

## Comparing the effect of lovastatin and exercise on serum lipid profile in hyperlipidaemic patients

Taghadosi M<sup>1</sup>, Fath-Gharib B.J<sup>2</sup>, Piroozmand A<sup>3\*</sup>

<sup>1</sup>Departments of Medical-Surgical Nursing, <sup>2</sup>Medical Student, <sup>3</sup>Microbiology, Kashan University of Medical Sciences, Kashan, Iran.

\*Corresponding author: apiroozmand@gmail.com

Received: 13.09.12; Accepted: 28.12.12

### ABSTRACT

**Background:** Hyperlipidaemic is a risk factor of cardiovascular diseases. Recently, statins, life style modification and diet have been used to treat hyperlipidaemia. **Aim:** The present study was performed to evaluate the effect of lovastatin and exercise on hyperlipidaemic patients. **Methods:** This double-blind randomized clinical trial was performed on 80 patients over 30 years old, whose lipid profile was HDL-C  $\leq 35$  mg/dl, LDL-C  $\geq 160$  mg/dl, triglyceride  $\geq 200$  mg/dl, and cholesterol  $\geq 200$ . At first, 96 hyperlipidemic patients were included in this study, 7 out of them were excluded because of HTN (hypertension) and HLP (hyperlipidaemia) and 9 due to diabetes. The patients were randomly divided into two groups: the first group took lovastatin 40 mg daily, the second group was instructed to walk 35 minutes a day, 3 days a week. After 6 weeks trial, data were analyzed using t-test, Wilcoxon signed sample test, Kolomogorou-Smirnov test, Mann-Whitney test, and Leveus test. **Results:** The average age was  $55.18 \pm 9.9$ . 59 out of 80 (73.7%) were men and 21 were women (26.3%). The average age of group 1 (with lovastin) was  $55.12 \pm 8.4$  years and in group 2 (exercise) was  $55.35 \pm 9.2$ . The average decrease in TG level in lovastatin treated (I) and subjected to exercise (II) groups was 21.4 mg/dl and 20.5 mg/dl ( $P < 0.2$ ) respectively. Cholesterol decrease in two groups was  $41.3 \pm 44.3$  mg/dl and  $1.57 \pm 41.8$  mg/dl ( $P < 0.001$ ) respectively. The average decrease in LDL level in I and II groups was  $35.82 \pm 34.1$  and  $8.55 \pm 28.1$  ( $P < 0.001$ ), whereas, an average increase was shown in HCL level:  $5.45 \pm 14.4$  mg/dl and  $0.4 \pm 12.3$  mg/dl ( $P$ -value = 0.09) respectively. **Conclusion:** The results showed that exercise could reduce LDL, but lovastatin can reduce total cholesterol, TG and can increase HDL. Therefore in the management of hyperlipidaemia, exercise should be combined with lovastatin therapy to achieve a better outcome.

**Keywords:** Hyperlipidaemia, lovastatin, exercise, HDL, LDL, triglyceride

### INTRODUCTION

One of the most important risk factors of coronary artery diseases is hyperlipidaemia, which is the trigger of arteries closure process (atherosclerosis). This is why focus should be on blood lipid control especially LDL-C.<sup>[1-10]</sup> Increase in blood level of cholesterol and triglycerides (TG) is one of the most prevalent problems with which a

physician faces daily.<sup>[1]</sup> It might be hereditary, primary or secondary to other disorders and disease.<sup>[2,11]</sup> More than  $10^5$ - $10^6$  Americans have blood cholesterol higher than 200 mg/dl.<sup>[3]</sup> People whose lipid levels are 10% higher than normal are assumed hyperlipidaemic. In a review study, it was shown that 25-40% decrease in LDL-C can reduce coronary heart disease (CHD) risk up to 35% and there is a direct relation between decrease in LDL-C and reduced risk of

CHD.<sup>[12]</sup> Considering all risk factors of CHD, laboratory results show that controlling blood lipids especially LDL-C can reduce ischemic events.<sup>[13-15]</sup> There is a reverse relation between HDL and coronary artery diseases. An increase in HDL is accompanied by decrease in CHD mortality. HDL-C lower than 40mg/dl shows high risk of CHD and HDL-C more than 60 mg/dl has a negative risk in proportion to CHD. Each 1 mg/dl increase in HDL is along with 2% (men) to 3% (women) decrease in CHD risk and a decrease of 3.7% (men) to 4.7 (women) in mortality due to CHD.<sup>[16-18]</sup> Results of new studies have shown that using medications especially statins can decrease serum level of LDL-C and then CHD and patients mortality.<sup>[19,20]</sup>

Some drugs are desirable choices for treatment because of high serum level, high tolerance, anti-lipid trait and simplicity in administration. Lovastatin is a statin which is frequently used in hyperlipidaemia treatment.<sup>[18,21-22]</sup> Franceschini<sup>[23]</sup> showed that simvastatin 40mg per day reduces LDL-C but does not change HDL-C.<sup>[24]</sup> In a study in patients with hypercholesterolemia, simvastatin caused more increase in HDL than other anti-hyperlipidaemic drug.<sup>[23]</sup> Researches have shown that with exercise, in addition to decrease in LDL-C biochemically, profitable changes are created in LDL structure.<sup>[25-30]</sup>

Nieman<sup>[31]</sup> showed that exercise for 12 weeks did not reduce cholesterol level, but exercise produced remarkable improvement in LDL-C in comparison to medications.<sup>[32]</sup> In order to investigate the different treatment recommendations, the present study was done to compare the effect of lovastatin and exercise on hyperlipidemic patients in Kashan Shahid Beheshti Hospital.

## METHODOLOGY

A randomized clinical trial was conducted on out-patients in Kashan Shahid Beheshti Hospital in 2006. The patients older than 30 who had TG>200, LDL-C≥160 or HDL≤35 were included in the study. The blood glucose and lipid level were measured. Then the participants who had only hyperlipidaemia and without other known diseases (including diabetes, previous hyperlipidaemia, HTN, history of myocardial infarction, regular exercise program) and were able to do exercise (based on the cardiologist examination), and the ones who

did not have severe hyperlipidaemia (TG>400) were requested to participate in the study. After 12 hours of fasting, 5 cc blood samples were taken for TG, LDL, HDL and cholesterol. To measure cholesterol and HDL, calimetry enzyme method with CHOD-PAP photometry was used. LDL-C level was calculated according to the following formula:

$$\text{LDL} = \text{total chol} - (\text{HDL} + \text{TG}/5).$$

96 people were studied. 16 out of them were excluded; 9 because of severe HLP (hyperlipidaemia) and HTN (hypertension) and 7 because of diabetes. 80 patients were randomly divided into two groups. The first group had lovastatin 40 mg daily and the second walked for 35 minutes daily 3 times a week. Both groups received similar education on diet and exercise. After 6 weeks, all came to hospital to give 5 cc fasting blood samples. TG, LDL, HDL and cholesterol were measured with same kits used at the beginning.

## Statistical analysis

T-test, Mann-Whitney, Kolomogorou-Smirnov, Wilcoxon Signed Rank Test were used to analyze the differences in the two groups.

## RESULTS

At the end of the study, 80 patients (40 in lovastatin group and 40 in exercise group) completed this process. Out of them, 59 women and 21 men participated in this study. Average age in case and control group was 55.12±8.5 and 55.35±9.2 respectively. Lovastatin reduced cholesterol, TG, and LDL significantly ( $P<0.001$ ). Also exercise decreased LDL from 145.6 mg/dl to 137.1. This difference was significant ( $P<0.001$ ). The reduction in TG, cholesterol was not significant. Exercise did not show significant increase in serum HDL (Table 1).

Exercise as well as lovastatin reduced TG, but the difference was not significant. Lovastatin reduced LDL 4 times more than exercise ( $P<0.001$ ). HDL was increased in lovastatin users; although the difference was not significant (Table 2).

## DISCUSSION

Results showed that lovastatin could reduce cholesterol, TG, LDL and increase HDL significantly whereas exercise revealed

significant effect only on LDL. Studies done by other researchers show that lovastatin 20mg /day for 10 weeks reduces TG as much as 10%. There is a 10% reduction in

LDL and 15% increase in HDL with exercise.<sup>[33]</sup> In a study in US, total cholesterol was reduced by 14-28% due to lovastatin.<sup>[34]</sup>

Table 1: Serum lipids before and after treatment with lovastatin and exercise in patients with hyperlipidaemia

Treatment type	Serum Lipids	Statistical indices n=40		P-value
		Before treatment X±SD	After treatment X±SD	
Lovastatin	HDL	42.25±1.12	47.7±12.6	0.021
Exercise		45.22±12.5	45.62±10.8	0.839
Lovastatin	LDL	164.37±50.2	128.55±41.1	<0.001
Exercise		145.65±41.4	137.1±36.2	0.001
Lovastatin	Cholesterol	255.92±56.1	214.6±45.3	0.001
Exercise		225.32±43.6	223.75±45.8	0.813
Lovastatin	TG	216.9±112.1	195.42±87.6	0.001
Exercise		200.97±82.8	180.47±124.1	0.062

Table 2: Changes in serum lipids after treatment in patients with hyperlipidaemia

Intervention	Exercise	Lovastatin	P-value
Lipid	X±SD N=40	X±SD N=40	
TG	20.5±122.6	21.47±97.2	0.2
Cholesterol	1.57±41.8	41.3±44.3	<0.001
LDL	8.55±28.1	35.82±34.1	<0.001
HDL	0.4±12.3	5.45±14.4	0.09

In another study, it was shown that lovastatin 40mg/day for 3 weeks reduced cholesterol by 23%.<sup>[35]</sup> As we may know, among non-medical treatments, the simplest and the most effective recommendation is regular exercise.<sup>[13]</sup> Hata showed that walking can reduce TG to 10mg/dl.<sup>[30]</sup> 90% of people with

TG>250 mg/dl have small and dense LDL-C particles. These small particles are more dangerous than bigger ones.<sup>[18]</sup> It is believed TG>200 mg/dl is a basis for the pathogenesis of atherosclerosis, but there is still some suspicion.<sup>[17,36]</sup>

In order to compare the effects of simvastatin and fenofibrate on HDL biomarker, it was shown that simvastatin 40mg does not change serum HDL.<sup>[23]</sup> In other studies in patients with hypercholesterolemia, simvastatin could cause more increase in HDL in comparison with other anti-hyperlipidemic drugs.<sup>[24,36,23]</sup> Studies show that aerobic activities increase serum HDL by 9-15%.<sup>[24,26,27,30]</sup>

The results of present study also showed that lovastatin can reduce serum cholesterol significantly but exercise does not make any change in serum cholesterol. Also the average decrease in lovastatin group was 26 times more than the exercise group. The previous studies showed 14-28% decrease in total cholesterol following lovastatin treatment.<sup>[31,34-35]</sup> The results of another study showed that lovastatin could reduce LDL significantly in comparison to exercise. The decrease of LDL in lovastatin group was 4.2 times.

To offer the new methods of screening for hyperlipidaemic patients and prevention of atherosclerosis with respect to the proven effect of LDL-C in CAD, there is a remarkable emphasis on measuring the density of this lipoprotein in plasma; its amount is different for everyone based on the number of risk factors.<sup>[1,8]</sup> Recent guide for the prevention of CHD shows that LDL decrease is a primary goal and statin therapy can be used as the first medical therapy; because these drugs have important effects on LDL levels and CHD.<sup>[23]</sup> A co-working group of interventional studies in cholesterol treatment in a meta-analysis on 90,000 persons under treatment of statin showed that a decrease of 39% in LDL-C was accompanied by 21% decrease in cardiovascular events.<sup>[37]</sup> Although optimal goal for LDL-C level in patients with known coronary heart disease (CHD) has been less than 100mg/dl, there are findings which showed that achieving even lower LDL-C levels has a profitable effect with statin therapy.<sup>[13]</sup> Aerobic exercise reduces LDL-C between 10-18%.<sup>[26,28-29]</sup> Exercise influences platelets functions and oxidized LDL, and as a result help reduce heart disease risk factors. The researches have shown that exercise both decreases LDL and beneficially changes its structure.<sup>[33,38]</sup> The results of the most of the studies show that exercise is not able like lovastatin to reduce all serum lipid indices alone and each one can be used in an appropriate place.

## CONCLUSION

The results showed that 35 minutes exercise daily, 3 times a week for 6 weeks can reduce LDL and TG, and lovastatin 40mg/day for 6 weeks can reduce total cholesterol and LDL and increase serum HDL. So we can use the former results (exercise) in proper treatment of HLP.

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doi: <http://dx.doi.org/10.14194/ijmbr.214>

**How to cite this article:** Taghadosi M, Fath-Gharib B.J, Piroozmand A. Comparing the effect of lovastatin and exercise on serum lipid profile in hyperlipidaemic patients. *Int J Med Biomed Res* 2013;2(1):18-22

**Conflict of Interest:** None declared