Influence of one-year treatment with lovastatin on myocardial remodeling and ischemia in patients with coronary artery disease

Koroner arter hastalığı olan hastalarda miyokardiyal yeniden şekillenme ve iskemiye bir yıllık lovastatin tedavisinin etkisi

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ABSTRACT

Objective: Emerging evidence assumes that statins have a benefit to influence the myocardial remodeling and ischemia in patients with coronary artery disease (CAD). Our aim was to investigate the possible and direct favorable effects of lovastatin on left ventricular (LV) systolic, diastolic function and myocardial ischemia in patients with CAD.

Methods: This randomized prospective study consisted of 83 patients (46 males; mean age 54.3±6.5 years) with CAD and dyslipidemia. All patients were randomized to following groups: the 1st group (n=44) received lovastatin (20-60 mg/day), hypolipidemic diet and physical training; the 2nd group (n=39) - hypolipidemic diet and physical training. Lipid spectrum, Doppler-echocardiography, bicycle exercise test and 24-hour ambulatory electrocardiographic monitoring were done at baseline and were repeated after 12 months of treatment. The data were analyzed by using the paired and unpaired Student's t-tests.

Results: In the 1st group there was an improvement of lipid spectrum ($p<0.05$) without significant changes of liver transaminases and other side effects. After treatment LV ejection fraction increased from 59.8±8.04 to 62.9±4.43% in lovastatin alone group ($p=0.01$). Unlike 2nd group, the 1st group's patients had also reduction of myocardial ischemia: increased exercise time (5.21±1.81 vs. 5.96±1.76 min; $p<0.05$), METS (4.42±0.6 vs. 4.78±0.7; $p<0.05$), magnitude (1.12±0.34 vs. 0.81±0.19 mm; $p<0.05$) and duration (2.16±0.67 vs. 1.04±0.46 min, $p<0.01$) of ST segment depression, as well as number of leads with ST segment depression (2.18±0.72 vs. 1.31±0.67; $p<0.05$).

Conclusion: Lipid-lowering therapy with lovastatin improved the LV systolic function and decreased myocardial ischemia.

(Anadolu Kardiyol Derg 2011 1: 16-21)

Key words: Statins, myocardial remodeling, ischemia, lovastatin

ÖZET

Amaç: Koroner arter hastalığı (KAH) ve dislipidemili hastalardaki iskemi ve miyokart yeniden şekillenme üzerine statinlerin yararlı etkileri olduğu kanıtlanmıştır. Amacımız, lovastatinin sol ventrikül (SV) sistolik ve diyastolik fonksiyonları ile miyokart iskemisi üzerine olası ve doğrudan yararlı etkilerini araştırmaktı.

Yöntemler: Bu randomize prospektif çalışma, koroner arter ve dislipidemi hastalığı olan 83 hastadan (46 erkek; ortalama yaş, 54.3±6.5 yıl) oluşmaktadır. Bütün hastalar, gruplara randomizeydi: 1. grup (N= 44), 20-60 mg/gün lovastatin aldı, hipolipidemik diyet ve beden eğitimi uygulandı; 2. grup (N=39) - hipolipidemik diyet ve beden eğitimi uygulandı. Başlangıçta lipit spektrumu, Doppler ekokardiyografi, bisiklet egzersiz testi ve 24-saat ambulatuvar elektrokardiyogram izlemesi, yapıldı ve 12 aydan sonra tekrarlandı. Veriler, eşleştirilmiş ve eşleştirilmemiş Student's t-tests kullanarak analiz edildi.

Bulgular: Birinci grupta, karaciğer transaminazlarında önemli değişiklikler ve diğer yan etkiler olmaksızın lipit spektrumunda ($p<0.05$) düzelme vardı. Tedaviden sonra, SV ejeksiyon fraksiyonu yalnız lovastatin grubunda 59.8±8.04'den %62.9±4.43'e yükseldi ($p=0.01$). İkinci gruptan farklı olarak birinci grup hastalarında da miyokardiyal iskemi azalması vardı: Egzersiz zamanında (5.21±1.81 vs. 5.96±1.76 dk; $p<0.05$) ve METS'de artma: (4.42±0.6 vs. 4.78±0.7; $p<0.05$), ST segment depresyon büyüklüğü (1.12±0.34 vs. 0.81±0.19mm; $p<0.05$) ve süresi (2.16±0.67 vs. 1.04±0.46 dk.; $p<0.01$) ve ST segment depresyonlu derivasyon sayısında (2.18±0.72 vs. 1.31±0.67; $p<0.05$) azalma.

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Accepted Date/Kabul Tarihi: 23.11.2010 **Available Online Date/Çevrimiçi Yayın Tarihi:** 24.12.2010

doi:10.5152/akd.2011.004

Sonuç: Lovastatinle lipit-düşürme tedavisi, miyokardiyal iskemiyi azalttı ve SV sistolik fonksiyonunu arttırdı.
(Anadolu Kardiyol Derg 2011 1: 16-21)
Anahtar kelimeler: Statinler, miyokardiyal yeniden şekillenme, iskemi, lovastatin

Introduction

Coronary artery disease (CAD) is the main cause of mortality and disability of population in many countries (1). In addition to multiple risk factors of CAD, recent epidemiological studies emphasized the role of increased left ventricular myocardial mass on sudden cardiac death (2).

It has been demonstrated that lipid lowering treatment with statins can improve clinical course and prognosis of CAD and atherosclerosis-associated illnesses. It has been derived from randomized controlled trials, that using of statins can decrease the frequency of acute coronary syndrome (fatal and nonfatal myocardial infarction, unstable angina pectoris) episodes, stroke, necessity of invasive interventions and hospitalization (3). Studies have also revealed multiple beneficial, "pleiotropic" effects of 3-hydroxy-3-methyl-glutaryl-CoA reductase inhibitors: improvement of endothelial function, stabilization of coronary plaques, suppression of proliferation of smooth muscle cells in vessels and platelet aggregation, reduction of inflammation (4). At present time, scientists and physicians have a great interest to beneficial effects of statins, especially on myocardial remodeling and myocardial ischemia. Evidence of beneficial effects on myocardial remodeling after statin therapy has been explored among different patients, mostly in patients with non ischemic cardiomyopathy (5).

However, effects of statins on myocardial remodeling in patients with CAD and dyslipidemia remain unclear.

The aim of this study was to investigate possible effects of lovastatin on myocardial remodeling and myocardial ischemia in patients with CAD and dyslipidemia.

Methods

Study design

The study was designed as prospective, randomized.

Patients and protocol of the study

Overall, 83 patients aged between 42 and 65 (mean age 54.3±6.5 years) years, with CAD and dyslipidemia were selected for the study after they took part in the 6- week hypolipidemic diet according to National Cholesterol Education Program (NCEP) of the American Heart Association (6). Inclusion criteria were: stable CAD, confirmed by positive exercise testing, plasma concentration of total cholesterol (TC) ≥200 mg/dl, triglycerides (TG) ≥150 mg/dl, low-density lipoprotein (LDL) cholesterol ≥100 mg/dl and normal level of liver transaminases. The exclusion criteria were: myocardial infarction within the past 6 months, chronic heart failure (functional class II and more according to the New York Heart Association (NYHA)), severe valvular heart disease, systolic blood pressure >170 mmHg and diastolic blood pressure >100 mmHg, arrhythmia (atrial fibrillation, AV block II degree and higher), insulin-treated diabetes, alcoholism, premenopausal women; hepatic, renal, inflammatory, metabolic and malignant diseases.

Total of 83 consecutive subjects by the instrumentality of random number sequence were randomized to receive either lovastatin 20-60 mg/day (1st group), hypolipidemic diet and physical training or standard care-hypolipidemic diet and physical training (2nd group, control) for a 12-month period. Starting dose of lovastatin was 20 mg/day. If target level of low-density lipoprotein (LDL) cholesterol (less then 100 mg/dl) would not be achieved after 6 weeks, the dose of lovastatin would be titrated to 40 mg/day, accordingly the ATP III recommendations (6). Subsequently lipid spectrum and liver transaminases were checked after 1.5, 3 and 12 months.

Lipid-lowering drugs were withdrawn 3 months before randomization. During study, all patients received only standard antiaggregant (aspirin 125 mg/day) and antianginal (beta-blockers, nitrates, calcium channel antagonists) therapy. Cardiovascular medication was kept unchanged during the study.

Investigations performed at baseline and at the end of the study (after 12 months) included checking of full lipid spectrum (assessment of total cholesterol (TC), triglycerides (TG), LDL-, high-density lipoprotein (HDL)- cholesterol), liver transaminases, electrocardiogram (ECG), bicycle exercise test, 24-hour ambulatory electrocardiographic (AECG) monitoring and Doppler echocardiography.

The study protocol was approved by the Institutional Ethics committee. Written informed consent was obtained from all patients.

Effectiveness and safety measurements

During the follow-up visits, the patients had a complete medical examination with analysis of lipid spectrum, liver transaminases and ECG. They were also questioned on experiencing any symptoms that could have been related to statin treatment. We identified whether the patients had had any intercurrent illness or complication requiring interruption of statin treatment. We verified the compliance by monitoring the amount of drug dispensed.

Laboratory analyses

Plasma lipid concentrations were obtained after 12-hour overnight fasting period. TC and TG concentrations were determined by standard enzymatic methods ("Sinchron CX4 DELTA", Beckman, USA) (7), HDL concentrations - by selective precipitation with dextran-magnesium chloride. LDL cholesterol levels were calculated using Friedewald's formula (8): LDL cholesterol=TC-[HDL+(TG/5)]. Those patients whose TG levels were more than 400 mg/dl were excluded from the LDL cholesterol analysis, because LDL cholesterol levels could not be calculated in these patients (8). Atherogenic index (AI) was calculated by A. Klimov`s formula: AI=TC/HDL cholesterol (9).

Echocardiography

Echocardiographic ("Acuson / Sequoia 256", USA) measurements were performed by a single technician using the 2.5-MHz transducer. Patients were examined in the left lateral decubitus position. Two-dimensional, M-mode and Doppler echocardiography were performed. The 2-dimensional images were acquired in parasternal long-axis, short-axis, and apical 2-, 4-, and 5-chamber views. Echocardiographic measurements included: left ventricular (LV) end-diastolic and end-systolic dimensions, ejection fraction (EF). LV EF was computed by using a modified Simpson's biplane method from apical 2- and 4-chamber views. The transmitral pulse Doppler velocity recordings: early diastolic velocity (E), late diastolic velocity (A), E/A ratio and isovolumetric relaxation time (IVRT) were averaged from 3 cardiac cycles (10).

Echocardiographic LV mass was determined using the corrected formula according to the American Echocardiography Society (11):

LV mass (grams)=0.8x[1.04x((EDD+VS+PW)^3-EDD^3)]+0.6.

LV mass was indexed using the D. DuBois` formula (12):

S=0.007184x$H^{0.725}$x$W^{0.425}$,

Where S-body surface (m^2), H-height (cm), W-weight (kg).

Bicycle exercise stress test

Bicycle exercise stress testing was performed with a 12-lead ECG according to the standard protocol (sitting bicycle ergometry, with stress periods of 2 min, starting at 50W and increased by 25W) (13). Tests were performed on a bicycle ergometer ("Tunturi", Finland), using Marquette Hellige Medical System (Marquette Hellige GmbH, CardioSmart, Germany). Anti-anginal medication gradually was discontinued 72 hours before the test. Blood pressure and heart rate were measured throughout the test or when clinically indicated. Exercise testing was terminated upon physical exhaustion, onset of angina, or when ST segment depression was 1.0 mm or more. Exercise testing was considered as positive at first appearance of 1.0 mm ST segment depression 80 ms after the J-point compared to the resting ECG.

The following parameters were assessed: exercise time (min), rate-pressure product (RPP), metabolic equivalents (METS), ischemia index. The ischemia index was calculated using the formula:

Ischemia index=(ST segment depression, mm) x (Duration of ST segment depression, min)x(number of leads with ST segment depression).

Ambulatory ECG monitoring

Ambulatory ECGs were recorded on a three-channel "Memo Port 2000-4000" tape recorder ("Memo Port 2000-4000", Hellige, Germany) with electrodes positioned to obtain pseudo V1, V5 and aVF leads. The recordings were made over a continuous period of 24 h, during which the patient completed a diary of physical activity and symptoms. The tapes were subsequently analyzed ("Memo Port 2000-4000", Hellige, Germany). Transient myocardial ischemia was defined as the presence of episodes showing 0.1mV (1mm) horizontal or down-sloping ST segment depression, 80 ms after the J-point, lasting for 60s and separated by at least 60s from the next ischemic episode. The total number of ischemic episodes, the total duration of ischemia were assessed. For ischemic episodes and ischemic duration, any overlapping episodes in the different channels were not summed.

Statistical analysis

All statistical analyses were conducted with the use of statistical software (Statistica), version 6.0, 2001 from StatSoft, Inc. (Tulsa, Oklahoma, USA). All values for samples were expressed as mean±SD. Differences in baseline characteristics, hemodynamic variables and LV mass among the groups were determined by using an unpaired Student's t test. For comparison of continuous variables within groups at baseline and 12-month follow-up- a paired Student's t-test was used. A p value <0.05 was considered to be significant.

Results

There were no significant differences in baseline characteristics among groups shown in Table 1.

Effects of lovastatin on lipid levels

Laboratory testing data are listed in Table 1. At the end of 6 - week period in the 1st group the target level of LDL-cholesterol (6) was achieved in 25 (56.8%) patients only. They continued taking the lovastatin 20 mg/day. Lovastatin dose was increased to 40 mg/day in 19 (43.2%) patients because LDL-cholesterol levels were not decreased to <100 mg/dl after 6 weeks of therapy. Laboratory analyses were repeated at the end of 12-week period and 2 (4.5%) patients had LDL-cholesterol more than 100 mg/dl, that is why the lovastatin dose was increased up 60 mg/day in these patients.

Thus 12-month lovastatin therapy (Table 1, Fig. 1) has decreased TC by 26.7% (p<0.01), LDL-cholesterol - by 32.8% (p<0.01), atherogenic index-by 26.8% (from 235.9±62.2 to 172.5±61.8 mg/dl; p<0.01); TG - by 17.8% (p<0.01). There was no significant change in HDL-cholesterol (p>0.05).

The lipid spectrum (TC, LDL-, HDL-cholesterol and TG) was not changed significantly in the control group. Both groups had no significant increase of liver transaminases (Table 1).

Lovastatin and myocardial remodeling (Table 2)

At the end of 12-month period in the 2nd group there was significant increase in LV end-diastolic and end-systolic volumes (p<0.05 for both). There were no significant changes of these parameters in the 1st group.

LV EF was not changed significantly in the control group during 12-month follow-up, while the patients, receiving lovastatin, had significantly increased LV EF at the end of 12-month period (p=0.01).

Diastolic function parameters (E, A, E/A) did not change significantly in both groups (Table 2).

At the end of 12-month period LV index mass increased (from 77.4±12.2 to 80.6±13.6 g/m^2; p<0.05) in the control group. However in patients receiving lovastatin we could not detect significant changes of LV mass.

Table 1. Clinical characteristics and lipid profiles at baseline and 12-month therapy

Variables	Group 1 (n=44)		Group 2 (n=39)	
	Baseline	12 months	Baseline	12 months
Average age, years	52.8±4.7	-	53.1±7.3	-
Men/female, n	24/20	-	22/17	-
Blood pressure, mmHg				
Systolic	134.1±10.1	133.8±9.3	131.2±10	131.9±8.5
Diastolic	84.1±4.3	84.3±3.1	83.9±4.2	84.2±5.1
Smokers, n (%)	8 (18.1)	8 (18.1)	7 (17.9)	7 (17.9)
BMI, kg/m^2	28±2	28±3	27±2	27±4
Type II diabetes, n (%)	6 (13.6)	6 (13.6)	5 (12.8)	5 (12.8)
History of MI, n (%)	8 (18.2)	8 (18.2)	4 (10.3)	4 (10.3)
Beta-blockers, n (%)	23 (52.3)	23 (52.3)	21 (53.8)	21 (53.8)
Ca channel blockers, n (%)	13 (29.5)	13 (29.5)	12 (30.8)	12 (30.8)
Nitrates, n (%)	7 (15.9)	7 (15.9)	6 (15.4)	6 (15.4)
ACE inhibitors, n (%)	14 (31.8)	14 (31.8)	12 (30.8)	12 (30.8)
Cholesterol, mg/dl				
Total	230.1±41.3	172.5±47.9**	231.9±35.5	246.3±42.5
HDL	38.9±7.3	44.01±8.1	39.4±8.1	40.9±9.3
LDL	147.8±36.3	99.2±33.6**	150.1±27.8	151.3±31.3
Triglycerides, mg/dl	95.7±25.5	77.9±23.2*	97.1±21.6	96.9±23.2
AST, IU/L	24.8±5.3	26.2±4.9	23.5±5.2	24.1±4.1
ALT, IU/L	26.0±4.61	26.9±3.1	25.6±4.4	26.2±4.1

Values are expressed as mean±SD and number/percentage.
Unpaired and paired Student's t tests:
*p<0.01; **p<0.001 compared with group 1 baseline data;
ACE - angiotensin converting enzyme, ALT - alanine aminotransferase, AST - aspartate aminotransferase, BMI - body mass index, HDL - high-density lipoprotein, LDL - low-density lipoprotein, MI - myocardial infarction

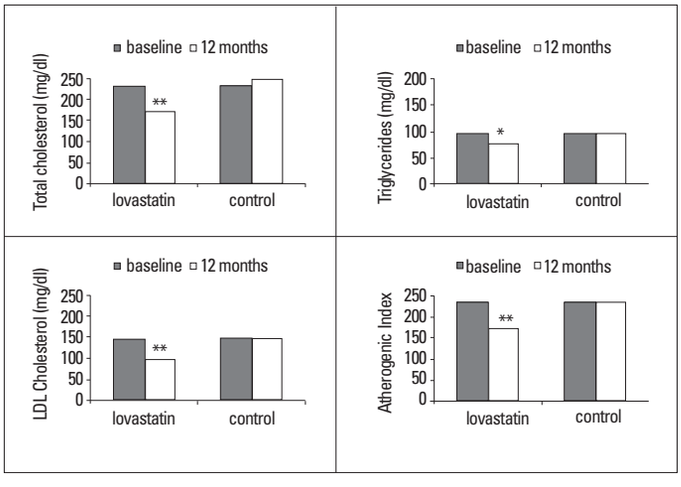

Figure 1. Bar graphs showing lipid levels at baseline and after treatment for total cholesterol, triglycerides, LDL, and atherogenic index with lovastatin and control groups. Values are average baseline and 12 months data
Paired Student t test: *- p<0.01, **p<0.001 - as compared with baseline
LDL - low-density lipoprotein

Antiischemic effect of lovastatin

Antiischemic effect of lovastatin was assessed by using bicycle tests and AECG monitoring.

Bicycle exercise test (Table 3)

All patients underwent bicycle test. 47 (56.6%) of them had angina pectoris functional class II (25 in the 1st group, 22 patients-in the 2nd group), 36 (43.4%)-had angina pectoris functional class III (19-in the 1st group, and 17 patients-in the 2nd group).

At the end of 12 months there was significant reduction in the parameters of ischemia in lovastatin group, but not in the control group: ST segment depression magnitude ($p<0.05$), and duration ($p<0.01$), number of leads with ST segment depression ($p<0.05$) and ischemia index ($p<0.05$) during exercise testing. Patients, receiving lovastatin, had also significant increase in METS ($p<0.05$) and exercise time ($p<0.05$). Parameters of bicycle exercise testing in the control group remained unchanged during 12 months.

Ambulatory ECG monitoring (Table 4)

At baseline, both groups had the same amount and duration of ischemic episodes. There were no significant differences between the changes in baseline ischemic episodes ($p=0.35$), duration ($p=0.73$), or burden ($p=0.54$) in both groups (Table 4). After 1 year, there was a significant decrease in number of ischemic episodes by 32.5% ($p<0.05$) and duration of ST segment depression by 38.7% ($p<0.05$) in the lovastatin group. Besides, there were reductions in number of painful (by 32.4%; $p<0.05$) and silent (by 38.4%; $p<0.05$) ischemia episodes. There were no significant changes in number ($p=0.43$), duration ($p=0.62$), or magnitude ($p=0.75$) of ischemic episodes in the control group.

During 12-month period there were no any side effects and complications of lovastatin treatment.

Discussion

In the present study, we observed that patients receiving lovastatin had increasing of left ventricular ejection fraction ($p=0.01$), whereas patients following only diet had consistent increase of the left ventricular size and mass. Patients in lovastatin group, but not in the control group, had also consistent reduction of myocardial ischemia: increased exercise time ($p<0.05$) and METS ($p<0.05$); decrease in magnitude ($p<0.05$) and duration ($p<0.01$) of ST segment depression, number of leads with ST segment depression ($p<0.05$). One- year treatment with lovastatin improved lipid spectrum without significant changes of liver transaminases and other side effects.

Lipid-lowering effect of lovastatin was confirmed by previous randomized clinical trials (14).

The analyses of echocardiographic data have revealed significant increase in LV end-diastolic, end-systolic volumes, LV mass in control group, compared to patients from the lovastatin group. These results may be due to prevention of myocardial structural and functional changes during lovastatin treatment.

Inhibition of 3-hydroxy-3-methylglutaryl coenzyme A reductase by statins slows cholesterol synthesis in the liver, thereby decreases the hepatic production of cholesterol (15). Simultaneously there is a block of synthesis of important isoprenoid intermediates-farnesyl-pyrophosphate and geranyl-geranyl pyrophosphate. They take part in posttranslational modification of GTP-binding proteins (Rho, Ras, Rac, Rab, Rap). These proteins are the key mediators in the hypertrophic response of myocardium and regulate proliferation, apoptosis in different cells (16). Using of statins leads not only to decrease of atherogenic lipoproteins in serum, but also to the reduction of the synthesis of several isoprenoid intermediates and thereby, prevents myocardial hypertrophy development (17). This fact has been proved in experimental (16) studies and less-in clinic trials (17).

Table 2. Left ventricular systolic and diastolic function in both groups

Variables	Group 1 (n=44)		Group 2 (n=39)	
	Baseline	12 months	Baseline	12 months
LV EF, %,	59.8±8.04	62.9±4.43**	61.1±3.4	60.04±6.4
LV mass, g/m^2	77.5±9.7	74.6±10.4	77.4±12.2	80.6±13.6*
Peak E, m/s	0.64±0.15	0.65±0.18	0.62±0.12	0.61±0.1
Peak E, m/s	0.58±0.11	0.57±0.12	0.59±0.11	0.6±0.12
E/A ratio	0.97±0.2	1.0±0.21	0.98±0.19	0.97 ±0.23
IVRT, s	0.089±0.01	0.089±0.01	0.090±0.02	0.092±0.01

Values are expressed as mean±SD
Unpaired and paired Student's t tests: *- p<0.05; **-p=0.01 as compared with baseline
A - late diastolic transmitral velocity, E - early diastolic transmitral velocity, IVRT - isovolumetric relaxation time, LV EF - left ventricular ejection fraction

Table 3. Comparison of exercise test parameters between control and lovastatin groups

Variables	Group 1 (n=44)		Group 2 (n=39)	
	Baseline	12 months	Baseline	12 months
Exercise time, min	5.21±1.81	5.96±1.76*	5.32±1.35	5.31±1.14
Peak RPP	270.7±58.7	279.4±39.8	271.3±42.1	270.7±33.5
METS	4.42±0.6	4.78±0.7*	4.43±0.9	4.41±1.1
Ischemia index	5.8±1.4	2.7 ±0.87**	5.9±1.3	5.9±1.2

Values are expressed as mean ± SD
Unpaired and paired Student's t tests: *- p<0.05; **- p<0.01 as compared with baseline
METS - metabolic equivalents, RPP - rate-pressure product

In present study of 12-month treatment with lovastatin (20-60 mg/day) there was no significant decrease of LV mass. However there was an increase in LV mass in the control group, thereby we hypothesized that lovastatin prevents myocardial structural and functional changes.

Treatment with lovastatin in our study also improved the LV myocardial systolic function: there was a significant increase of the LV EF in lovastatin group (p=0.01), in comparison to the control group. Similar result also was reported in literature (18).

Lovastatin and myocardial ischemia

Development of myocardial ischemia during routine daily activities is likely due to the presence of vasoconstriction resulting from impaired vasomotor function. Increased levels of LDL cholesterol induce endothelial dysfunction and promote vasoconstriction of coronary arteries (19). Therefore, LDL lowering can improve endothelial function and prevent coronary vasoconstriction (20).

In this study, a significant reduction in ischemia after 12 months is noted in the lovastatin treated group versus control group. This can probably be attributed to normalization of endo-

Table 4. Parameters for ischemia in patients with complete AECG data

Variables	Group 1 (n=44)		Group 2 (n=39)	
	Baseline	12 months	Baseline	12 months
Total number of episodes with ST segment depression, n/24 h	3.91±0.97	2.64±0.7*	3.85±1.02	3.79±0.84
Number of silent ischemia episodes, n/24 h	2.84±0.69	1.64±0.7*	2.76±0.63	2.69±0.83
Number of episodes with chest pain, n/24 h	1.81±0.61	1.47±0.6*	1.51±0.33	1.64±0.42
Total duration of episodes with ST segment depression, min/24 h	17.8±5.1	10.9±3.7*	18.1±6.3	18.3±7.1
Duration of silent ischemia episodes, min/24 h	12.31±2.1	7.85±2.13*	12.47±2.6	11.78±2.1
Duration of episodes with chest pain, min/24 h	3.94±1.13	2.67±0.94*	3.72±1.13	3.81±1.05
Maximum ST segment depression, mm	1.37±0.55	1.12±0.43*	1.25±0.49	1.30±0.31

Values are expressed as mean±SD
Unpaired and paired Student's t tests: * - p<0.05 as compared with baseline
AECG - ambulatory electrocardiography

thelial function (21). On the other hand, it is more likely that the reduction of myocardial ischemia was not solely due to LDL lowering. Recent studies indicate that statins among many other effects are able to modulate inflammation in the vessel wall and enhance neovascularization (22).

Antiischemic effect of lovastatin treatment may be attributed to complex influence of statins on process of coronary atherogenesis, endothelial function, stabilization of plaques and anti-inflammatory, anti-thrombotic, and anti-arrhythmic properties. These multifactorial effects of statins in aggregate may lead to reduction of myocardial ischemia.

Therefore, the treatment with lovastatin in addition to conventional antiaggregant and antianginal treatment of patients with CAD and dyslipidemia had improved myocardial remodeling. It was manifested in increase of the LV EF and unchanged the LV mass.

The antiischemic effect of lovastatin, which has been shown in increased exercise tolerance during bicycle exercise test, shortened ischemic episodes during 24-hour ECG monitoring, defines beneficial clinical influence of statin in CAD.

Study limitations

There are further limitations in our study: lack of angiography confirmation of CAD diagnosis, small number of patients. Moreover, patients from the control group did not receive hypolipidemic drugs, they kept hypolipidemic diet only accordingly to NCEP recommendations (6). Other studies with larger number of patients including evaluation of the effects of lovastatin on wall motion abnormalities are required in future.

Conclusion

The results of present study demonstrate that one-year therapy with lovastatin can improve the LV EF and decrease myocardial ischemia in patients with CAD and dyslipidemia. We hope that our findings will pave the way for additional large-scale clinical trials to evaluate the benefits of statins in patients with CAD.

Conflict of interest: None declared.

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