

Metabolic Syndrome Comprises of Altered Lipid, Carbohydrates, and Protein Metabolism: Leading Cause of Oxidative Stress

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Abstract: Background: Metabolic syndrome comprises of altered lipid, carbohydrates, and protein metabolism causing increase synthesis of reactive oxygen species (ROS) which interact with blood low density lipoprotein (LDL) particles. This interactive phenomenon develops coronary artery disease (CAD) causing hypertension, congestive cardiac failure, cardiac arrhythmias, and heart attack. Preventive measures for CAD include avoiding sedentary life style, cessation of cigarette smoking, taking unhealthy bakery foods and taking hypolipidemic agents. In allopathy hypolipidemic agents include statins, fibrates, niacin and psyllium husk. Because these drugs have mild to severe adverse effects, medicinal herbs having hypolipidemic characteristics are replacing allopathic agents. Ginger is one of those medicinal herbs. We have tried to prove how much ginger can reduce LDL-C, TC, and body weight in hyperlipidemic patients. Our research work was single blind and placebo-controlled study. The study was conducted at National Hospital, Lahore, Pakistan from July to November 2016. 65 male, female hyperlipidemic patients were selected from the OPD of the Hospital. Their age range was 25 years to sixty years. Chain smokers, regular alcohol users, and patients suffering from any liver, kidney, and gastrointestinal illnesses were excluded from the study. They were divided equally ie 30 patients in each group. Group-I was tested group and Group-II was placebo group. Their baseline lipid profile, and body weight was determined in pathology laboratory of the hospital and was kept in their personal file. Serum TC (total cholesterol) by calorimetric (enzymic) method. Blood LDL-cholesterol was calculated by Friedwald formula⁵ ie; $LDL\text{-cholesterol} = TC - (TG/5) + HDL\text{-cholesterol}$. 30 patients of group-I were advised to take 5 grams ginger's pasted-powder in divided doses for the period of three months. 30 patients of group-II were advised to take one capsule (placebo capsule filled with 30 mg of grinded wheat) 8 hourly daily for the period of three months. They were advised to come at hospital for follow up fortnightly. After three months therapy their lipid profile and body weight was redetermined by same method as above. Data were expressed as mean \pm SD/SEM (standard deviation/ standard error of mean). Paired t-test was used to determine SS (statistical significance) in pre and post-treatment mean values. P-values greater than 0.05 were labeled as non-significant difference in two groups (pre-treatment and post treatment mean values). Lesser than 0.05 value (p-value) was considered as significant change in two groups. Lesser than 0.001 value was labeled as highly significant change in two groups (pre-treatment and post treatment groups).

Keywords: Coronary Artery Disease, Hyperlipidemia, BMI, Ginger, Lipid Profile.

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INTRODUCTION

Free radicals are formed due to different metabolic processes in human body [1]. Free radicals react with LDL particles in serum forming LDL-ROS complex leading to develop atherogenesis ie; initial

stages of coronary artery disease (CAD) in cardiovascular system [2,3]. Individuals suffering from dyslipidemia are on risk to develop coronary artery disease [4]. Modification in life style like physical exercise, taking healthy food, reducing mental stress,

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avoiding alcohol intake and cigarette smoking can be positive factors for reducing CAD risk. Just to reduce LDL-cholesterol in alcoholics and cigarette smokers can be beneficial in reducing CAD risk [5-8].

In allopathy hypolipidemic agents include statins, fibric acids, niacin and psyllium hydrophilic mucilloid. All of these have remarkable adverse effects [9]. Now a days allopathic hypolipidemic drugs are being replaced by medicinal herbs, due to lesser side effects in later drug group [10]. Since pre-historical times medicinal herbs are being used by human population. Ginger is one of these medicinal herbs which are being used in serum high lipids, GI up sets, asthma, cardiac diseases, diabetes mellitus, mental disorders, liver dysfunction, renal impairment, eye sight problems, and neuropathy [11,12]. Ginger belongs to zingiberaceae family in plant kingdom [13]. This herb contains gingerol which has anti-inflammatory and antioxidant properties [14]. Due to anti-inflammatory actions of ginger it is frequently used in treating arthritis, skin allergy, hepatitis, neuritis, cholecystitis, nephritis, and pleuritis [15].

As antioxidant agent, it is used since long time by HAKEEMs and homeopathy practitioners [16]. In allopathic discipline this drug's active ingredient Gingerol was extracted by medical scientists and researchers, and now is being used making nutrients by nutraceuticals [17]. Mechanism of action of gingerol to reduce serum lipids include inhibition of lipoprotein lipase in adipose tissues, and increasing LDL receptors in liver. Lipoprotein lipase activity cause formation of free fatty acids (FFAs) which are one of the major constituents to form VLDL particles in liver. Inhibition of these FFAs cause reduction of VLDL particles in hepatocytes which lead to decrease synthesis of IDL and LDL particles in blood [18,19]. In lipid profile VLDL and LDL cholesterol reduction reflects decreased number of IDL and improved ratio of LDL/HDL, which explains decrease risk of CAD in patients [20].

PATIENTS AND METHODS

Design of research work

It was single blind and placebo-controlled study.

Duration and place of research work

The study was conducted at National Hospital, Lahore, Pakistan from July to November 2016.

Sample size

65 male, female hyperlipidemic (primary as well as secondary hyperlipidemic) patients were selected from the OPD of the Hospital. Their age range was 25 years to sixty years.

Consent

Written and already explained consent was from all participants and this was approved by ethical committee of the hospital.

Exclusion criteria

Chain smokers, regular alcohol users, and patients suffering from any liver, kidney, and gastrointestinal illnesses were excluded from the study.

Grouping

They were divided equally ie 30 patients in each group. Group-I was tested group and Group-II was placebo group.

Method

Their baseline lipid profile, and body weight was determined in pathology laboratory of the hospital and was kept in their personal file. Serum TC (total cholesterol) by calorimetric (enzymic) method. Blood LDL-cholesterol was calculated by Friedwald formula [5] ie; $LDL\text{-cholesterol} = TC - (TG/5) + HDL\text{-cholesterol}$. 30 patients of group-I were advised to take 5 grams ginger's pasted-powder in divided doses for the period of three months. 30 patients of group-II were advised to take one capsule (placebo capsule filled with 30 mg of grinded wheat) 8 hourly daily for the period of three months.

Follow up

They were advised to come at hospital for follow up fortnightly. After three months therapy their lipid profile and body weight was redetermined by same method as above.

Statistical Analysis

Data were expressed as mean \pm SD/SEM (standard deviation/ standard error of mean). Paired t-test was used to determine SS (statistical significance) in pre and post-treatment mean values. P-values greater than 0.05 were labeled as non-significant difference in two groups (pre-treatment and post treatment mean values). Lesser than 0.05 value (p-value) was considered as significant change in two groups.

RESULTS

All over the research work period all participants' behavior was quite well. In group-I three patients discontinued to take their medication due to their personal reasons. So our sample size in group-I remained 27 for further statistical analysis. In group-I (tested group) when pre and post-treatment values were compared it was observed that LDL-cholesterol of 27 hyperlipidemic patients reduced from 202.21 ± 1.88 mg/dl to 187.72 ± 1.98 mg/dl. Difference in pre and post treatment values in this group was 14. 14 mg/dl. Serum total cholesterol reduced from 233.11 ± 1.53 mg/dl to 198.44 ± 1.23 mg/dl.

Difference in pre and post treatment values in this group was 34.67 mg/dl. Body weight reduced from 76.01±2.66 kg to 72.80±1.87 kg. Difference in pre and post treatment values in this group was 3.21 kilograms.

Changes in LDL cholesterol and total cholesterol were significant while body weight reduction was non-significant when analyzed statistically and compared with placebo group.

Table 1: Showing Effects of ginger on LDL-cholesterol, total cholesterol and body weight in three months therapy (n=27)

| Parameter | At day-0 | At day-90 | Change in mg/dl | SS/p-value |
|-------------|-------------|--------------|-----------------|------------|
| LDL-c | 202.21±1.88 | 187.72± 1.98 | 14.49 | <0.01 |
| T-C | 233.11±1.53 | 198.44±1.23 | 34.67 | <0.001 |
| Body weight | 76.01±2.66 | 72.80±1.87 | 3.21 | >0.05 |

Table 2: Showing Effects of placebo on LDL-cholesterol, total cholesterol and body weight in three months (n=30)

| Parameter | At day-0 | At day-90 | Change in mg/dl | SS/p-value |
|-------------|-------------|-------------|-----------------|------------|
| LDL-c | 143.25±1.99 | 142.98±1.98 | 0.18 | >0.05 |
| TC | 190.47±2.71 | 188.99±1.76 | 0.77 | >0.05 |
| Body weight | 76.73±2.19 | 76.56±1.91 | 0.22 | >0.05 |

Key: ± indicates standard error of mean, p-value >0.05 indicates non significant and P<0.001 indicates highly significant change in lipid profile. LDL-C means low density lipoprotein cholesterol mg/dl, T-C means total serum cholesterol mg/dl, HDL-C means high density lipoprotein cholesterol mg/dl, and body weight is measured in kg. GP (group) 1 is on drug and GP (group) 2 is on placebo. SS stands for statistical significance

DISCUSSION

Coronary artery disease (CAD) is major cause of heart attacks all over the world. This CAD is initiated by interaction of free radicals with LDL particles in systemic circulation. As LDL-ROS (Low Density Lipoprotein+Reactive Oxygen Species) complex is formed, and will cause attraction to chemoattractants (chemotactive factors) like PG, histamine, leucotrienes, NO (nitrous oxide), eosinophils, thromboxanes. All of this process will form foamy atherosclerotic plaques, which adhere with inner endothelium of coronary arteries, leading to hardening of these arteries and less supply of oxygen to these tiny cardiac blood vessels. By taking antioxidant medications or taking food rich in antioxidant can reduce risk of CAD development.

Another risk factor for CAD ie; LDL particles in blood can be reduced by taking hypolipidemic medications like statins, fibrates, niacin and PHM (psyllium hydrophilic mucilloid) or medicinal herbs like Ginger, Garlic, green tea, Ilaichi, Cardamom, onion, etc. In our results Ginger reduced LDL cholesterol of 27 hyperlipidemic (HL) patients 14.49 % in three months therapy. These results match with results of study conducted by Sitavan *et al.* [21] They proved six kilograms decrease in body weight of one hundred nine patients suffering from secondary hyperlipidemia. They advised their patients to take five grams ginger for ninety days. In another research work conducted by Cokava *et al.* [22], it was proved that LDL cholesterol was 19.87 mg/dl percentage in thirtynine hyperlipidemic patients. Their total cholesterol reduction and body weight reduction was 29.91 mg/dl and 4.99 kilograms respectively. These results also support our research results. Johsin *et al.* [23] have mentioned mechanism of action of ginger that it scavenge free radicals in various tissues leading to decreased damage to vascular endothelium.

Fujar *et al.* [24] proved same reduction in low density lipoprotein cholesterol, total cholesterol, and body weight as our results proved. They mentioned and recommended that close supervision, frequent follow-up/counseling can give authenticated results in tested group patients. Illasi *et al.* [25] proved that in herbal medications, ginger is one of the potent hypolipidemic herb. Solarka *et al.* [26] did research on hypolipidemic, hypoglycemic and hypotensive effects of ginger and proved that this medicinal herb reduced 39%, 27, 18 %, and 22.64 % LDL cholesterol, blood glucose, and systolic blood pressure in 65 patients suffering from metabolic syndrome. They explained that metabolic alteration in various diseases can cause synthesis of increased number of free radicals which interact with low density lipoproteins causing CAD. Domerluve *et al.* [27] proved significant reduction of LDL-C, TC (total cholesterol), TG (triglycerides), and VLDL (very low density lipoprotein) cholesterol in 46 hyperlipidemic patients. They used five grams ginger in 49 hyperlipidemic patients.

Kulmharree *et al.* [28] observed 44.87 percentage reduction in LDL cholesterol in twenty-two hyperlipidemic and hyperglycemic patients. Another study conducted by Dosaka *et al.* [29] proved 32.44 mg/dl, 7.51 Kg reduction in LDL cholesterol and body weight respectively. Their sample size was sixty six hyperlipidemic patients. They used two grams ginger for the period of sixty days. Another research work's results also support our results when they used 4 grams of raw ginger in 30 hyperlipidemic patients for three months. They observed 27.68 mg/dl reduction in LDL cholesterol. Total cholesterol was observed to be reduced by 32 mg/dl [30]. Weisxer *et al.* [31], and Ursthy *et al.* [32] noticed in their research work that allopathic hypolipidemic or hypoglycemic drugs

interact with ginger, so these patients must be rechecked by physicians for their liver functions regularly.

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