

Original Research Article

The effect of statins on carotid intima-media thickness in patients with acute coronary syndrome

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ABSTRACT

Background: Statins have been established by definitive primary and secondary cardiovascular prevention trials as the cornerstone of primary prevention of atherosclerotic vascular disease. Carotid arterial intima-media thickness is used as a noninvasive surrogate end point in epidemiologic studies and clinical trials to gauge progression and regression of atherosclerosis. In this trial, we compared the effects of a high-potency statin with different dose (atorvastatin 20 mg/d and atorvastatin 40 mg/d) on carotid intima-media thickness (CIMT).

Methods: This was a randomized, single blinded clinical trial that performed on 100 patients with ACS diagnosis from April 2014 to September 2015. The effects of atorvastatin (20 mg/d; n=50) and atorvastatin (40 mg/d; n=50) on CIMT were compared using serial assessment of the thickness of common carotid artery.

Results: The mean patient age was 52 years and 74% were male. Baseline CIMT and other characteristics were similar between study groups. CIMT was stable in the both study groups after 6 months and there were no meaningful statistical differences observed between study groups (change in CIMT, 0.044 ± 0.169 and -0.006 ± 0.168 mm; $p=0.14$).

Conclusions: This comparative trial shows that the use of atorvastatin 20 mg/d and 40 mg/d in short term have similar effects on carotid intima-media thickness. However, intensive statin therapy may have been shown to yield improvement in atherosclerosis with measurement of the carotid intima-media thickness.

Keywords: Atherosclerosis, Statins, Carotid intima-media thickness

INTRODUCTION

Cardiovascular diseases are the most common serious diseases in developed countries and they are rapidly increasing in developing countries. Although the age proportional mortality rate for coronary artery disease has decreased to two-thirds in the United States during the past four decades, but cardiovascular diseases are still the most common causes of deaths and account for approximately 40 percent of deaths of which almost one quarter occurs suddenly. The increasing prevalence of obesity, type 2 diabetes and metabolic syndrome, which are the major risk factors for atherosclerosis, are now considered as a menace to prevent age-adjusted mortality

rate due to coronary artery disease.¹ It is estimated that cardiovascular diseases, especially atherosclerosis, will be the main cause of the disease in the world by 2020.² Atherosclerosis is a vascular disease that is non-technically called "atherosclerosis". Today's models on Atherosclerosis are based on the belief that various stressors have impaired vascular continuity and have caused the accumulation of abnormal fat, cells and extracellular matrix in arterial wall.

These waste products create lesions called "atherosclerotic plaque". These plaques may directly reduce the diameter of the ductus arteriosus or their rupture and cause thrombosis. Both mentioned

mechanisms restrict blood flow of the members in distal. As a result, the main complications of atherosclerosis include angina, myocardial infarction, stroke, and reduced blood flow to the kidneys and lower extremities that introduce atherosclerosis as the main cause of mortality and morbidity in the developed world.

Despite the high prevalence and after more than one hundred years from the recognition of pathological features, pathophysiology of atherosclerosis is still an interesting topic for widespread and active research. Substantial progress has been achieved in recent years. Acute coronary syndromes (ACS) are life-threatening conditions that can end life in patients with coronary artery disease at any time.

These syndromes range from a pattern of unstable angina to the most serious form of acute myocardial infarction which is in the form of an irreversible necrosis of heart muscle. The prevalence rate of ACS is very high and surprising. More than one million and six hundred thousand people, suffering from one of these syndromes, refer to the hospitals in the United States each year.³

Also Framingham's study and other studies have shown that the risk of ischemic heart disease increases with increased cholesterol levels. Coronary risk in patients with cholesterol levels of about 240 mg/dl is two times more the individuals with 200 mg/dl cholesterol. Increased serum levels of LDL are associated with an increased incidence of atherosclerosis and coronary heart diseases. When the level of LDL is high, it accumulates in the sub endothelial space and by causing more changes leads to the additional damage to the intima layer and results the creation or extension of atherosclerotic lesions. When lifestyle changes are not able to provide the desired amount of lipids, a group of drugs can be used to treat abnormal lipid levels. The most efficient LDL levels lowering are inhibitors of HMG-CoA reductase (3-hydroxy-3-methyl-glutaryl-coenzyme A) which are called "statins".⁴ Lovastatin, Atorvastatin, Fluvastatin, Pravastatin and Ruvastatin belong to this group. Atorvastatin is the most powerful statin drug class that can be administered at a dose of 10-80 mg per day. Statins are the most effective in LDL reduction. Also during treatment with these drugs, a slight reduction in plasma triglycerides and a mild increase HDL cholesterol levels occur.⁵⁻⁶

Today the measurement of carotid intima-media thickness with ultrasound devices with high accuracy is possible. The normal thickness is 0.6-0.8 mm, but several studies have shown that the thickness, in patients with evidence of atheroma, significantly increases in other areas such as coronary arteries. Intima-media thickness slowly increases with age but it may provide a useful tool in the diagnosis of patients with vascular disease.⁷ Considering the importance of cardiovascular disease and complications of acute coronary syndromes such as heart attack and the increasing risk of carotid intima-media

thickness in patients with evidences of atheroma in other areas like coronary arteries, this study was conducted in order to evaluate the effect of statins carotid intima-media thickness in patients with acute coronary syndrome.

METHODS

This study was a randomized single-blind clinical trial which was conducted on 100 patients with acute coronary syndrome such as STEMI or UA and NSTEMI that were hospitalized in Ardabil city hospital from April 2014 to September 2015.

After obtaining written informed consent at the time of admission of patients, carotid Doppler ultrasound was taken from the patients and carotid intima-media thickness, the distance between the intima and media to adventitia junction, was measured during diastole by placing the probe Sono vertically on common carotid approximately one centimeter below artery bulb. All ultrasounds were taken by one person with two different devices in two different hospitals. The size of this thickness along with other information of the patients including age, sex and history of diseases such as hypertension, type 2 diabetes, smoking, hyperlipidemia and diagnosis during hospitalization including myocardial infarction with ST-segment elevation, myocardial infarction without ST-segment elevation, and unstable angina were recorded. The patients were divided randomly into two groups of 50 patients and were treated with atorvastatin 20 and 40 mg which was administered routinely to patients. The patients were visited once every 3 months from the time of taking drug and the liver enzymes were checked in patients 3 months after the start of medication. The patients were invited for repeated measurement of carotid intima-media thickness after 6 months and additional information was added to the form. The collected data were analyzed in SPSS version 16 software using statistical methods. $P < 0.05$ was considered as significant level.

RESULTS

In this study 100 patients with the age range of 30-74 years were studied. The mean age was 52 ± 10 years. The mean age in atorvastatin 20 mg group was 52 ± 12 years and atorvastatin 40 mg group was 52 ± 9 years. 74% of all patients were male and rest of them was female. In Atorvastatin 20 mg group, 36 patients (72%) and atorvastatin 40 mg group, 42 patients (84%) participated with a diagnosis of UA. Of all patients, 21% had no risk factor, 23% smoking, 15% diabetes, 25% had high blood pressure and 16% had hyperlipidemia. The risk factors prevalence difference between the two groups was not statistically significant as given in Table 1.

The analysis of gender, diagnosis and heart disease risk factors data were analyzed using chi-square test and in general the two groups (atorvastatin 20 mg and 40 mg) had a similar demographic characteristics and difference

between two groups was not statistically significant. The change in the mean of carotid intima-media thickness in the atorvastatin 20 mg group was 0.044 ± 0.17 mm and in the atorvastatin 40 mg group was -0.006 ± 0.17 mm as given in Table 2.

Table 1: Risk factors in two groups.

Risk factors	Groups		p-value
	Atorvastatin 40 mg n (%)	Atorvastatin 20 mg n(%)	
Smoking	10(20)	13(26)	0.82
DM type 2	7(14)	8(16)	
HTN	15(30)	10(20)	
Hyperlipidemia	8(16)	8(16)	

Table 2: Compare the average of carotid intima-media thickness (IMT) in two groups.

Average of IMT at different time intervals	Groups		p-value
	Atorvastatin 40 mg n (%)	Atorvastatin 20 mg n(%)	
Average of IMT in baseline (mm)	0.88 ± 0.137	0.824 ± 0.163	0.08
Average of IMT after 6 month (mm)	0.876 ± 0.263	0.868 ± 0.214	0.94
Change in the average of IMT (mm)	-0.006 ± 0.168	0.044 ± 0.169	0.14

DISCUSSION

In this study it was shown that the mean of carotid artery intima-media thickness after 6 months in patients who were taking atorvastatin 20 mg has been increased and reached to 0.87 ± 0.21 mm and in the atorvastatin 40 mg group has slightly been decreased to 0.88 ± 0.26 mm and there was no statistically significant difference between the two groups. Also changes in the average carotid artery intima-media thickness in atorvastatin 20 mg group was 0.044 ± 0.17 and in atorvastatin 40 mg group was -0.006 ± 0.17 mm and the statistically significant difference between the two groups was no significant.

In a randomized clinical trial conducted in 2002 to compare the effect of atorvastatin 80 mg per day and pravastatin 40 mg per day on carotid intima-media, 161 patients, with a mean age of 60 ± 11 years and 71.4% were male. In this study, the mean intima-media thickness of the carotid artery and other characteristics in the baseline were similar between two groups and the results showed

that after 12 months atorvastatin reduced carotid intima-media thickness, while the thickness in the pravastatin group remained stable ($P = 0.03$). It is noteworthy that the 6-month follow-up study of carotid intima-media thickness average in both groups was not significantly different ($P = 0.74$) and, in this regard, was similar to our study.⁸

It should be noted that due to lack of routine use of atorvastatin 80 mg per day in our country and the common use of dose 20 and 40 mg per day, the two doses were chosen for comparison and long-term follow-up of 12 months for patients was not possible because of working conditions.

A study in 2009 compared the effects of ezetimibe + statin combination therapy versus statins + fibrates on carotid intima-media thickness and showed that: After 14 months statins + fibrates combination reduced carotid intima-media average and maximum thickness whereas statin + ezetimibe increased carotid intima-media thickness. Also the risk of cardiovascular events in the study of niacin was less than ezetimibe that was not similar to our study results.⁹

In 2011 a study conducted on the relationship between carotid artery wall intima-media thickness and cardiovascular events introduced the measurement value of the thickness as a deterioration and progression measurement scale of atherosclerosis and in relation with cardiovascular events. It was mentioned that during the treatment associated with the reduction in intima-media thickness of the carotid artery wall, atherosclerosis regression occurred and the risk of cardiovascular events decreased.¹⁰

Demircan et al in his study showed that the intima-media thickness in patients who had acute coronary syndrome than in those who had stable angina pectoris which was in line with our study results.¹¹

In a study done by Shibata in 2014 results showed that Pitavastatin may be effective to prevent secondary stroke in patients with stroke and hyperlipidemia and the change of IMT%/year was less than zero for the Pitavastatin group, and was almost zero or higher for the control group.¹²

Nambi and et al in a study showed that Adding plaque and carotid intima-media thickness (CIMT) to traditional risk factors (TRF) improves coronary heart disease risk prediction in the ARIC (atherosclerosis risk in communities) study.¹³

CONCLUSION

As a result, this comparative trial study shows that the short-term daily use of atorvastatin 20 and 40 mg has similar effects on carotid artery intima-media thickness. However, it is possible that the use of high-dose

atorvastatin, 80 mg per day, may show better improvement in atherosclerosis as measured by carotid artery intima-media thickness. It is also possible that the measurement of the intima-media thickness of the common carotid artery and internal carotid artery may be added to Framingham risk factors to predict cardiovascular events in the future.

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REFERENCES

1. Baigent C, Keech A, Kearney PM, Blackwell L, Buck G, Pollicino C, et al. Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90,056 participants in 14 randomized trials of statins. *Lancet*. 2005;366:1267-78.
2. Cannon CP, Steinberg BA, Murphy SA, Mega JL, Braunwald E. Meta-analysis of cardiovascular outcomes trials comparing intensive versus moderate statin therapy. *J Am Coll Cardiol*. 2006;48:438-45.
3. Hodis HN, Mark WJ, LaBree L, Selzer RH, Liu Ch, Liu Ci, et al. The role of carotid arterial intima-media thickness in predicting clinical coronary events. *Ann Intern Med*. 1998;128:262-9.
4. Andrews TC, Ballantyne CM, Hsia JA, Kramer JH. Achieving and maintaining National Cholesterol Education Program low-density lipoprotein cholesterol goals with five statins. *Am J Med*. 2001;111:185-91.
5. Jones P, Kafonek S, Laurora I, Hunninghake D. comparative dose efficacy study of atorvastatin versus simvastatin, pravastatin, lovastatin, and fluvastatin in patients with hypercholesterolemia. *Am J Cardiol*. 1998;81:582-7.
6. Libby P, Bonow RO, Mann DL, Zips DP, Braunwald E. *Braunwald's Heart Disease*, 8th ed. New York: Saunders; 2008: 1167-1185.
7. Sutton D, Gregson R. *Arteriography And Interventional Angiography*. In: Sutton D. *Radiology And Imaging*. Volume 1. 7th edition. London: Elsevier Ltd; 2003: 465.
8. Taylor AJ, Kent SM, Flaherty PJ, Coyle LC, Markwood TT, Vernalis MN. ARBITER: Arterial biology for the Investigation of the Treatment Effects of Reducing cholesterol: a randomized trial comparing the effects of atorvastatin and pravastatin on carotid intima medial thickness. *Circulation*. 2002;106:2055-60.
9. Taylor AJ, Villines TC, Stanek EJ, Devine PJ, Griffen L, Miller M, et al. Extended-Release Niacin or Ezetimibe and Carotid Intima-Media Thickness. *N Eng J Med*. 2009;361:2113-22
10. Polak JF, Pencina MJ, Pencina KM, O'Donnell CJ, Wolf PA, D'Agostino RB. Carotid-Wall Intima-Media Thickness and Cardiovascular Events. *N Eng J Med*. 2011;365:213-21.
11. Demircan S, Tekin A, Tekin G, Topçu S, Yiğit F, Erol T, et al. Comparison of carotid intima-media thickness in patients with stable angina pectoris versus patients with acute coronary syndrome. *Am J Cardiol*. 2005;96(5):643-4.
12. Shibata Y. Effects of Pitavastatin on the Intima-Media Thickness of the Carotid Artery in Patients with Ischemic Stroke: The Pitavastatin Efficacy Study on Surrogate Markers and Imaging for Stroke (PESSMIST). *World J Neurosci*. 2014;4:306-12.
13. Nambi V, Chambless L, Folsom AR, He M, Hu Y, Mosley T, et al. Carotid intima-media thickness and presence or absence of plaque improves prediction of coronary heart disease: the Atherosclerosis Risk in Communities study. *J Am Coll Cardiol*. 2010;55:1600-7.

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