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The effect of herbal medicine Lowerchol (Cyclanthera pedata and phytosterols extract) on the lipid profile and blood pressure in patients with dyslipidemia

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ABSTRACT

Introduction: *Changes in plasma lipid profile and hypertension are the risk factors for acquired heart disease that can be controlled to reduce the risk of heart attack and developing heart disease. The fundamental mechanism controlling these factors is the use of drugs such as cholesterol and LDL levels, blood fats and blood pressure lowers. This study aimed to investigate the effect of herbal medicine Lowerchol on the lipid profile, blood pressure and enzymes AST and ALT in dyslipidemia patients with a history of cholesterol-lowering drug, atorvastatin, and individuals who consumed the cholesterol level lowering drugs for first time.*

Material & Method: *In this clinical trial, 100 patients with dyslipidemia and hypertension were selected. Patients were asked to take the capsule containing 888 mg of phytosterols and 500 mg of Cyclanthera pedata fruit extract after their meals, 2 times daily for 2 months.*

Results: *Compare lipid profile and enzyme concentration of people who had a history of atorvastatin showed no significant changes in ALT, AST, and HDL and triglyceride enzyme levels, but after taking Lowerchol, the amount of cholesterol at a rate of %10.04 (P<0.0001) and LDL at a rate of %14.37 (P≤0.0008) increased. In contrast, in people who had no lipid-lowering drug history showed a significant decrease of enzymes ALT and AST, and decrease in cholesterol level was %10.66 (P≤0.0018) and in triglyceride was%17.49 (P=0.0014). However, it was not seen any significant changes in LDL and HDL enzyme levels. All the patients undergoing treatment of Lowerchol showed decrease in their blood pressure as much as 2 to 3 unit and its stability. According to the mentioned results, it is not suggested replacement of Lowerchol for common cholesterol endogenous lowering drugs. The drug should be taken as a supplement of lowering cholesterol synthesis drugs or be prescribed as a medicine of lowering blood pressure.*

Keywords*: Lowerchol, atorvastatin, phytosterols, dyslipidemia, hypertension, cardiovascular disease*

INTRODUCTION

One of the major causes of heart disease and brain stroke is considered dyslipidemia. Dyslipidemia is an increase in total cholesterol or low-density lipoproteins (LDL) and decrease in high-density lipoprotein (HDL) [1,2]. The prevalence of dyslipidemia is so high and a study in 2000 indicated almost %25 of adults in America have a total cholesterol of 239.4 mg/dl. As a result of getting high level of cholesterol through diet can augment the level of LDL in serum[3]. There is a direct correlation between serum lipid and other factors with cardiovascular disease, so that a reduction of%1 in the blood cholesterol level has

demonstrated %2 reduction in the incidence of cardiovascular diseases[4]. In addition to dyslipidemia, the high prevalence of blood pressure and its close relevance with cardiovascular disease, blood pressure is considered as one of the most important public health problems in many countries [5,6]. In spite of easily diagnosis and treatment of high blood pressure, it is very common and often asymptomatic and if it is not controlled or managed properly, it can lead to deadly complications [7]. Pharmacological interventions for the treatment of dyslipidemia and hypertension is regarded useful to deal with heart disease patients. Thus, plasma lipid profile regulation by a range of natural drug materials has been studied. Among these compounds, one can be noted phytosterols which is plentiful in many herbal ingredients [8,9]. The main effect of these compounds in lowering cholesterol, happens by competing with cholesterol absorption in enterocytes [10]. Absorption takes place by the NPC1L1 receptor through a simple transfer or guided (facilitated) diffusion. The role of NPC1L1 membrane receptor (transporter) has been more identified in recent years. The NPC1L1 transporter blockage can reduce %50 of cholesterol and phytosterols uptake [11,12]. After absorption by enterocytes, a large amount of plant sterols depending on the length of the chain are secreted into the intestinal lumen through ABCG5 and ABCG8 transporter [13-15]. As a result, the blood phytosterols level is about %0.5 of blood cholesterol, which reflects the low efficiency of intestinal absorption of plant sterols as mentioned above, plant sterols compete with cholesterol absorption and lead to a decrease in plasma cholesterol.

Although statin drugs are used for the treatment of dyslipidemia and prevention of primary or secondary cardiovascular diseases abundantly, it is pointed to their side effects such as myopathy and hepatopathy and their limitation usage to some people, including pregnant and lactating women, and patients with liver failure [16,17]. Additionally, according to the manufacturing of herbal medicines containing phytosterols including Lowerchol for the treatment of dyslipidemia and blood pressure, we aim to evaluate the efficacy of Lowerchol (Cyclanthera pedata extract and phytosterols) on the lipid profile and blood pressure as well as serum levels of AST and ALT in patients with dyslipidemia and hypertension to be introduced or confirmed its effectiveness as a viable alternative for drugs statin.

METHODS

Patients

100 patients with the age range of 30 to 70 who had dyslipidemia and hypertension were selected for this clinical trial. Two days before the beginning of the study, the serum cholesterol, triglycerides, LDL, HDL and AST and ALT enzyme levels were measured (after 12 hours of fasting). The main criteria for the patient selection were the high concentration of at least one of the lipid profile components and systolic blood pressure higher than 12 and body index between 18 and 37. If patients were taking

statin drugs before the study, they were asked to take Lowerchol instead of statin. Thus, selected patients were divided into two groups: patients with a history of atorvastatin (20 mg) and who had no history of any cholesterol-lowering drug.

Study Design

Patients were asked to take the capsule containing 888 mg of phytosterols and 500 mg of Cyclanthera pedata fruit extract after their meals (breakfast and dinner), 2 times daily for 2 months. They were followed up for side effects and blood pressure during these 2 months. Finally, patients who took Lowerchol drug completely for two months, were called to be measured (equipment: Hitachi 912 auto analyzer) the concentration of serum lipid profile components (LDL, HDL, TG, cholesterol) and AST and ALT enzymes by taking 5ml of blood from the patient's blood in clinical laboratory of Vali-Asr and Imam Sajad Hospitals of Tehran University of Medical Sciences. Serum was separated from whole blood through centrifugation for 15 min at 1500 rpm.

Statistical Analyses

For comparing, the results and detecting of probable significant differences between two groups, patients with a history of atorvastatin (20 mg) drug and who had no history of any cholesterol-lowering drug, T-test and ANOVA were done. $P<0.05$ was regarded as a significant difference.

RESULTS

From total of 100, 20 patient's dues to various reasons, such as a sharp drop in blood pressure, headache, dizziness, palpitations and bloating after a week, discontinued taking the drug and 80 patients fully participated in this clinical trial. The mean age of these patients was 54.46±12.14 (years), %54.46 were male and %45.54 were women. The mean BMI was 30±2.3.

57 patients had the history of atorvastatin (20 mg) with the mean age was 57.61±9.8 (years). 23 patients had no history of atorvastatin with the mean age was 40.95± 7.36 (years). The model of lipids and enzymes AST and ALT change after 8 weeks of taking drug Lowerchol is reported in Table-1.

Table 1: change pattern of variables (indexes) before and after taking Lowerchol in all patients

Variable (indexes)	Before taking Lowerchol (Mean±SD)	After taking Lowerchol (Mean±SD)	Difference between before & after	P value
AST U/L	19.05 ± 5.33	19.09 ± 5.53	0.04+	0.952
ALT U/L	20.88 ± 6.87	21.67 ± 8.47	0.79+	0.826
Cholesterol mg/dl	181.2 ± 33.57	199.4 ± 41.56	18.2+	≤0.0001*
TG mg/dl	148.5 ± 54.36	144.4 ± 51.23	4.1-	0.074
LDL mg/dl	114.4 ± 34.15	130.8 ± 34.49	16.44+	0.0008*
HDL mg/dl	46.9 ± 10.4	43.69 ± 8.13	2.73-	0.0011*

Note: *p≤0.05 is significant

According to the results shown in Table-1, there was no significant difference between before and after treatment by Lowerchol for ALT and AST enzyme levels (p>0.05). The amount of cholesterol at a rate of %10.04 (P<0.0001) and LDL at a rate of %14.37 (P≤0.0008) increased. The reduction of triglyceride by %2.7 was no significant (P=0.074) and the amount of HDL also fell by %5.8 (P≤0.0011).

In contrast, patients who had no history of atorvastatin showed a significant decrease in the most lipid profile after taking Lowerchol reported in Table 2. Based on the results listed in Table 2, in this group of patients, there was a reduction in AST

%9.67 (P=0.013) and ALT %5.6 (P= 0.0021) after taking Lowerchol. Additionally, reduction in cholesterol %10.66 (p≤0.0018) and triglycerides %17.49 (P = 0.0014) were not significant but considerable changes in LDL and HDL levels were observed.

Table 2: change pattern of variables (indexes) before and after taking Lowerchol in patient group with no history of atorvastatin

Variable (indexes)	Before taking Lowerchol (Mean±SD)	After taking Lowerchol (Mean±SD)	Difference between before & after	P value
AST U/L	24.8 ± 6.17	22.74 ± 4.09	2.4-	0.0134
ALT U/L	26.41 ± 8.88	24.91 ± 7.69	1.5-	0.0021*
Cholesterol mg/dl	225.1 ± 55.7	201.5 ± 28.91	24-	0.0018*
TG mg/dl	226.9 ± 108.9	187.2 ± 59.08	39.7-	0.0014*
LDL mg/dl	134.0 ± 26.8	139.2 ± 22.19	5+	0.184
HDL mg/dl	42.96 ± 6.9	40.17 ± 8.06	2.78-	0.146
*p≤0.05 is significant				

10 patients with the history of atorvastatin (6 women and 4 males) with the mean age of 61.63±9.59, the lipid profile increased so that they complained from heart beating at the end of taking Lowerchol period. Detailed information about the variables in this group are shown in Table 3. In this group, there was no significant change in the amount of AST, ALT and HDL levels while considerable increase in cholesterol, triglyceride and LDL, %31.5 (P≤0.0001), %20.22 (P=0.028) and %38.8 (P=0.0069), respectively.

Table 3: change pattern of variables (indexes) before and after taking Lowerchol in patient group with the history of atorvastatin

Variable (indexes)	Before taking Lowerchol (Mean±SD)	After taking Lowerchol (Mean±SD)	Difference between before & after	P value
AST U/L	18.88 ± 5.85	20.56 ± 10.38	1.72+	0.630
ALT U/L	20.44 ± 6.75	19.75 ± 7.44	0.69-	0.534
Cholesterol mg/dl	173.3 ± 28.83	227.2 ± 49.20	53.81+	≤0.0001*
TG mg/dl	141.56 ± 59.45	170.2 ± 97	28.63+	0.028*
LDL mg/dl	102.8 ± 38.0	142.8 ± 48.61	39.94+	0.0069*
HDL mg/dl	54.11 ± 11.4	56.0 ± 32.7	1.81	8.265
*p≤0.05 is significant				

DISCUSSION

Recent surveys have shown that phytosterols along with a healthy diet can reduce blood cholesterol and LDL [8]. Meta-analyses have demonstrated that daily consumption of 2gr of phytosterols in the diet can reduce cholesterol levels and LDL to %10. However, the effect of phytosterols packaged in capsule form has been less studied [18,19]. In addition, previous studies have often been done as phytosterols effects on lipid profile in patients with hypercholesterolemia or along with the use of a statin or in studies of placebo-controlled [20].

In this study, the effect of Lowerchol (capsule contains extract Cyclanthera pedata and phytosterols) in patients who had a history of atorvastatin (20 mg) and they were asked to use Lowerchol instead of atorvastatin and the patients who first used cholesterol-lowering drugs were investigated.

Phytosterols show low oil solvability state and inadequate solubilization of the phytosterols has indicated as a probable explanation of ineffectiveness of free phytosterols capsules [21,22]. In order to make them more fat soluble for usage in fatty

diet, Phytosterols are generally esterified. Adding both sterol and stanol esters into various food products and encapsulated form have shown cholesterol lowering effects [23,24]. Studies have recommended that phytosterols should be dissolved properly and hydrolyzed rapidly in the duodenum for interaction with cholesterol in the micellarization. It is necessary to obtain optimal cholesterol lowering results [25,26]

In some studies, the effect of capsulated phytosterols in the form of placebo-controlled, have reported a reduction of %5-9 in the LDL-cholesterol level [27-29]. while other several studies have not reported a considerable reduction in LDL-cholesterol. The latter one is consistent with our findings since in a group with a history of atorvastatin (20 mg) consumption cholesterol and LDL level did not decrease (we expected to be unchanged or increased insignificantly cholesterol and LDL) while cholesterol (to %10.04) and LDL levels (to %14.37) increased significantly. In this group of patients, the HDL also fell by %5.8.

However, the results were different between the patient group without a history of atorvastatin (who their mean age was 17 years younger than other group) and the group with the history of taking atorvastatin. Although we found no significant decrease in LDL level, dramatic changes in cholesterol and triglyceride levels were observed. Our findings showed in this group, a reduction in cholesterol level by%10.66 and triglycerides by %17.49. While in this group, the LDL rose by %3.7, this increase was not statistically significant. On the other hand, because of the group showed higher levels of AST and ALT enzymes, after taking Lowerchol, the level of AST by %9.67and ALT by %5.6 declined.

Due to the different results that occurred in the study groups and the age difference between the two groups, it is possible the effect of Lowerchol is associated with the age. Additionally, the consent by the younger patients was evident after taking Lowerchol. Lowerchol capsules containing 500 milligrams of fruit juice, Cyclanthera pedata, in addition to phytosterols that reduce blood pressure, according to previous studies. During this study, the majority of applicants also showed a decline and stabilization in the blood pressure so that several patients left the study due to the large drop in blood pressure that prevents the daily chores.

CONCLUSION

In general, the results can be indicated that Lowerchol cannot be a suitable replace for statins especially in the elderly patients (older than 50 years). It should be taken along with statin drugs as a supplement to the endogenous cholesterol synthesis and absorption of exogenous cholesterol be controlled in patients with hypercholesterolemia.

For people who possess much higher concentrations of the lipid profile components, and patients younger than 50 years who are consent of their hypertension, Lowerchol can be taken as a cholesterol-lowering drug. In addition, Lowerchol can replace synthetic drugs that reduce blood pressure in people suffering from hyper-tension due to the significant reduction in blood pressure of the participants in this clinical trial.

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