Adverse Effects of HMG CoA Reductase Inhibitor and Garlic on Renal Function in Patients with Diabetic Dyslipidemia

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Abstract

Objectives: To analyze the adverse effects of HMG CoA reductase inhibitor (statin) and garlic (Allium sativum) on renal function in diabetic dyslipidemic patients.
Methods: This clinical trial was conducted at Surgeon Munawar Memorial Hospital, Karachi from 1st March 2019 to 30th August 2019. Total of 60 patients of 30-70 years of age with abnormal lipid profile were enrolled for this study after a written consent. The study was conducted to assess the side effects of statin (20 mg/day) and garlic (300 mg/day) in diabetic dyslipidemia patients. The study period consisted of six months. 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. The initial inclusion criteria of the patient were 1) Age between 30-70 years old of either sex, 2) Patients with diabetic dyslipidemia. 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.
Results: This study included 60 patients with an abnormal lipid profile of age 30-70 years. International statin product (20 mg/day) and local garlic product (300 mg/day) for 08 weeks were used for oral administration in patients. Urea and creatinine levels in the serum of diabetic dyslipidemic patients were measured before and after treatment with an international statin (20 mg/day) and a local garlic product (300 mg/day).
Conclusion: According to the findings of this study, statins increase the serum level of urea and creatinine while garlic has no effect on urea and creatinine serum level.
Keywords: Urea, Creatinine, Diabetic dyslipidemia, HMG-CoA reductase inhibitor, Coronary heart disease.
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Introduction

Diabetes mellitus type 2 is getting more normal all through the world, and it is very nearly turning into a pandemic. Diabetes mellitus burdened roughly 285 billion patients in, 2010, and this figure is required to ascend to 439 million adults around the year 2030, with an expansion of up to 69 percent contrasted with 20 percent in developed countries between the year 2010 and year 2031. By 2025, it is expected that developing countries of the world would represent around 75% of the diabetes population[1,2]. Heightening age has huge impact on the event of diabetes. By 2030, it is expected that the quantity of diabetic patients of matured 64 and more established in agricultural nations would outperform 82 million, while the number in developed countries will surpass 48 million[3]. Roughly 25% of patient's very age of 45 years is disappeared with DM anticipated by American Diabetic Affiliation. It totally was likewise detailed constantly of 2000 there have been roughly 5.2 million patients of diabetes and this may go higher to 13.9 million by year of 2020 and to 14.5 million by 2025, making

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Pakistan among the fourth most populated nation of the world in regards to diabetic patients. Diabetic ketoacidosis and hyperosmolar non-ketotic trance state are the most well-known inconveniences of ongoing hyperglycemia, though long haul issues are separated into microvascular (nephropathy, retinal changes, neuropathy) and macrovascular infections (heart disease)[4,5]. Intermittent claudication, diabetic foot, and gangrene are instances of macrovascular and microvascular ailments that can cause issues and raise the danger of removal. A high glucose level is significant in the movement of diabetic intricacies. Epidemiological investigations have uncovered a connection between expanded lipid and protein focuses and passing from macrovascular disease. Plasma LDL cholesterol levels are straightforwardly connected with the continuous improvement of atherosclerotic cores and macrovascular disease, while plasma HDL cholesterol levels are contrarily related[6]. As per the directed proposals by NCEP were resolved that patients with macrovascular disease have LDL-C upsides of under 100 mg/dl[7]. Essential hyperlipidemia is a condition brought about by an acquired quality insufficiency and an assortment of different conditions. The ordinary notable danger factors for coronary vascular disease assume a significant part in the acceleration and development of large scale vascular illness in individuals with type 2 diabetes. The prevalence of lipoproteins, containing low-density lipoprotein (LDL), very low-density lipoprotein (VLDL), and remainder lipoprotein are by far the most part engaged with dyslipidemia. The oxidative rebuilding of LDL cholesterol, which is embroiled in the development of atherosclerotic sores, is brought about by receptive oxygen species (ROS). Regardless of the significance of statin treatment, family doctors face ordinary obstructions while recommending statin medications because of the ascent in serious results. The result of statin medication is a considerable expansion in serum liver enzymes[8,9]. Statin-related antagonistic impacts envelop myopathy, muscle touchiness/torment alongside shortcoming, fatigue, and, in uncommon cases, rhabdomyolysis, which are altogether motivations to consider for ceasing statins treatment. In past late many years, Allium sativum has been the focal point of clinical interest because of its enemy of hyperlipidemic properties. Garlic has likewise been displayed to bring down cholesterol levels and assume a part in an assortment of physiological conditions that add to a high cardiovascular danger, like vasoconstriction, high essential signs, expanded platelet collection and deferred fibrinolysis[10].

Subjects and Methods

This study was conducted at a private hospital from 1st March, 2019 until 30th August, 2019 to research the harmful effects of antilipemic drugs. This research is focused on a Pakistani populace with diabetic dyslipidemia. The study was conducted after the approval of United Medical & Dental College, Karachi. In this study, we used non-probability convenient technique. The study time-period was six months. Sixty patients were selected for the study. The patients were divided into two groups. Group I consisted of 30 patients with diabetic dyslipidemia. Group I was orally administered with international product of statin i.e. 20mg/day for 8 weeks and group II with other 30 patients were orally administered with herbal product of allium sativum i.e. 300 mg/day for 8 weeks. The urea and creatinine was estimated in the serum of diabetic dyslipidemic patients before and after treatment with international product of statin i.e. 20 mg/day and allium sativum (300 mg/day). Before the experiment began, patients were asked to fill a consent form. Weight force per unit area, and height of subjects were assessed. The initial inclusion criteria of the patients were 1) Age between 30 to 70 years of either sex, 2) Patients with diabetic dyslipidemia. The exclusion criteria were 1) Pregnancy or lactation, 2) Patients with liver diseases, 3) Patients with renal diseases. All patients received a thorough case history and physical examination. Before and after the treatment, serum urea and creatinine levels were measured. For a period of six months, patients were given simvastatin i.e. 20 mg/day and garlic orally. After six months, blood samples were drawn again to assess urea and creatinine levels. A

sample of blood was taken and centrifuged for ten minutes. Till further analysis, serum was separated, obtained and stored. Utilizing commercially available kits, the serum levels of urea and creatinine were measured enzymatically on a micro lab. The sample size of sixty was calculated by using software SPSS version 11.

Results

A total of sixty patients were chosen for the study. Before and after the treatment, serum urea and creatinine levels were measured. Table 1 depicts the changes in serum urea and creatinine in diabetic dyslipidemia patients before and after treatment with an international statin drug for six months. Patients who were administered statin at a portion of 20 mg/day showed an ascent in serum urea and creatinine from a baseline worth of 28.46 to ± 0.75 mg/dl, to 31.10 to ± 0.70 mg/dl, and 1.02 to ± 0.04 mg/dl, to 1.17 to ± 0.03 mg/dl. In comparison to before and after therapy, these increases were spotted to be of highly statistically significant (p 0.05). Table 2 shows the changes in urea and creatinine levels in diabetic dyslipidemia before and after treatment with a local garlic product for six months. The urea and creatinine levels of patients who were administered 300 mg of allium sativum per day showed no significant change.

Table 1. Effects of Statin on Urea and Creatinine in Diabetic dyslipidemic patients

	Urea (mg/dl)	Creatinine (mg/dl)
Before treatment	28.46 ± 0.75	1.02 ± 0.04
After treatment	31.10* ± 0.70	1.17* ± 0.03

*By t-test, p< 0.05 is statistically significant when compared to the respective control.

Table 2. Effects of Garlic on Urea and Creatinine in Diabetic dyslipidemic patients

	Urea (mg/dl)	Creatinine (mg/dl)
Before treatment	29.80 ± 0.79	0.86 ± 0.03
After treatment	30.36 ± 0.92	0.84 ± 0.04

Discussion

Hyperlipidemia is a catch-all term for a variety of acquired or hereditary illnesses characterized by a high amount of lipids (fats, cholesterol, and triglycerides) in the bloodstream. Many patients don't seem to be ready to accept statin due to poor compliance for several reasons like rhabdomyolysis resulting in arthralgia and myalgia[11]. Statin may produce adverse effects in many patients. Because none of the anti-hyperlipidemic drugs are without side effects, are hazardous, or are a cost-effective way to manage hyperlipidemia, the use of plant-based herbal remedies has grown significantly over the ages and is now a popular alternative management choice. Simvastatin can raise urea and creatinine levels if taken for an extended period of time. Urea and creatinine levels typically restored to pre-treatment levels once the medicine was stopped. Simvastatin monotherapy has been linked to oliguric acute renal failure, which causes blood urea nitrogen and creatinine levels to rise. Increased serum urea and creatinine in a dose-dependent manner[12]. Diabetes may also cause diabetic nephropathy and may deteriorate renal function. Thanks to poor compliance of statin, there's an urgent need of other therapy/backup to handle these issues[13,14]. The increasing use of different and complementary therapies for diabetes and hyperlipidemia makes it timely to style a test analyzing the results of garlic and statin on these important and customary cardiovascular and their related contributing factors. Statin is a reductase inhibitor that inhibits cholesterol synthesis[15,16,17]. Since none of the anti-hyperlipidemic drugs are without adverse side effects and are a cost-efficient way of managing hyperlipidemia, the use of plant-based herbal remedies has grown significantly over the centuries and has become a popular alternative management strategy. Herbal medicine made from Allium sativum has been shown to help with a variety of ailments[18,19,20]. In keeping with Pakistan's low-income structure, it indicates that indigenous herbs can assist people lower their lipids (cholesterol, triglycerides, LDL, and HDL) without causing harm[21]. The current study was designed to "Evaluate the conse-

quences of garlic and statin on diabetic dyslipidemia with relation to its ability to exhort a discount in risk and to ascertain the time and dose that the utmost decrease would require and to look at and record any adverse effects during therapy with statin and allium sativum". In the current study, impact of statin on renal boundaries is contrasted with the results of garlic in diabetic dyslipidemic patients. In present investigation, when diabetic dyslipidemic patients were medicated with drug simvastatin, their serum creatinine and urea levels were fundamentally expanded after treatment when contrasted with before treated patients. The usage of statins for an extended period of time may result in a rise in urea and creatinine levels. When the medication was taken off, the amount of urea and creatinine gradually reverted back-to their pre-treatment levels. Statin monotherapy has been linked to an increased risk of oliguric acute nephropathy, which results in an increase in blood urea nitrogen and creatinine levels. Statins have previously been shown to increase serum urea and creatinine levels in a dose-dependent manner[22]. These alterations were constant in patients using a high-dose statin for 20 days, resulting in an increase in blood nitrogen, urea and creatinine levels[23]. In patients with high dose of simvastatin 80 mg, Schmidt (2007) diagnosed oliguric acute nephrosis for a duration of 27 days. The majority of anti-hyperlipidemic drugs have adverse side effects. Because of the link between hyperlipidemia and the development of atherosclerosis, as well as the risk of side effects associated with traditional antihyperlipidemic medications, plant-based substances that exhibit antilipidemic actions without or with fewer adverse effects have been recommended[24]. Within the present study effects of garlic on renal functions of dyslipidemic patients was monitored. In current study, as diabetic dyslipidemic individuals were treated with a local garlic product, no significant differences in serum urea and creatinine levels were identified following therapy when compared to individuals who were not treated.

Conclusion

However, these lipid decreasing drugs don't seem to be freed from toxic consequences. As a result, a medicine that is less toxic while still being effective would be advantageous. Statin therapy has been linked to a variety of renal adverse effects, including elevated serum urea and creatinine levels. In any case, these expanded degrees of serum urea and creatinine weren't seen in diabetic dyslipidemic patients treated with garlic. Because of the negative effects and high costs of statin drugs, the National Drug Policy encourages the use of locally manufactured herbal remedies. In diabetic dyslipidemic patients, there were no detrimental effects on urea and creatinine levels after administering allium sativum.

Conflict of Interest

Authors have no conflict of interest and no grant/funding from any organization.

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