

Presence of High Plasma LDL-Cholesterol and Lower Plasma Concentrations of HDL-Cholesterol May Lead to keep Heart Unhealthy

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Abstract:

Cholesterol is carried through the bloodstream attached to two different compounds called lipoproteins: low-density lipoproteins (LDL) and high-density lipoproteins (HDL). LDL is commonly known as the “bad” cholesterol because it transports cholesterol from the liver throughout the body, and potentially allows it to be deposited in artery walls. HDL, known as the “good cholesterol,” picks up cholesterol from the blood and delivers it to cells that use it, or takes it back to the liver to be recycled or eliminated from the body. The focus has shifted to the novel risk factors as well as characteristics and stability of atherosclerotic plaque; the genetic predisposition has further broadened the pathogenetic mechanisms. This review focuses on the molecular mechanisms involved in the evolution of the atherosclerotic plaque that may pave the way for selecting optimal therapies and preventing plaque complications. Atherosclerosis is no longer a disease attributed mainly to the high lipid content of the body. New insight into the disease pathology has shown it to be a disease of much greater ramifications. Endothelial damage and reactive oxygen species (and other free radicals) have predominantly emerged as factors in virtually all pathways leading to the development of atherosclerosis due to hyperlipidemia, diabetes, hypertension or smoking. Novel risk factors such as hyperhomocysteinemia, infections and systemic lupus erythematosus have emerged. Hypolipidemic herbs can normalize lipid profile of patients suffering from primary or secondary hyperlipidemia. Psyllium husk and Ficus Carica (Anjeer) are being used successfully for treatment of both types of Hyperlipidemias. This research study was single blind placebo-controlled, and was conducted at General Hospital Lahore-Pakistan from January to June 2018. One hundred hyperlipidemic patients were enrolled for the research work. Base line lipid profile was measured in Biochemistry Lab of the hospital. Patients were divided in four groups, 25 patients in each group. Group-I was on Figs, Group-II was on Psyllium, Group-III was on combination of these two herbal medicines. After three months therapy, their lipid profile was determined and mean values with \pm SEM were compared before and after treatment. When analyzed statistically and compared with placebo effects, all patients' LDL-cholesterol was reduced significantly. HDL-cholesterol was increased in all groups of patients. We concluded from this study that when used in good amount/dose, Psyllium husk and Figs reduce LDL-cholesterol and increase HDL-cholesterol significantly.

Keywords: immunotherapy related adverse effects; pembrolizumab; toxic epidermal necrolysis

Introduction

Recently, localization of eNOS to specialized plasma membrane invaginations termed caveolae has been proposed to be required for maximal

eNOS activity. Because caveolae are highly enriched in cholesterol, and hypercholesterolemia is associated with increased NO production, we first

studied the effects of cholesterol loading on eNOS localization and NO production in cultured bovine aortic endothelial cells (BAECs). Caveolae-enriched fractions were prepared by OptiPrep gradient density centrifugation. Treatment of BAECs with 30 µg/mL cholesterol for 24 hours stimulated significant increases in total eNOS protein expression (1.50-fold), eNOS associated with caveolae-enriched membranes (2.23-fold), and calcium ionophore-stimulated NO production (1.56-fold). Because reactive oxygen species (ROS) contribute to endothelial dysfunction in hypercholesterolemia. Primary or secondary Hyperlipidemia is major cause of these cardiac problems [2]. Start from birth to death for human being's life is concerned with sedentary life and taking Fatty/Junk Food, for which individuals are used to ignore is free radical formations in their body. These free radicals are key factors for initiation of inflammatory processes known as atherogenesis leading to develop coronary artery disease (CAD). Major heart diseases like hypertension, angina, congestive cardiac failure, myocardial infarction and cardiac arrhythmias are end stage of progression of coronary artery disease. Formation of atherosclerotic plaques leading to develop CAD is due to presence of high plasma LDL-cholesterol and lower plasma concentrations of HDL-cholesterol [3]. Conventional method of hypolipidemic drug's therapeutic philosophy is going to lost or at least being to be unpopular due to unwanted pharmacological effects of these drugs [4]. At least in low economic human population, peoples are getting benefits from hypolipidemic medicinal herbs like Psyllium Husk (PH), and Ficus Carica (FC). Psyllium Husk decreases plasma cholesterol by two mechanisms. First PH inhibit enterohepatic circulation of bile acids from gastrointestinal tract, leading to depletion of bile store in gall bladder, which signals hepatocytes to form bile acid instead of cholesterol synthesis. Second, ingested lipids are adsorbed with PH particles and are excreted in stool [5-8]. Ficus Carica or Figs (anjeer) has been used traditionally to treat various ailments such as Hyperlipidemia, diabetes mellitus, gastric problems, inflammation, and cancer [9]. Figs are rich in phenolics, organic acids, and volatile compounds. Regarding phenolics, numbering over 4,000 distinct species, many of these compounds have antioxidant activity. They may affect cell-to-cell signaling, receptor sensitivity, inflammatory enzyme activity or gene regulation, which play part to scavenge free radicals formed in many biotransformatory processes in human body [10-12]. Processed and dried figs are superior to natural figs when it comes to antioxidants. These dried figs have superior quality of antioxidants, called phenols, compared to other fruits that attribute their antioxidant property to vitamin C and E [13]. The high levels of antioxidants in dried figs help to eliminate free radicals that can damage blood vessels and result in heart disease. And, as mentioned earlier, they prevent hypertension, a huge risk factor for development of coronary artery disease (CAD) [14]. Synthesis of nitric oxide (NO) by endothelial nitric oxide synthase (eNOS) is critical for normal vascular

homeostasis. eNOS function is rapidly regulated by agonists and blood flow and chronically by factors that regulate mRNA stability and gene transcription.

Patients & Method

TYPE/PLACE? DURATION OF STUDY: It was single blind placebo-controlled research work, conducted from January 2018 to June 2018 at General Hospital, Lahore, Pakistan. **SAMPLE SIZE:** One hundred male and female hyperlipidemic patients were selected for research, age range from 20 to 65 years. **Inclusion criteria** were primary, secondary hyperlipidemic patients, without medical history of victimization of patient by any major cardiac disease like Angina, Congestive Cardiac Failure, Myocardial Infarction, and Cardiac Arrhythmias. **Exclusion Criteria** were any thyroid, renal, hepatic disease, alcohol users, chain smokers, and taking any medicine on regular basis. **CONSENT AND STUDY APPROVAL:** Written and explained consent was taken from all participants and approved by research ethics committee of the hospital. Patients were divided in four equal groups, comprising 25 patients in each group. Their baseline determination of LDL-cholesterol and HDL-cholesterol was made at Biochemistry laboratory and was kept in specially formatted Performa. Group-I was advised to take dried Figs 10 grams daily in three equally divided doses. Group-II was advised to take 10 grams of Psyllium husk daily in three divided doses before each meal for three months. Group-III was advised to take 10 grams Figs and 10 grams Psyllium husk in three divided doses daily for three months. Group-IV was advised to take one capsule (containing grinded wheat) with each meal time, thrice daily for the period of three months. They were advised to come for follow up monthly. Their LDL-cholesterol and HDL-cholesterol was measured monthly. After three months their lipid profile was measured. Resulted were compiled and statistically analyzed by using SPSS version 5.0 2014. Mean values of the tested parameters were expressed with \pm SEM and paired 't' test was applied to determine significant changes in mean values before after treatment. P-value >0.05 was considered as non-significant change, p-value <0.01 was considered as significant and p-value <0.001 was considered as highly significant change in tested parameters.

Results

After three months therapy by Ficus Carica (Figs), Psyllium husk and combination of these two herbs, results were compiled and analyzed statistically by SPSS version 5.0 2014. Before and after treatment mean values with \pm SEM of LDL-cholesterol and

HDL-cholesterol, with three drugs are shown in following table, which is self-explanatory:

Drug	Parameter	At day-0	At day-90	Change	% change	p-value
Ficus Carica (n=24)	LDL-c	236.17 \pm 1.87	216.08 \pm 1.66	20.1	8.5	<0.001
	HDL-c	40.05 \pm 2.19	47.74 \pm 1.45	7.7	16.1	<0.01
Psyllium husk (n= 24)	LDL-c	228.76 \pm 2.91	210.92 \pm 2.86	17.8	7.8	>0.001
	HDL-c	33.33 \pm 1.61	38.60 \pm 2.10	5.3	13.7	<0.01
FC+PH (n=22)	LDL-c	234.65 \pm 3.76	208.97 \pm 1.32	25.7	11.0	<0.001
	HDL-c	38.87 \pm 1.42	47.54 \pm 2.86	8.7	18.3	<0.01
PLACEBO (n=25)	LDL-c	221.97 \pm 2.10	220.12 \pm 2.00	1.9	0.9	>0.05
	HDL-c	35.43 \pm 2.50	36.19 \pm 3.76	0.8	2.2	>0.05

KEY:all parameters and change before and after treatment in parameters are measured in mg/dl, and their mean values are written with \pm SEM. P-value <0.01 = significant, p-value >0.05 = non-significant changes in lipid profile. HDL-c and LDL-c values are measured in milligrams per milliliter. n = sample size. FC stands for Ficus Carica, and PH stands for Psyllium Husk

Table: Effects of Ficus Carica, Psyllium husk, and Ficus Carica+Psyllium husk combination on HDL-c and LDL-c in HYPERLIPIDEMIC patients

Discussion

Psyllium husk is well known, since long for its hypolipidemic actions. Figs are one of the earliest fruits grown by man. Though figs are not available throughout the year, dried figs (popularly known as anjeer in Pakistan) are

not only is dried fig tasty to eat, it has numerous health benefits to offer as well. Figs being used by layman and health related persons for digestion of foods, for treating hypertension, diabetes mellitus, anemia, obesity, bones deformity, and for prevention of complications leading to cause heart diseases like oxidative stress and Hyperlipidemia. *Ficus Carica* (Figs) contain Flavonoids, various phytochemicals, wide variety of organic acids, furanocoumarins, polysaccharides, all compounds have one way or other antioxidant effects. In our research Figs consumption by 25 hyperlipidemic patients for three months decreased LDL-cholesterol 20.1 mg/dl, and increased HDL-cholesterol 7.7 mg/dl. Macdonald-wicks LK et al¹⁵ proved near to same results as ours. They mentioned mechanism of antioxidant activity of this herb that active ingredients present in Figs scavenge and use free radicals and prevent cell damage in body. Mawa Set al used combination of Psyllium husk and Figs and proved 30.1 mg/dl reduction in LDL-cholesterol. These results match with ours as in our observation, combination of two herbs reduced LDL-cholesterol 25.7 mg/dl and increased HDL-cholesterol 8.7 mg/dl in three months therapy by two herbs [16]. Bozin B et al¹⁷ used Figs (*Ficus Carica*) in 78 hyperlipidemic patients and proved that this herbal medicine reduced plasma total cholesterol 34.88 mg/dl, LDL-cholesterol 9.96 mg/dl and increased HDL-cholesterol 2.04 mg/dl. These results are in contrast with our results. Reason to contrast in these two studies are due to selective patients in these researchers' study as they only selected secondary hyperlipidemic patients and used 5 grams Figs for one week only. We proved LDL-cholesterol reduction 17.8 mg/dl when Psyllium husk was used by 25 patients for the period of 3 months. HDL-cholesterol increased 5.7 mg/dl in our patients. These results match with results of study conducted by Liu F et al who proved 20.04 mg/dl reduction in LDL-cholesterol when they advised their patients to take Psyllium for 8 weeks. Tatsis EC et al used combination of Figs with Psyllium seeds in 12 patients and proved LDL-cholesterol reduction only 8.07 mg/dl, while in our patients this decrease was 25.7 mg/dl [18,19]. This contrast in results we guess is due to their small sample size (only 12 patients) and form of drug used was Psyllium seeds not husk. She-Ching WU et al have favored utilization of husk form of Psyllium, as it has more adsorbent effect as compared to their seeds. Research studies by Nawakillv J et al [20,21]. have had proved same effects of seeds and husk on secondary hyperlipidemic patients. Active ingredients present in Figs scavenge and use free radicals and prevent cell damage in human body. And combination of psyllium and Figs are superb to reduce ROS burden in human being [22-24].

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