



PRIMARY HYPERLIPIDEMIC PATIENTS; DIFFERENCES IN LIPID PROFILE WITH ORIGINAL PRODUCT OF SIMVASTATIN AND HERBAL PRODUCT OF ALLIUM SATIVUM

Dr. Naveed Ali Siddiqui¹, Muhammad Asadullah²

1. MBBS, MPhil, PhD
Assistant Professor,
Department of Biochemistry
United Medical & Dental College,
Karachi, Pakistan
2. United Medical & Dental College,
Karachi, Pakistan

Correspondence Address:

Dr. Naveed Ali Siddiqui
Flat No. A-407, Bisma Residency,
Block 13, Near Habib University,
Gulistan-e-Johar Karachi.
naveed_sddq@yahoo.com

Article received on:

11/01/2016

Accepted for publication:

29/03/2016

Received after proof reading:

04/05/2016

ABSTRACT: The ratio of cardiovascular disease (CVD) in Pakistan is high as compare to western world and is one of the chief reasons of disability around the world. When CVD is diagnosed, following preventive measures should be taken which include regular exercise, proper diet, weight control and lipid reducing drugs to overcome the risk of morbidity or mortality. Primary hyperlipidemia is common factors for the progression and development of atherosclerosis and coronary heart disease. This study was designed to evaluate the effects of simvastatin and allium sativum (garlic) on lipid profile and to compare the lipid decreasing efficacy of simvastatin and herbal product of allium sativum in primary hyperlipidemic patients. **Objectives:** To evaluate the changes in lipid profile in patients with primary hyperlipidemia using original product of simvastatin and herbal product of the allium sativum (garlic). **Study design:** Cross-sectional study. **Setting:** The study was conducted at Surgeon Munawar Memorial Hospital, Karachi in year 2013 -2014. **Material and Methods:** Total of 60 patients of 30-70 years of age with abnormal lipid profile was enrolled for this study after a written consent. The patients were divided into group I and II with primary hyperlipidemia. Patients of group 1 and II were orally treated with simvastatin (20 mg)/day and allium sativum (garlic) (300 mg/day) for 8 weeks. All patients were evaluated before and after treatment with product of simvastatin and herbal product of allium sativum. **Results:** In this study the cholesterol, triglyceride (TG), high density lipoprotein (HDL) and low density lipoprotein (LDL) were estimated in the serum of patients before and after treatment with Simvastatin (20 mg)/day and herbal product of allium sativum (garlic) (300 mg/day). It is observed in the present study that treatment with simvastatin significantly reduced the level of serum total cholesterol, triglycerides, LDL and increase serum HDL level. Allium sativum significantly reduces serum total cholesterol, serum LDL and increase serum HDL level in primary hyperlipidemic patients but there was no effect on triglyceride levels. **Conclusion:** We concluded that simvastatin significantly reduced the level of serum total cholesterol, triglycerides, LDL and increase serum HDL level and allium sativum significantly reduces serum total cholesterol, serum LDL and increase serum HDL level in primary hyperlipidemic patients but there was no effect on triglyceride levels.

Key words: Lipid profile, hyperlipidemia, herbal product, Allium sativum.

Article Citation: Siddiqui NA, Asadullah M. Primary hyperlipidemic patients; differences in lipid profile with original product of simvastatin and herbal product of allium sativum. Professional Med J 2016;23(5):564-570. DOI: 10.17957/TPMJ/16.3247

INTRODUCTION

Coronary heart disease is a leading cause of morbidity and mortality and high blood cholesterol is a major risk factor for coronary heart disease.^{1,2} Cardiovascular disease (CVD) is a primary reason of disability and premature transience throughout the threat to world wide and the number of patients of CVD is increasing gradually around the world.^{3,4} Among non-communicable diseases, CVD contributes a very huge proportion in Asian countries.⁵ The prevalence of cardiovascular heart disease

related mortality and morbidity was seemed to be increase in under developed countries. The development of atherosclerotic cardiovascular disease is an essential pathological process.⁶ In formation and progression of atherosclerosis, the major role plays by the inflammation of arteries and endothelial dysfunction. The progression and formation of atherosclerotic lesion is determined by various macro-vascular related diseases.⁷ Hyperlipidemia is an elevated level of fats in the blood stream. Primary hyperlipidemia caused by inherited gene defect and numerous

contributing factors. It is also a contributing factor for cardiovascular disease related morbidity and mortality and increased cholesterol level are linked to progression of macro-vascular disease throughout the world.⁸ Cholesterol is transported in the form of lipoproteins. Most of lipoproteins are VLDL, LDL, and HDL. Epidemiological researches have shown relation between increased concentration of lipid and proteins and mortality from macro-vascular disease.⁹

In patients with increased levels of total cholesterol or LDL cholesterol, or with risk of coronary artery disease, anti-lipidemic therapy should be initiated at an early stage.¹⁰ The drugs used in primary hyperlipidemia contain simvastatin. Simvastatin is butanoic acid 2, 2-dimethyl-, 1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)-ethyl]-1naphthalenylester. The empirical formula of simvastatin is C₂₅H₃₈O₅ and its molecular weight is a 418.57. Simvastatin is an insoluble in water, consist of crystalline powder and freely soluble in methanol, chloroform and ethanol. Simvastatin, like other statins, is an inhibitor of HMG-CoA (3-hydroxy-3-methylglutaryl-CoA) reductase—a rate limiting enzyme in the cholesterol-biosynthesis. Simvastatin, lovastatin, and pravastatin are all derivatives of a fungal compound and are described 'natural' statins. They all have been reported to decrease LDL-C, progression of coronary artery stenosis, cardiovascular mortality. Recently, synthetic statins have been introduced, and three of the class – Cerivastatin, Atorvastatin, and Fluvastatin are in clinical use.¹¹ Statins are more beneficial in their lipid decreasing effect than the other agents, which recommend that the statins would be more likely to significantly reduce mortality and clinical events.¹² Scandinavian Simvastatin survival study reported that all cause of coronary events and mortality were substantially decrease by the use of a statin in patients with coronary heart disease and increased lipid levels.¹³ The usage of plant based medicines is becoming a popular alternative management. The affiliation of atherosclerosis and hyperlipidemia and associated side effects with standard anti-dyslipidemic drugs has led to

extensive hunt for herbal compounds that safely in lipid profile. Various herbal products have been reported for their effects on various cardiovascular contributing factors such as dyslipidemia but few has given results to sufficient dosage required for maximum improvement in macro-vascular disease.¹⁴ *Allium sativum* is used in plant based herbal medicine for past few years. *Allium sativum* has been the focus of medical attention in last few centuries for beneficial effects on hyperlipidemia.¹⁵ *Allium sativum* can produce an antilipidemic role by prevention of lipid aggregation and other atherogenic manifestations at the vascular wall.¹⁶ *Allium sativum* consist of a number of organo-sulfur constituents. It is proved that allicin is the primary compound for cholesterol biosynthesis inhibition. Many clinical trials have observed that *Allium sativum* and its ingredients inhibit enzymes involved in fatty acid and cholesterol biosynthesis. Diallyl sulfide, diallyl disulfide, diallyl trisulfide, dipropyl trisulfide, and dipropyl sulfide (Lipid-soluble sulfur compounds) inhibit synthesis of cholesterol^[17]. *Allium sativum* and their constituents inhibiting human squalene monooxygenase and HMG-CoA reductase, a rate limiting enzymes involved in cholesterol biosynthesis.¹⁸

MATERIAL AND METHODS

Patients Selection

The population under study was representative of Pakistani population with primary hyperlipidemia. The study period consist of 8 weeks. Blood pressure, body weight and height of subjects were assessed. The patient answered the questionnaire on health complaints, smoking, social role, drug usage, family history and dietary pattern. Patients were asked to fill a consent form before starting the experiment. The initial inclusion criteria of the patient were 1) Age between old of either sex, 2) Patients with primary hyperlipidemia. The exclusion criteria were 1) Pregnancy or lactation, 2) Patients with liver diseases, 3) Patients with renal diseases. Detailed medical history and physical examination of all patients were carried out.

Study Design

Sixty patients were selected for the study. Patients of group 1 and II were orally treated with Simvastatin (20 mg)/day and Allium sativum (garlic) (300 mg/day) for 8 weeks. All patients were evaluated before and after treatment with product of Simvastatin and herbal product of Allium sativum. Serum lipid profile was done before and after the treatment. Patients were orally administered with original product of simvastatin and herbal product of Allium sativum (300 mg/day) for 8 weeks. After 8 weeks, blood samples were collected again for the estimation of lipid profile.

Collection of Samples

The blood sample was drawn using 5ml syringe and centrifuged at 3000 rpm for 10 minutes. Serum was separated and collected in clean and dry Eppendorfs and was stored at -70 C till further analysis.

Biochemical Analysis

The serum levels of total cholesterol, TG, and HDL were determined enzymatically on microlab using commercially available (Randox laboratories limited, UK) kits. LDL was calculated using Friedwald formula.

Statistical Analysis

The data was analyzed statistically using SPSS version-11.

RESULTS

In the present study 60 patients were investigated with primary hyperlipidemia. The individual of group 1 consist of 30 patients were orally administered with original product of Simvastatin (20mg)/day for 8 weeks and group 11 consist of other 30 patients were orally administered with herbal product of Allium sativum (300mg)/day for 8 weeks. In group 1, table-I and figure-1 represents the variation of serum lipids including Cholesterol, High density lipoprotein (HDL), Triglyceride (TG) and Low density lipoprotein (LDL) in primary hyperlipidemia before and after 8 weeks of treatment with original product of Simvastatin. Patients who have been given

Simvastatin at a dose of 20mg/day showed a reduction in total cholesterol from baseline value of 210.46 to \pm 6.33 mg/dl to 181.80 to \pm 3.24 mg/dl at week 8. This decreases was found to be statistically highly significant ($p < 0.005$) when compared from before and after treatment. Patients who have been given Simvastatin at a dose of 20mg/day showed a reduction in serum triglyceride from baseline value of 160.83 to \pm 3.24 mg/dl to 136.10 to \pm 2.36 mg/dl at week 8. This decreases was found to be statistically highly significant ($p < 0.005$) when compared from before and after treatment. Patients who have been given simvastatin at a dose of 20mg/day showed an increase in serum high density lipoprotein (HDL) from baseline value of 38.23 to \pm 0.40 mg/dl to 39.53 to \pm 0.19 mg/dl at week 8. This increases was found to be statistically highly significant ($p < 0.005$) when compared from before and after treatment. Patients who have been given simvastatin at a dose of 20mg/day showed a reduction in serum low density lipoprotein (LDL) from baseline value of 138.80 to \pm 6.74 mg/dl to 113.76 to \pm 3.38 mg/dl at week 8. This decreases was found to be statistically highly significant ($p < 0.005$) when compared from before and after treatment.

In group 2 table-I and figure-2 represents the variation of serum lipids including Cholesterol, High density lipoprotein (HDL), Triglyceride (TG) and Low density lipoprotein (LDL) in primary hyperlipidemia before and after 8 weeks of treatment with herbal product of Allium sativum (300mg)/day. Patients who have been given Allium sativum at a dose of 300mg/day showed a reduction in total cholesterol from baseline value of 222.00 to \pm 5.23 mg/dl to 199.06 to \pm 3.16 mg/dl at week 8. This decreases was found to be statistically significant ($p < 0.05$) when compared from before and after treatment. Patients who have been given Allium sativum at a dose of 300mg/day showed baseline value of serum triglyceride from 165.53 to \pm 3.63 mg/dl to 164.83 to \pm 3.54 mg/dl at week 8. This was not significant when compared from before and after treatment. Patients who have been given Allium sativum at a dose of 300mg/day showed an

increase in serum high density lipoprotein (HDL) from baseline value of 36.40 to \pm 0.32 mg/dl to 38.00 to \pm 0.26 mg/dl at week 8. This increases was found to be statistically significant ($p < 0.05$) when compared from before and after treatment. Patients who have been given Allium sativum at a dose of 300mg/day showed a reduction in serum low density lipoprotein (LDL) from baseline value of 136.03 to \pm 2.00 mg/dl to 113.43 to \pm 1.28 mg/dl at week 8. This decreases was found to be statistically significant ($p < 0.05$) when compared from before and after treatment.

	Cholesterol mg/dl	TG mg/dl	HDL mg/dl	LDL mg/dl
Before treatment	210.46 \pm 6.33	160.83 \pm 3.24	38.23 \pm 0.40	138.8 \pm 6.74
After treatment	181.80** \pm 3.24	136.10** \pm 2.36	39.53** \pm 0.19	113.76** \pm 3.38

Table-I. Effects of Simvastatin on serum lipid profile in Primary hyperlipidemic patients

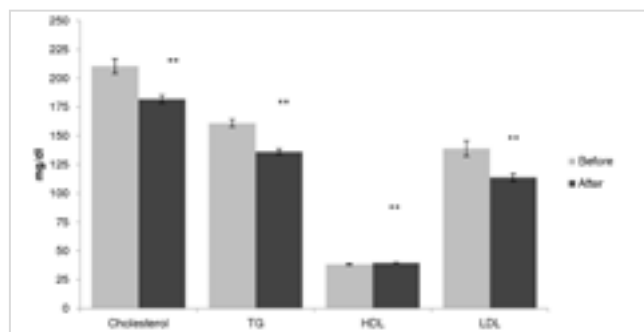


Figure-1. Effects of Simvastatin on serum lipid profile in Primary hyperlipidemic patients

Values are Mean \pm S.E (n=30). ** $p < 0.005$ significant difference by t-test as compared to respective control.

	Cholesterol mg/dl	TG mg/dl	HDL mg/dl	LDL mg/dl
Before treatment	222.00 \pm 5.23	165.53 \pm 3.63	36.40 \pm 0.32	136.03 \pm 2.00
After treatment	199.06* \pm 3.16	164.83 \pm 3.54	38.00* \pm 0.26	113.43* \pm 1.28

Table-II. Effects of Allium Sativum on lipid profile in Primary hyperlipidemic patients

Values are Mean \pm S.E (n=30). * $p < 0.05$ significant difference by t-test as compared to respective control.

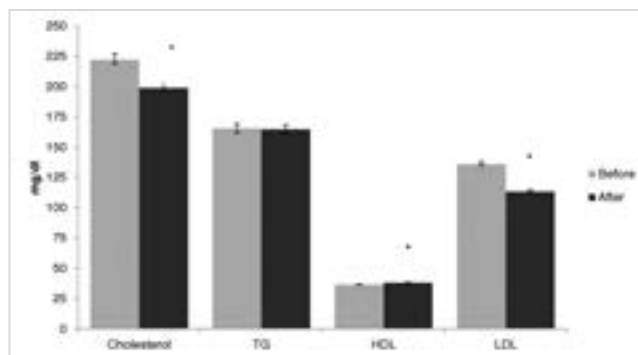


Figure-2. Effects of Allium Sativum on serum lipid profile in primary hyperlipidemic patients

Values are Mean \pm S.E (n=30). * $p < 0.05$ significant difference by t-test as compared to before treatment.

DISCUSSION

Diagnosing and managing hyperlipidemia can prevent cardiovascular heart disease is a common activity for family physicians. Formation of atherogenic dyslipidemia is an essential risk factor for the progression of cardiovascular disease. Many clinical studies are reported that risk of developing macro-vascular disease in South Asians countries is increased as compared with other countries. Macro-vascular disease in population of Asia is found to be increased in the worldwide and is supposed to be the major reason of death in the Pakistan. In the urbanized life style and higher socio-economic areas, higher incidence of CVD has been reported as compared to lower socio-economic areas. Hyperlipidemia develops macro-vascular disease has a major public health issue in Pakistan.¹⁹ Allium Sativum and Simvastatin are lipid lowering agents. HMG-CoA reductase inhibitors commonly are effective in primary as well as secondary prevention of coronary disease. Therefore, these agents are used as the first choice for hypercholesterolemia in this subset of the population, especially simvastatin and atrovastatin. Simvastatin is an inhibitor of HMG-CoA reductase in the cholesterol synthesis.²⁰ As none of the anti-hyperlipidemic agents are devoid of adverse effects, harmful efficient and cost effective agent for managing hyperlipidemia. Allium sativum based herbal medicine has proved to decrease many disorders.²¹ According to low income structure

in Pakistan, it appears to analyze indigenous plants which can help in decreasing their lipids (cholesterol, triglycerides, LDL, and HDL) with no harmful manifestation.²² In present study effect of Simvastatin on lipid profile along with their lipid lowering efficacy is compare with the effect of *Allium sativum* in primary hyperlipidemia patients. 14 hour fasting lipid profile was done at baseline i.e. at week 0 and were repeated after week 8. In present study when primary hyperlipidemic patients were treated with product of Simvastatin, their serum cholesterol, triglyceride and low density lipoprotein (LDL) were significantly decreased while significant increased has been observed in serum HDL levels after treatment as compared to before treated patients. Increase blood levels of cholesterol play a leading role in the formation of atherosclerotic lesion in the intima of coronary arteries. Formation of atherosclerosis begins with deposition of LDL.²³ Treatment with Simvastatin for 6 weeks at a dose of 20mg/day decreases total cholesterol, triglycerides, low-density lipoprotein cholesterol (LDL-C), and increases high-density lipoprotein cholesterol (HDL-C).²⁴ Low concentrations of total cholesterol, triglycerides and low-density lipoprotein cholesterol (LDL-C) following Simvastatin treatment also reported previously.²⁵ Dose dependent decrease in triglycerides and low-density lipoprotein cholesterol (LDL-C) and increase in high density lipoprotein cholesterol (HDL-C) is observed.²⁶ Similar changes in lipid profile are evaluated in present study in patients treated with 20 mg Simvastatin for 8 weeks.

Most of anti-hyperlipidemic agents produce adverse effects. The correlation between the hyperlipidemia and formation of atherosclerosis and the risk of side effects associated with standard antihyperlipidemic agents has promoted use of plant based compounds that produce anti-lipidemic effect without or less side effects. Garlic is one of the medicinal plants known for its excellent qualities like cardiovascular protective effects, antiaging effects and anti-inflammatory effects. Garlic is antioxidant phytochemicals that include organo-sulphur compounds and show hypolipidemic effects on experimentally induced

hyperlipidemia.²⁷

In the present study effects of *Allium sativum* on lipid profile of primary hyperlipidemic patients was monitored. In primary hyperlipidemic, serum cholesterol and low density lipoprotein were significantly decreased following the treatment of *Allium sativum* while significant increased has been observed in serum high density lipoprotein levels after treatment as compared to before treated patients but there were no significant effects on triglycerides. Long term treatment with garlic is more effective in reducing serum total cholesterol levels and serum triglycerides (TG) levels (Zeng *et al.*, 2012). Consonance with Javad *et al.*, 2007, showed significant decrease in total cholesterol, low density lipoprotein (LDL-C) and increase in high density lipoprotein (HDL-C) levels but triglycerides were not statistically significant. Significant decrease in serum total cholesterol, LDL- cholesterol, non-significant reduction in serum triglyceride and increase in HDL- cholesterol observed in the present study, also reported previously.³⁰ Decreased in total cholesterol concentration observed with *Allium sativum* is because of decrease in LDL - cholesterol which is due to blockage of biosynthesis of hepatic cholesterol possibly via inhibition of hydroxyl methylglutaryl CoA (HMG-CoA) reductase by allicin, an organo-sulfur constituent of garlic.³¹ It is observed in the present study that *Allium sativum* also improves lipid profile in primary hyperlipidemic patients.

CONCLUSION

A number of drugs that inhibit cholesterol synthesis have indicated to reduce and control serum lipid profile. However, these lipid decreasing drugs are not free of toxic effect. Therefore a drug that less toxic and yet effective would be beneficial. Present study was designed to compare the anti-lipidemic effect of *Allium sativum*, an herbal product, with a standard lipid lowering drug, Simvastatin. *Allium sativum* and simvastatin improves lipid profile in primary hyperlipidemic and patients. Due to adverse effect and rising cost of product of Simvastatin, the National Drug Policy promotes the usage of locally made herbal products. In the

present study, *Allium sativum* did not have any noticeable problem in patients, the desirable cause for this tolerance is due to odorless enteric coated garlic tablet preparation used in this study. To handle with the issues of increasing demand for medicines and to help decrease the costs of imported products, a number of developing countries including Pakistan have set up various strategies, one of which is to promote the local (herbal) manufacture and usage of quality generic drugs. In conclusion it is observed that *Allium sativum* as well as Simvastatin tablets both reduce total cholesterol, low density lipoprotein cholesterol (LDL-C) and increase high density lipoprotein cholesterol (HDL-C). However further clinical research and studies are needed to confirm the safety and quality of the plants to be used by clinicians as therapeutic agents.

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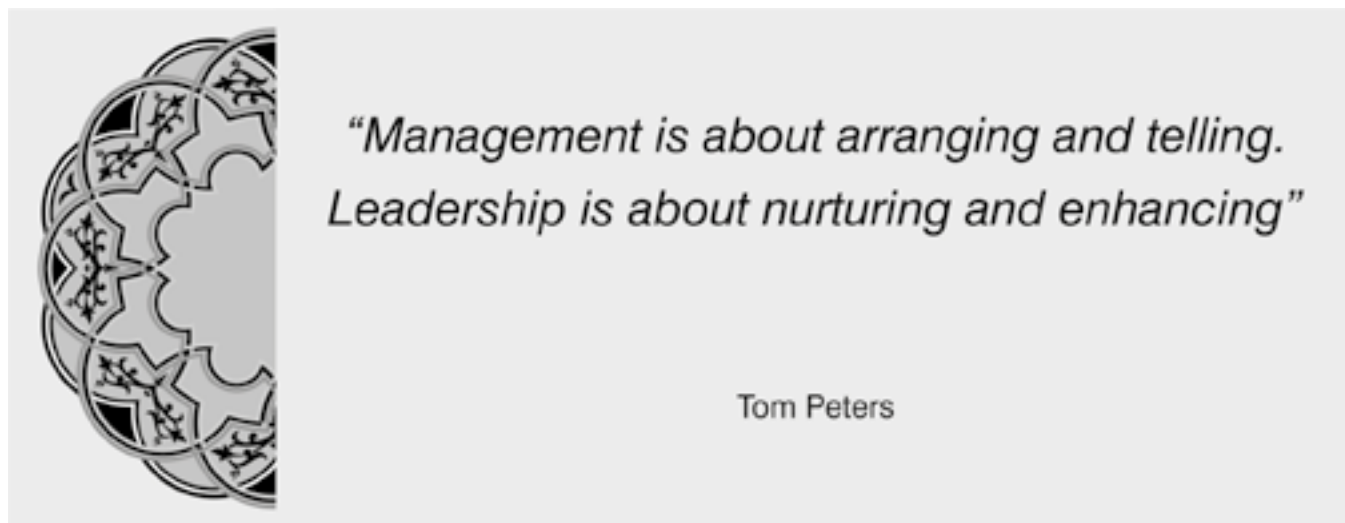
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AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Dr. Naveed Ali Siddiqui	Contribution of each author is equal	
2	Muhammad Asadullah		