Original Article

The Effect of Two Different Doses of Atorvastatin on Lipoprotein-a on Patients with Acute Coronary Syndrome

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ABSTRACT

Background and Objectives: Lipoprotein-a potentially represents a useful tool for risk stratification in cardiovascular accidents. The aim of this study was to evaluate the atorvastatin effect on serum lipid profile & lipoprotein A.

Material & Methods: In 2009, 405 patients with acute coronary syndrome randomly were divided into 2 groups, taking 20 & 40 mg atorvastatin daily for 3 months. Lipid profile & lipoprotein-a serum levels were checked at the beginning of the study and also one and three months later.

Results: There was no statistical difference between the two groups in all measurements except in patients with unstable angina. The difference lay in the change of LP-a level after one month (P=0.045) and in apo-a level in all patients in the second and the third measurements compared with the first one (P=0.001 & P=0.002).

Discussion: It appears that the two doses (20mg and 40mg) of atorvastatin have a reduction effect on lipoprotein-A and serum lipid levels, but no difference is seen in the level of reduction. The 40 mg atorvastatin leaves more effects on reduction of apo-a than on the 20 mg after one and three months.

Keywords: Atorvastatin calcium, Lipoprotein-a, Acute Coronary Syndromes

Introduction

Lipoprotein-a (Lp-a) is present in both humans and primates. It shares many properties with low-density lipoprotein (LDL), but contains a unique protein moiety designated apo (a), linked to apolipoprotein B-100 by a single disulfide bond. Lp-a is an independent but moderate risk factor for coronary artery disease, and smaller

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size apo (a) is associated with coronary artery disease (1,2).

Statins reduce cholesterol by inhibiting 3-hydroxy-3-methylglutaryl coenzyme-A (HMG-CoA) reductase (3,4),which plays the main role in cholesterol production (4).

Statins competitively inhibit HMG-CoA reductase, the first committed enzyme of the HMG-CoA reductase pathway (1,3). Since statins are similar to HMG-CoA on a molecular level they replace HMG- CoA in the enzyme and reduce the rate of its production of mevalonate, the next molecule in the cascade that finally produces cholesterol, in addition to a number of other compounds. In the end, it reduces cholesterol through certain mechanisms(3,4).

Any increase in the cholesterol level has proven to raise the risk of cardiovascular diseases (4).

Therefore, statins can help prevent cardiac diseases while they could be also used as secondary preventive treatment(4). Statins scarcely cause complications, but they seriously damage muscles when complications emerge (3). Cardiac diseases are less likely when the level of Serum LDL-C is below 60 mg/dl than when the level is above 80 mg/dl(4).

From the available clinical trial data, atorvastatin can be considered one of the most effective statins, not only by taking into account its effects on LDL-C and ability to meet recommended treatment guidelines for this parameter, but also its effect on triglyceride (TG) levels and capacity to modify lipoprotein composition in a non-atherogenic manner(2,4,5).

By the way, a few studies have been conducted to examine the atorvastatin effect on apoparoteins and lipoproteins. This study was designed to evaluate the effect of atorvatatin on serum level of Lp-a in patients with acute coronary syndrome (ACS).

Materials and Methods

In a randomized clinical trial, 405 patients with acute coronary syndrome, admitted into Imam Khomeini Hospital's CCU from Sep. 2009 to Sep 2010, were selected. ACS includes unstable angina (UA), ST-elevation myocardial infarction (STEMI) and non-ST-elevation myocardial infarction (NSTEMI). Diagnosis was carried out by cardiology residents aided by relevant professors. Exclusion criteria include impaired liver function test & serum LDL less than 30mg/dL & more than 200mg/dL.

Employing the method of allocation concealment, patients were randomly divided into two groups. The first group was treated by atorvastatin 80 mg (40mg BD) for 2-3 days then followed by 20mg/d while the latter continued by 40mg/d for 3 months. All patients were advised to take first step diet of National Cholesterol Education Program (5).

Prior to treatment as well as one and three months after the beginning, the serum levels of Lp-a, apo(a), total cholesterol (Chol), LDL, High density lipoprotein (HDL) & triglyceride (TG) were checked at the hospital lab. The method used for cholesterol was CHOD-PAP, for HDL & LDL was photometry, for TG was GPO-PAP and for Lp-a was imunoturbidometric. All the kits were made by BioSystem S.A. company in Spain. The study was carried out according to the principles of declaration of Helsinki. The local Ethics Committee of Tehran University of Medical Sciences approved the study protocols.

The statistical analysis was performed by SPSS 13th version software using descriptive, frequencies, t-test & bivariate correlation. Data reported in form of mean ± standard deviation (SD). The level of significance assumed 0.05.

Since there was no trial, patients did not undergo additional procedures. Nor did they

pay for any test. The Helsinki statement was followed in this study. The data are confidential.

Result

Out of 405 patients, 227 proceeded with the first follow up one month & 89 others went ahead with the second follow up 3 months after the beginning of the treatment.

There were 113 (49.8%) of them in first group (taking 40mg/d atorvastatin) & 114 (50.2%) in second group (taking 20mg/d). A total of 49 patients from the first & 40 patients from the second groups continued into the 2nd follow up. Demographic data of total & both studied groups are summarized in Table 1.

Table 1- Demographic data of patients

		Group I	Group II	Total	*P*-value
Gender		F*: 41 (36.3%) M**: 72 (68.7%)	F: 37 (32.5%) M: 77 (67.5%)	F: 78 (34.4%) M: 149 (65.6%)	0.544
Age (yr)		61.32±8.43	61.48±7.89	61.4±8.15	0.88
Diagnosis	U/A***	41 (36.3%)	47 (41.2%)	88 (38.8%)	0.784
	STEMI****	46 (40.7%)	35 (30.7%)	81 (35.7%)	
	NSTEMI*****	26 (23%)	32 (28.1%)	58 (25.5%)	

*Female ** Male ***Unstable angina
****st-elevation myocardial infarction *****non st-elevation myocardial infarction

Lipid profile was checked in all three sessions. Table 2 shows the results. Except for Apo-a, none of other variables indicated any significant difference in the two groups. The studied groups were different in Apo-a in the second (*P*=0.055) and the third (*P*=0.031) follow up.

Table 2- lipid profile of patients in three measurements

		Group I (n=113)	Group II (n=114)	*P*-value
HDL* (mg/dl)	First	41.6±15.4	40.6±15.2	0.534
	Second	43.9±21.4	40±15.3	0.291
	Third	41.4±19.2	40.1±14.2	0.934
LDL (mg/dl)**	First	90.5±35.4	87.7±30.7	0.578
	Second	78±39.9	75.5±48.2	0.258
	Third	68.8±43.2	72.7±47.7	0.632
Cholesterol (mg/dl)	First	167±54.6	162±46.8	0.557
	Second	145.1±51.5	151±59.6	0.633
	Third	135±47.1	141.9±55.7	0.581
TG* (mg/dl)**	First	138.5±58.5	138.4±55.3	0.811
	Second	142.3±72.6	138.5±72.2	0.502
	Third	117.5±82.1	102±57.2	0.632
Lp-a** (mg/dl)**	First	54.2±69.6	46.1±47.9	0.708
	Second	45.6±74.7	41.9±53.9	0.987
	Third	31.5±42.1	33.1±32.4	0.405
Apo-a (mg/dl)	First	146.6±95	185.8±116.4	0.886
	Second	141.3±58	141.6±60	0.055
	Third	121.1±59.1	145.1±85.3	0.031

*High-density lipoprotein **Low-density lipoprotein
*** Triglyceride **** Lipoprotein-a

The increase/decrease of serum levels of variables during the study period was measured and examined by *t*-test. Results are summarized in Table 3.

Table 3- Differences of variables between three evaluations in groups

	Changes between	Group I (n=113)	Group II(n=114)	*P*-value
HDL* (mg/dl)	Second -First	2.3±14.9	-0.6±12.7	0.119
	Third -Second	-4.5±73.6	-30.2±60	0.412
	Third-First	-1±14.9	-13.4±15.2	0.869
LDL (mg/dl)**	Second -First	-12.5±41.5	-12.2±38.2	0915
	Third -Second	42.2±39	47.3±38.4	0.473
	Third-First	-15.5±49.4	-13.4±40.6	0.837
Cholesterol (mg/dl)	Second -First	-21.9±45.9	-11±42.4	0.065
	Third -Second	-0.1±29.7	-6.1±25.2	.0315
	Third-First	-24.3±48.6	-18.9±45	.0335
TG* (mg/dl)**	Second -First	3.8±47.8	0.1±52.1	0.579
	Third -Second	-23.9±70.4	-51.6±56.6	0.073
	Third-First	-28.5±90.2	-44±62	0.463
Lp-a** (mg/dl)**	Second -First	-8.6±42.4	-4.2±37.1	0.245
	Third -Second	-10.1±21.4	-11.9±25.1	0.853
	Third-First	-23.9±32.9	-22.5±35.5	0./195
Apo-a (mg/dl)	Second -First	-9.4±92.3	34.7±112.2	0.001
	Third -Second	13.6±62	30.1±77.4	0.279
	Third-First	-9.4±92.3	30.4±112.2	0.002

*High-density lipoprotein **Low-density lipoprotein
*** Triglyceride **** Lipoprotein-a

In patients with unstable angina (U/A), Lp-a status of group I in the first follow up was significantly lower than group II (*P*=0.045), but in all others the Lp-a did not change.

As far as gender is concerned, both groups were statistically identical in changes between all of three measurements.

Table 4 shows the results of test of correlation between Lp-a serum level changes and age in the studied groups. No significant correlation was determined between age and lp-a level in the three measurements.

Table 4- Correlation between age and LP-a in both groups

Changes etween		Group I (n=113)	Group II (n=114)
Second & first	Pearson (r)	-0.141	0.05
	P-value	0.136	0.597
Third & second	Pearson (r)	-0.038	0.197
	P-value	0.796	0.222
Third & first	Pearson (r)	-0.068	-0.005
	P-value	0.641	0.977

Discussion

Although the study faced the challenge of the patients' refusal to be followed up upon, researchers had to get more patients to fulfill the whole sample size. Moreover, a proper use of drugs could not be exactly monitored throughout the study.

To test the effects of atorvastatin on serum lipids and Lp-a levels, 90 dyslipidaemic, patients treated with 20 mg of atorvastatin for 24 weeks, were studied by Goudevenos *et al*. in 2001 (6). Atorvastatin was highly effective in normalizing the serum lipid profile, but no significant change in median serum Lp-a levels was observed in the whole group of patients. Therefore, no evidence was found of atorvastatin influencing serum Lp=a levels (6). Similarly, we showed in our study that serum Lp-a levels is not correlated with two studied doses of atorvastatin.

Gonbert *et al*. in 2002, described the serum levels of Lp (a) and of apo (a) in patients with hypercholesterolemy before and after treatment (6 weeks) with atorvastatin 10 mg/day or simvastatin 20 mg/day. After treatment, both statins significantly diminish Lp-a levels but did not significantly lowered Lp (a), although this effect was of greater magnitude in atorvastatin-treated patients (7). Our study approves this pattern and according to them Lp-a levels in both groups decreased during time.

Also in previous studies (8-10) it showed that atorvastatin significantly lowered Lp-a. It appears that 40mg atorvastatin can reduce significantly the serum level of Apo-a in comparison with 20mg (9-12). Based on our study, 20mg and 40mg of atorvasatin usually have similar effect on serum lipid profile.

Conclusion

The two different doses of atorvastatin had no difference in serum lipid and Lp-a levels. In the view of other studies mentioned above, we can conclude that the adjustment of atorvastatin dose in ACS patients can be based on other factors such as drug availability and patient tolerance. Drug side effects also can play this role. Since no difference was found between 20mg and 40mg; these conditions will determine the final dose of atorvastatin for each patient.

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