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Research Article

Compare the effect of high and low doses of atorvastatin on the levels of high-sensitivity C-reactive protein in patients with acute coronary syndrome

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ABSTRACT

Background: Findings of other researches indicate that inflammation process is one of the most important molecular interactions mediated in atherosclerosis and the inflammation indexes of plasma level such as high-sensitivity C-reactive protein (hs-CRP) is regarded to predict the risk of cardio-vascular diseases. According to various studies, statins are certainly effective in the prevention of atherosclerosis and anti-inflammatory role of atorvastatin by lowering effect on hs-CRP can be considered. The aim of this study was to compare the effect of high and low doses of atorvastatin on levels of hs-CRP in patients with acute coronary syndrome.
Methods: This is a clinical trial study that has been done on 180 patients with acute coronary syndrome who referred to Imam Khomeini hospital in Ardabil. Patients were divided in 2 groups randomly. Atorvastatin with low dose (20mg) and high dose (40mg) with routine treatments were given to first and second groups, respectively. The hs-CRP level was evaluated for all patients in hospitalized time and third month late. Data were collected and analyzed by statistical methods in SPSS.19.
Results: Of all patients, 40 patients (22.2%) was assayed with STEMI, 8 patients (4.4%) with N/Q WMI and132 patients (73.3%) with U/A. 125 patients (69.4%) were male and rest of them were female. The age average of patients was 59.1±8.1 years. 74 (41.1%) of patients had blood pressure and 35 (19.4%) use smoke. After three months, in group with low dose, 81 patients (90%) and in group with high dose 85 patients (94.4%) improved. The atorvastatin with high dose could significantly decrease the hs-CRP ratio with 40% more than other group with 13.3%.
Conclusions: In this study high dosage of atorvastatin could lessen significantly the hs-CRP and LDL ratio compared to atorvastatin with low dosage.

Keywords: Acute coronary syndrome, Atorvastatin, HS-CRP

INTRODUCTION

Acute coronary syndrome (ACS) includes myocardial infarction with elevated ST segment, without elevated ST segment and unstable Angina.[1,2] In America about 1.68 million patients were diagnosed with ACS during 2001.[3] Chest pain has been the second major complaint in the emergency of North America's hospitals.[4] Usually 10-30% of the patients with chest pain have ACS. 1-4% of ACS and 2-3% of the MI patients are mistakenly discharged from hospitals.[5-6] In Iran, cardiovascular disease, with 46% death rate, is the most common cause of death.[7] Atherosclerosis of coronary has been the most important cause of heart diseases and the findings of the recent studies showed that the inflammatory process involved in atherosclerosis is one of the most important molecular mechanisms.[8-11]

In this regard, the relationship between plasma levels of inflammatory markers has been considered in order to predict the risk of cardiovascular diseases. Cytokines, pro-atherogenic enzymes and CRP can be noted as Inflammatory markers which can be directly released from inflammatory cells and found in the platelets and tissues exposed to ischemia.[12] Hs-CRP is an acute phase protein is made in the liver under the control of serum concentrations of IL6 during the inflammatory process. In cases with low CRP levels that cannot be qualitatively revealed by symbol "+", it can be found by measuring of hs-CRP levels in blood.[13]

Different epidemiological studies have shown that plasma levels of hs-CRP is an independent and strong marker for determine the risk of heart attacks and peripheral artery diseases.[13-15] Statins are the inhibitors of Reductase HMG-COA enzyme that is essential for the synthesis of cholesterol and among the existing statins in Iran, atorvastatin is more efficiency than others. Anti-inflammatory effects of statins in lowering hs-CRP can have an important role in the treatment of ACS patients.[16]

The research findings show that the process of inflammation is one of the molecular mechanisms involved in atherosclerosis and in this regard plasma levels of inflammatory markers such as hs-CRP have been considered in order to predict the risk of cardiovascular disease. According to various studies, statins are certainly effective in the prevention of atherosclerosis and anti-inflammatory role of atorvastatin, by its lowering effect on hs-CRP, can be considered. The aim of this study was to compare the effect of high and low doses of atorvastatin on hs-CRP levels in patients with ACS.

METHODS

This clinical trial study was conducted on 180 patients, with acute coronary syndrome, that referred to Imam Khomeini hospital in Ardebil city. Patients were randomly divided into two groups. Along with routine treatments, low-dose atorvastatin in the first group (20mg) and high-dose atorvastatin in the second group (40 mg) was administered.

The patients were followed for 12 weeks and hs-CRP levels of the patients were measured on admission and three months later. The data were collected by using a checklist containing some questions about demographic data, risk factors for heart disease (such as high blood pressure, diabetes, hyperlipidemia, smoking, opioids and alcohol, and family history of heart disease in the patient and his relatives), the levels of primary and secondary hs-CRP, the levels of primary and secondary HDL and LDL. The collected data were analyzed using statistical methods in statistical software spss version 19.

RESULTS

Of the total patients, 40 patients (22.2%) with STEMI, 8 patients (4.4%) with the N / Q WMI and 132 patients (73/3%) with U/A were evaluated. 67 patients (74.4%) in the group receiving low-dose atorvastatin and 65 patients (72.2%) in the high-dose atorvastatin receiving group had unstable angina. The two groups were matched in terms of gender.

The average age in the group receiving low-dose atorvastatin was 60.6±7.9 and in the group receiving high-dose atorvastatin was 57.6±8.1 years (Table 1).

Table 1: Changes in mean of hs-CRP level before and after intervention.

Groups	Time	hs-CRP(mg/L)	hs-CRP decreasing rate (%)	p-value
Atorvastatin high dose	hs-CRP in baseline	4±2.5	40	0.001
	hs-CRP after three month	2.4±1.8		
Atorvastatin low dose	hs-CRP in baseline	3.03±2.53	13.3	
	hs-CRP after three month	2.6±2.58		

Table 2: Changes in LDL level during study in two groups.

Groups	Time	HDL	HDL decreasing rate (%)	p-value
Atorvastatin high dose	First (mean)	37.3±3.95	9	**0.001**
	Second (mean)	40.8±4.7		
Atorvastatin low dose	First (mean)	38.8±3.8	6	
	Second (mean)	41.4±3.9		

There wasn't any significant difference between the two groups in terms of hypertension, diabetes, hyperlipidemia, history of PCI, CABG, CAG, smoking and ACS history in family.

After a three-month follow-up period it was observed that in the group receiving low-dose atorvastatin, 81 patients (90%) were well, 8 patients (8.9%) again were suffering from ACS and one patient died. While in the group receiving high-dose atorvastatin, 85 patients (94.4%) were well and 5 patients again were suffering from ACS. There was no significant relation in the impact of high and low doses of Atorvastatin on the patient's clinical process. Also in baseline, Echo of patients was performed and ejection fraction for patients was calculated. Among the groups receiving low-dose atorvastatin, 72 patients (80 %) had normal EF and 18 patients (20%) had reduced EF. In the group receiving high-dose atorvastatin, 66 patients (73.3%) had normal EF and 24 patients (26.7%) had reduced EF and there was no significant difference between two groups.

Table 3: Changes in HDL level during study in two groups.

Groups	Time	LDL	LDL decreasing rate (%)	p-value
Atorvastatin high dose	First (mean)	104.9±14.5	23	0.001
	Second (mean)	82.1±10.84		
Atorvastatin low dose	First (mean)	95.8±13.8	10	
	Second (mean)	79.5±13.4		

The high-dose atorvastatin reduced the amount of hs-CRP about 40 %, while low-dose atorvastatin only 13.3% reduced the hs-CRP level and the difference was statistically significant (p=0.001) (Table 2).

It was also observed that atorvastatin at a low dose could only reduce the amount of LDL about 10 %, while atorvastatin at high dose could reduce LDL about 23% and the difference was statistically significant between two groups (P = 0.001) (Table 2). Also, the low-dose atorvastatin could increase HDL levels about 6% while high-dose atorvastatin reduced this amount about 9 % and the difference was statistically significant (P = 0.009) (Table 3).

In this study, no significant relationship was found between the level of hs-CRP and prognosis of the patients.

DISCUSSION

In this study of the total patients, 40 patients (22.2%) with STEMI, 8 patients (4.4%) with the N / Q WMI and 132 patients (73/3%) with U/A were evaluated which was different with other study results.[17-18] Unstable angina and myocardial infarction in patients who are hospitalized with acute coronary syndrome varies according to different studies. The ratio of patients with unstable angina to MI in our study was 3.3 to 1 which upper than other studies. This results perhaps because of more sensitive methods of measuring biochemical markers of myocardial necrosis such as troponin and CK_MB.[17-24]

In this study, there wasn't significant relationship between sex and the risk of acute coronary syndrome, the occurrence of unstable angina and QWMI. Meanwhile, various studies have different results.

The most obvious biological explanation for differences related to sex is coronary heart disease (CHD) demonstration.[25-28] The possible cause of the insignificancy of gender in this study can be attributed to the small sample size. In this study, no relationship was observed between the history of PCI, CABG and CAG with gender.

A study has shown that the percentage of men who undergo subcutaneous coronary angiography and angioplasty are significantly higher than women.[28] Also Jones in a review article in 2003 stated that men are referred for coronary angiography two times more than women. He also states that non-specific symptoms in women and failure to early detection of patients leads to a delay in receiving appropriate treatment.[29]

In this study, high-dose atorvastatin significantly increased HDL and decreased LDL levels, which was consistent with other similar studies.[30-32] In this study, consumption of high-dose statins could significantly reduce the amount of hs-CRP compared to lower doses. Meanwhile, in the studies conducted by Macin and Vasilieva it was revealed that CRP level in ACS decreased quickly after taking atorvastatin.[33]

In Gupta's study, atorvastatin significantly reduced the levels of hs-CRP and followed by the platelet aggregation in patients with high hs-CRP level.Also, in Gupta's study it was observed that in the group receiving atorvastatin the reduction of the level of hs-CRP was significantly more than the group who did not receive the medicine. After reviewing the study performed by Boon-baichaiapruck, it was observed that atorvastatin reduced LDL level about 44% and hs-CRP level about 10%, which was statistically significant (p=0.003).[34]

CONCLUSION

Results showed that although high-doses atorvastatin compared to the low-doses, significantly reduced LDL and hs-CRP levels but high-dose atorvastatin administration couldn't have more acceptable effects on the patient's clinical treatment and also prevent repeated ACD.

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