting its metabolic rate and reducing the level of LDL-C in blood plasma<sup>[7]</sup>.

This paper chooses 160 substandard plasma lipid patients with acute coronary syndrome after interventional therapy for a month. According to observing lipid - lowering therapy of separately taking statins in contrast with ezetimibe and atorvastatin calcium tablets, we assess the function of lowering blood lipids of ezetimibe in postoperative patients after interventional therapy of acute coronary syndrome. The results indicate that the clinical effect of ezetimibe and atorvastatin calcium tablets are better than taking atorvastatin calcium tablets alone; Ezetimibe in combination with atorvastatin calcium tablets can more effectively improve blood lipids, so as to effectively achieve the goal of lipid reduction, and don't increase the risk of bad reactions happening.

The metabolism of ezetimibe doesn't get through CYP450 enzyme system, hence without interaction with many drugs clinically, and particularly it has no significant influence on pharmacokinetics of statins; Ezetimibe without affecting cholesterol synthesis of the liver, bile acids excretion and absorption of other lipids and fat-soluble vitamins in the small intestine<sup>[8]</sup>, is especially suitable for elderly patients with CHD.

In conclusion, the obvious therapeutic effect of ezetimibe combined with atorvastatin calcium tablets in treating hyperlipemia is clearly superior to taking atorvastatin calcium tablets alone, to make the blood fat of patients with acute coronary syndrome after interventional treatment up to standard earlier.

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