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State of oxidative stress: Lethal phenomenon for heart and vessels

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ABSTRACT

Hyperglycaemia, hypertension, and hyperlipidemia are known as metabolic syndrome. In presence of high levels of blood LDL particles, free radicals (ROS), macrophages, cytokines, platelets, histamine, 5HT get involved in LDL oxidation, leading to formation of atherosclerotic plaques which get deposited in endothelium of coronary arteries causing coronary artery disease (CAD). Psyllium fibers and Ficus Carica (FC) are being considered to be useful in treating hyperlipidemia, hypertension, and hyperglycaemia. This study was conducted to determine hypotensive, hypolipidemic, and hypoglycaemic potential of Psyllium husk and FC. Study was conducted in National hospital, Lahore, Pakistan from January to April 2020. Seventy-five hyperlipidemic, hypertensive and diabetic patients were enrolled selected from the hospital with their consent. They were divided in three groups i.e. 25 patients in each group. Group-1 was on placebo, group-2 was on 15 grams psyllium husk to be used in three divided doses. Group-3 was on 12 grams FC to be taken in three divided doses daily for two months. Their Lipid profile, FBS, and hypertension were determined before and after two months therapy by these two agents. Two analyze data we used SPSS version 10.01.001 2015 and t test was applied to determine changes in the tested parameters. In two months, therapy by psyllium husk in 24 patients TG, TC, LDL-c was reduced 21.48, 10.09, 24.17 mg/dl respectively. HDL was increased 12.38 mg/dl in this group. FBS reduction was 28.66 mg/dl, systolic BP 6.30, and diastolic BP reduced in this group 7.52 mm of mg. We then concluded that FC and PH have good enough potential to normalize lipid profile, reduce BP, and FBS in patients suffering from metabolic syndrome.

Keywords: Hyperglycaemia, hypertension, and hyperlipidemia

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INTRODUCTION

Metabolic syndrome is associated with hyperglycemia, hyperlipidemia, and hypertension¹. Hypertension, and hyperlipidemia are directly related with oxidative stress in human body²⁻³. Increased LDL particles in blood interacts with reactive oxygen species (ROS) causing LDL-oxidation and leading to formation of atherosclerotic plaques which usually get deposited in endothelium of coronary arteries leading to develop CAD⁴. In presence of high glucose levels hyperlipidemia, and hypertension this atherosclerotic plaque formation process can be accelerated⁵. Preventable risk factors for these three metabolic aberrations include to stop over ingestion of junk foods, alcohol, carbohydrate/fats, stop smoking, and escaping sedentary life⁶. If individual still get

illness like this syndrome, he or she can start treating this metabolic syndrome by regular utilization of Psyllium Husk (PH) and Ficus Carica (FC)⁷. Psyllium husk are water soluble fibers which are not absorbed from stomach or intestine, rather they adsorb carbohydrates/glucose and lipids ingested by routinely taken foods⁸. These fibres also adsorb bile in GIT, inhibiting enterohepatic circulation of these bile acids. Pool of bile will thereafter be decreased in gall bladder, causing signalling hepatic cells to form bile instead of cholesterol synthesis⁹.

Phenolic compounds found in FC scavenge free radicals and thereafter reduce risk of development of coronary artery disease (CAD)¹⁰. FC also contain organic acids, vitamins,

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minerals, and volatile compounds like angelicin, bergapten, germacrene D, hydroxycaryophyllene, benzyl alcohol, benzylaldehyde, linalool, linalool oxides, cinnamic aldehyde, cinnamic alcohol, cinnamic indole, eugenol, sesquiterpene hydrocarbon. Many of these compounds found in FC lower blood lipid and glucose levels, and some are anti-inflammatory in characteristics¹¹.

Bergapten, and germacrene D may increase insulin secretion from regenerated pancreatic beta cells, so decrease hyperglycaemic state¹².

Linalool oxides and other volatile compounds get involve in various metabolic processes normally occurring in human body and decrease free radicals formation¹³. Organic acids, minerals, vitamins found in Figs (FC) have also been suggested to inhibit enterohepatic circulation, leading to decreased biosynthesis of cholesterol in liver cells¹⁴. Aim of this study was to determine hypolipidemic, hypotensive, and hypoglycaemic potential of PH and FC in Pakistani population so that ethnic considerations of drugs and their therapeutic potential may be determined.

METHODS

It was parallel t-type comparative and placebo-controlled study conducted in National Hospital Lahore, Pakistan from January 2020 to April 2020. Study work was approved by research ethics committee of the hospital. Seventy-five male/female already diagnosed moderately established Diabetic patients of type-2, and hyperlipidemic patients were enrolled. Written and well explained consent was taken from all participants. Their specified identifier proforma was prepared regarding their age, gender, occupation, residential address, contact phone number. Three groups were made, comprising 25 patients in each group. Group-1 was on placebo. They were advised to take one capsule (containing grinded moong bean), thrice daily for 2 months. Group-2 was advised to take psyllium husk 5 grams thrice daily after meal for two months. Group-3 were advised to take 4 grams FC (Anjir) thrice daily for two months. At day-0 their FBS (fasting blood sugar) was determine by Glucometer designed as On Call Extra CE 0123, provided by Alcon laboratories LTD Karachi Pakistan. Lipid profile of all patients was determined at laboratory of the hospital. They were advised to visit hospital weekly for follow-up and laboratory tests. They all were advised not to take junk foods and continue brisk walk for 30 minutes daily after dinner or at early in the morning. After two months trial, their FBS and lipid profile was redetermined by same procedure. Pre- and post-treatment Mean values \pm SD were compiled and analyzed by using SPSS version 10.01.001 of 2015. t-test was applied to get significance in results of pre- and post-treatment values, expressing it by p-values (like >0.05 non-significant change, <0.05 = significant change, <0.01 = moderately significant change, and <0.001 = highly significant change in the parameter)

RESULTS

After two months therapy by placebo, FC, and PH, it was observed that 12 grams of Figs reduced TG 43.00 mg/dl, TC 14.34 mg/dl, and LDL-c 48.80 mg/dl. All these changes are significant when analyzed biostatistically with p-values of <0.001 , <0.05 , and <0.001 respectively. HDL-c increased in this group was 5.86 mg/dl which is significant change with p-value of <0.05 . Fasting blood glucose (FBS) reduced in this

group was 19.82 mg/dl which is significant change with p-value <0.01 . Systolic BP reduction was 10.24, and diastolic BP reduced was 5.40 mm of Hg. Changes in both parameters are significant with p-value <0.05 . One patient discontinued therapy due to his personal reason. In Psyllium Husk group three patients withdrew from the trial due to low compliance of psyllium husk (due to its metallic taste). This drug reduced TG, TC, LDL-c 43.77, 21.43, 48.04 mg/dl respectively. All changes in these parameters are highly significant with p-value <0.001 . HDL-c increase was 5.03 which is significant enhancement when analyzed biostatistically with p-value <0.05 . 8.86, and 6.94 mm of Hg was reduced in their systolic and diastolic BP with significant p-value of <0.05 .

Table 1: EFFECTS OF Psyllium Husk, *Ficus carica* on hyperlipidemia, hyperglycemia, and hypertension in two months therapy

Para G-1 (PL) n=24	At day-0	At day-60	Change in mg/dl	Change in %	p-value
TG	157.01 \pm 1.91	154.87 \pm 1.11	2.14	1.36	>0.05
TC	210.76 \pm 1.46	207.40 \pm 2.86	3.36	1.59	>0.05
LDL-c	170.00 \pm 2.12	168.08 \pm 2.22	1.92	1.12	>0.05
HDL-c	39.97 \pm 2.77	40.97 \pm 2.12	1.00	2.50	>0.05
FBS	171.66 \pm 1.06	167.88 \pm 1.95	3.78	2.20	>0.05
BP Sis Dias	137.76 \pm 2.11 85.35 \pm 1.99	135.77 \pm 2.65 83.43 \pm 2.87	1.99 1.92	1.44 2.24	>0.05 >0.05

Para G-2 (PH) n=22	At day-0	At day-60	Change in mg/dl	Change in %	p-value
TG	203.76 \pm 2.87	159.99 \pm 2.23	43.77	21.48	>0.001
TC	212.19 \pm 3.11	190.76 \pm 1.64	21.43	10.09	>0.01
LDL-c	198.73 \pm 1.60	150.69 \pm 2.04	48.04	24.17	>0.001
HDL-c	40.61 \pm 1.84	45.64 \pm 2.54	5.03	12.38	>0.05
FBS	195.55 \pm 2.22	139.50 \pm 2.74	56.05	28.66	>0.001
BP Sis Dias	140.51 \pm 2.07 92.23 \pm 2.85	131.65 \pm 2.87 85.29 \pm 2.77	8.86 6.94	6.30 7.52	>0.05 >0.05

Para G-1 (PL) n=24	At day-0	At day-60	Change in mg/dl	Change in %	p-value
TG	202.61 \pm 2.19	159.61 \pm 1.46	43.00	21.20	>0.001
TC	212.22 \pm 2.19	197.88 \pm 2.11	14.34	6.75	>0.05
LDL-c	209.11 \pm 3.17	160.31 \pm 2.20	48.80	23.33	>0.001
HDL-c	38.81 \pm 2.16	44.67 \pm 2.75	5.86	15.09	>0.05
FBS	190.63 \pm 2.00	170.81 \pm 2.67	19.82	10.39	>0.01
BP Sis Dias	141.64 \pm 1.90 94.28 \pm 1.90	131.40 \pm 2.22 88.88 \pm 2.61	10.24 5.40	7.22 5.72	>0.05 >0.05

KEY: n = sample size, G-1 = placebo (PL) group, G-2 = Psyllium husk (PH) group, G-3 = *Ficus carica* (FC) group. N = sample size. TG = triglycerides, TC = total cholesterol, LDL-c = low density lipoprotein cholesterol, HDL-c = high density lipoprotein cholesterol, FBS means fasting blood sugar, BP stands for blood pressure, Sis = systolic BP, Dias = diastolic BP. TG, TC, LDL-c, HDL-c and Fasting blood sugar (FBS) are measured in mg/dl. Blood pressure is measured in millimetre of mercury.

DISCUSSION

Allopathic drugs are slowly and gradually being replaced by herbal medicine in few illnesses which need prolonged or lifelong treatment in some ethnic populations especially in subcontinent. Metabolic syndrome is one of those diseases which need preventive measures and if drug therapy is needed it costs much finance for its prolonged treatment.

This syndrome starts smoothly to effect human body, and if not prevented, morbid consequences are ensured¹⁵. Remarkable number of research studies proved its prevention by simple methods and considerations. Just leaving sedentary life, over consumption of processed foods, cessation of smoking, skipping from over ingestion of alcohol may prevent individual from its complications like cardiac arrhythmias, congestive cardiac failure and myocardial infarction or cardiac arrest¹⁶. If still person get started obesity, hypertension, uncontrolled hyperglycemia, and hyperlipidemia, he should consider taking fibers and nutraceuticals like psyllium husk and dried figs (*Ficus Carica*). Consumption of psyllium husk and figs has well proved hypoglycemic, hypotensive, and hypolipidemic effects¹⁷. Psyllium husk are known as psyllium hydrophilic muciloid and these fibres bind with bile acid secreted in GIT. Normally 94-96 % of secreted bile is reabsorbed from GIT to liver and stored in gall bladder. This process of bile reabsorption is called enterohepatic circulation, which is inhibited by these psyllium fibres. Hepatocytes start to make bile instead of cholesterol. Deficiency of cholesterol will lead to lesser requirement of VLDL and LDL synthesis. In our study results psyllium husk reduced 21.48, 10.09, 24.17 % TG, TC, and LDL-c respectively, HDL-c was increased 12.38 % in two months therapy by 15 grams daily intake of psyllium husk. It was unexpected that psyllium husk can increase HDL more than 12 % in two months therapy. Jabu E et al¹⁸ described mechanism of action of PH and explained that these fibers also increase formation of apoproteins required by HDL maturation ie; apo-A1 and apo-A2. They also mentioned TG synthesis reduction by hepatocytes, causing again lesser requirement of VLDL to be secreted in blood carrying TG. Forhavve C et al¹⁹ observed same amount of reduction in TG, TC, LDL-c in 133 hyperlipidemic patients which were diabetic type-2 victimized. Boharr G et al²⁰ warned the time of taking PH with meal as these fibers interact with other drugs like antidepressants, and anticoagulants. Vitamins and other nutritional value-having substances may be considered as these fibers decrease their absorption. *Ficus Carica* when used in 24 hyperglycemic, hyperlipidemic and hypertensive patients reduced TG, 43.00 mg/dl, TC 6.75 mg/dl, LDL 23.33 mg/dl, and increased HDL 5.86 mg/dl in two months therapy. FBS reduced in these patients was 10.39 mg/dl, systolic BP 10.24, and diastolic BP 5.40 mm of Hg. These results also associate with results of Ganji P et al²¹ who explained possible mechanisms of hypolipidemic, hypoglycemic and hypotensive actions of Figs. Angelicin, bergapten, germacrene D are found in FC and these compounds scavenge metabolites, ROS, and stabilize lymphocytes membrane thus decreasing chemotactic factors to reduce chances of atherosclerotic plaque synthesis. Organic acids, and vitamins found in FC act as antioxidants²². Vijay K et al²³, Toorah C et al²⁴, and Mulakarv T et al²⁵ proved lesser effects on HDL-c when used roots, leaves, and fruit of Figs. Benzyl alcohol, benzylaldehyde, linalool, linalool oxides are free radicals scavenger and transcription enhancers for synthesis of apo-A1 and apo-A2 which are essential for HDL's structural and functional features of the lipoprotein. More than 18 volatile oils are present in fresh fruit of FC which decrease inflammation, oxidative stress, and phagocytosis of chemicals necessary for synthesis of HDL particles²⁶. Hypotensive and hypoglycemic effects of FC are explained in research articles of Feghato R et al²⁷, and Erosj JK et al²⁸

that active ingredients of FC reduce reabsorption of sodium and chloride from various parts of nephron and reduce carbohydrates reabsorption from gastrointestinal mucosa. We concluded from this research that FC and PH are as efficacious as allopathic drugs used in hyperlipidemia, hypertension, and diabetes mellitus type-2.

CONCLUSION

In the light of the available literature, it is evident that Novel Corona virus can invade nervous system both directly and indirectly and can produce a wide array of signs and symptoms in both CNS and PNS. It is therefore important that healthcare workers from around the globe must have ample knowledge of these neurological manifestations. As stated above from multiple studies, these neurological symptoms can even constitute the first presenting symptom in COVID-19 positive patients, therefore, the possibility of any patient presenting with neurological manifestations to have concomitant SARS-CoV-2 infection should always be kept in mind. The need to further evaluate and assess more possible neurologic signs and symptoms associated with COVID-19 is therefore crucial for the better treatment and reduction in morbidity and mortality in all such patients. We therefore urge that more studies should be conducted on the above topic for better understanding and management of the disease.

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