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## ELABORATIVE SLANT ON LIPIDS, HYPERLIPIDEMIA, AND BILE ACID BINDING RESINS

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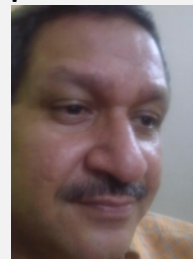
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### ABSTRACT

Since last 2 decades morbidity due to ischemic heart disease and myocardial infarction has been increased. Well known risk factors for MI and heart attack are obesity, increased bad-cholesterol (LDL-Cholesterol), decreased good-cholesterol (HDL-Cholesterol), frequent smoking, alcohol consumption, lazy life style. Purpose of this research work was to evaluate effects of bile acid binding resins on lipid profile of hyperlipidemic patients. It was single blind placebo-controlled research, conducted at Lahore General Hospital, Lahore, Pakistan. The methodology of research is Forty hyperlipidemic patients were included, in the study. Twenty patients were on placebo as control group, and twenty were on psyllium husk, 10 grams daily, in divided doses for the period of 12 weeks. Hyperlipidemic patients with other diseases were excluded from the study. Serum total cholesterol and triglycerides were estimated by the enzymatic calorimetric method. Serum HDL-cholesterol was determined by direct method, at day zero and at last day of the treatment. LDL-cholesterol was calculated by friedwald formula ( $LDL = Tc - (TG/5 + HDL-C)$ ). Data were expressed as the mean  $\pm$  SD and "t" test was applied to determine statistical significance of results. P value lesser than 0.05 was the limit of significance. It was resulted that two patients discontinued to take drug given, due to metallic test of psyllium husk. Psyllium decreased serum total cholesterol from  $228.27 \pm 4.89$  mg/dl to  $199.22 \pm 2.30$  mg/dl, triglycerides from  $169.27 \pm 9.92$  mg/dl to  $164.5 \pm 8.56$  mg/dl, LDL-Cholesterol from  $159.72 \pm 5.70$  to  $129.55 \pm 2.81$  mg/dl, and increased serum HDL-Cholesterol from  $34.61 \pm 1.85$  to  $36.77 \pm 1.96$  mg/dl in 90 days of treatment. Results of all parameters were significant when compared with results of placebo group. Student 't' test was applied for analysis of significance.

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## INTRODUCTION

Hyperlipidemia, in general, can be divided into two subcategories, i.e.; Hypercholesterolemia, in which there is a high level of cholesterol. And Hypertriglyceridemia, in which there is a high level of triglycerides, the most common form of fat. The majority of cases of hyperlipidemia in adults are not caused by primary disorders. They are most commonly due to secondary causes. The most common secondary cause of hyperlipidemia in adults is a sedentary lifestyle coupled with excessive intake of saturated fat, cholesterol, and trans fats. Other secondary causes of dyslipidemia include diabetes mellitus, hypothyroidism, chronic use of alcohol, and chronic kidney disease.<sup>1,2</sup> Although dyslipidemia usually doesn't cause symptoms, it can lead to symptomatic vascular disease, which includes coronary artery disease and peripheral arterial disease. Those with a high concentration of LDL in their blood can experience symptoms such as eyelid xanthelasma and arcus cornea. Severe elevations of triglycerides can lead to the formation of eruptive xanthomas over the hands, knees, back, and elbows. The latest research shows that hyperlipidemia or dyslipidemia is also linked to erectile dysfunction.<sup>3</sup> According to research, 20% of men who suffer from erectile dysfunction have dyslipidemia. Treatment of dyslipidemia is indicated for all patients who have cardiovascular disease and for some without. Treatment of dyslipidemia focuses primarily on reducing high levels of LDL cholesterol and secondarily on treating high levels of triglycerides, low levels of HDL cholesterol, and metabolic syndrome.<sup>4</sup> For treating primary hyperlipidemia, statins, nicotinic acid, bile acid binding resins, psyllium husk and fibric acids are main drugs in common use. Bile acids in gastrointestinal tract bound to oral anion-exchange resin, like cholestyramine or psyllium are lost in the feces and depletion of the bile acid pool stimulates conversion of cholesterol to bile acid synthesis causing fall in intracellular cholesterol in hepatocytes, and an increase or up-regulation of both LDL-receptors and cholesterol synthesis.<sup>5</sup> For many years psyllium husk has been used as an agent for gastrointestinal disturbances but it has hypolipidemic effects too. Psyllium husk binds bile acids in the intestine, thereby interrupting the

enterohepatic circulation of bile acids and increasing the conversion of cholesterol into bile acids in the liver.<sup>1-4, 6-10</sup>

## METHODOLOGY OF THE RESEARCH WORK

The place of research was Lahore general hospital, Lahore, Pakistan. It was conducted from January 2010 to July 2010. Forty patients of primary hyperlipidemia were selected from Cardiology OPD of the hospital. Hyperlipidemic male and female patients of 22-70 years old were selected. Written consent was obtained from all participants. The study period was three months. Important personal and medical data like name, age, sex, occupation, address, and previous medication, date of follow up visit and laboratory investigations, of each patient was recorded on a Performa. Detailed medical history and physical examination of all patients were carried out and recorded. Base line assessments were taken on the day of inclusion that was called Day-0 in the study and a similar assessment was taken on completion of research work called Day-90 of research design. Patients were divided into two groups, i.e. Drug-1 (Psyllium husk 10gm/day) and Drug-2 (placebo capsules, containing equal amounts of partly grinded wheat) groups. Patients of drug-1 group were advised to take psyllium husk fibers 10 gm daily in three divided times after or before each meal. Patients of drug-2 group were provided placebo capsules, i.e. one capsule, three times daily, after meal for 90 days. Patients were called fortnightly for follow up to check blood pressure, weight, pulse rate and drug compliance. Serum total cholesterol and triglycerides were estimated by the enzymatic calorimetric Method.

Serum LDL-Cholesterol was calculated by Friedwald formula ( $\text{LDL-Cholesterol} = \text{Total Cholesterol} - (\text{Triglycerides}/5 + \text{HDL-Cholesterol})$ ). Serum HDL-cholesterol was determined by direct method, at day-0 and day-90. Mean  $\pm$  SD was the expressive tool of data collected for all parameters of lipid profile and "t" test was applied to determine statistical significance as the difference in results of group I and group II patients. P-value < 0.05 was lower limit of significance.

**OBSERVATIONS AND RESULTS**

Treatment with bile acid binding resins, for the period of designed research, TC ie; total serum cholesterol decreased from 228.2±4.8 mg/dl on day-0 to 199.2±2.3 mg/dl on day-90. This reduction in total cholesterol was highly significant (P <0.001). The average percentage reduction in total cholesterol was -12.7%. Mean blood triglycerides level of 18 patients treated with psyllium husk was 169.2±2.9 mg/dl on day-0 which reduced to 164.5±4.5 mg/dl on day-90. The mean value differences were highly significant (P-value <0.001) when levels on day-0 and those on day-90 were compared. The percentage change between day-0 to day-90 was -2.81. Mean serum LDL-cholesterol reduced from 159.7±5.7 mg/dl to 129.5±2.8 mg/dl in 3 months. This change was highly significant (<0.001) when results of group I and group II were analysed. The percentage change was -18.88. In same group 18 patients treated with psyllium

husk, the mean HDL-cholesterol at day-0 was 34.6±1.8 mg/dl, which increased to 36.7±1.9 mg/dl on day-90. The result was highly significant (P <0.001) when values were compared at day-0 to day-90. The percentage increase in HDL-cholesterol from day-0 to day-90 was +6.24. In placebo group, 20 male and female patients of age range from 22 to 70 years, low density lipoprotein cholesterol at Day-0 was 150.75±2.67, which reduced to 148.80±2.28 at Day-90. Difference between these two values are non significant (P>0.05). In placebo group of patients high density lipoprotein cholesterol at Day-0 was 35.50±1.13 which increased to 35.75±1.07, which is non-significant change, when paired 't' test was applied for statistical analysis. The P-value was greater than 0.05. Results of total serum cholesterol and triglycerides in placebo group non significant (P-value >0.05). All results are elaborated in following table:

**TABLE NO: 1** Effects of drug and placebo on TC, TG, LDL-C, HDL-C in due period of Research Designed

Lipid	Placebo group (20 patients)			BABR group (18 patients)			
	Start	Stop	P Value	Start	Stop	P Value	Diff in %
T-C	215.95 ±2.47	208.70 ±5.38	>0.05	228.27 ±4.89	199.22 ±2.30	<0.001	9.37 %
TG	148.45 ±4.80	146.20 ±4.20	>0.05	169.27 ±9.92	164.50 ±8.56	<0.001	1.30 %
LDL-C	150.75 ±2.67	148.80 ±2.28	>0.05	159.72 ±5.70	129.55 ±2.81	<0.001	17.59 %
HDL-C	35.50 ±1.13	35.75 ±1.07	>0.05	34.61 ±1.85	36.77 ±1.96	<0.001	5.54 %

**Fote Note:** All observed parameters are measured in mg/dl. Start=start of treatment. Stop=end of the treatment. BABR = bile acid binding resins, T-C = Total-Cholesterol, TG = Triglycerides, LDL-C = low-density lipoproteins, HDL-C = high-density lipoproteins, P Value >0.05 means non significant, P Value <0.001 means highly significant, ± indicates standard error of mean.

**DISCUSSION**

Our research work results match with the study of Dodin S et al (2010)<sup>11</sup>, in which 60 primary hyperlipidemic patients were treated by psyllium husk 8 gram daily in divided doses for the period of 4 months. Triglycerides reduction was 4.11%, LDL-C was reduced to 27.21%. Our results also match with the result of . Pal S et al<sup>12</sup> who

observed almost same changes in lipid profile of thirty primary hyperlipidemic patients, treated with 6 gram of psyllium thrice daily for eight weeks. Our results match with the study of Khossousi A et al<sup>13</sup> in all parameters of lipid profile except their observation that HDL-C did not increase. It was only 0.49 % raised. Reason for this difference may be the genetic variation in patients suffering from primary hyperlipidemia. Various types of primary hyperlipidemia could respond in different manners with different drug regimen and duration of the treatment. Rosa Solà et al<sup>14</sup> did conduct placebo controlled trials, in which 15 male and female patients were treated with 16 gram psyllium husk in divided doses, thrice daily for the period of and half month. Results of the trial almost match with our results. In their results total-cholesterol reduction was 10.99%, triglycerides reduced from 184.99±12 mg/dl to 164±1.92 mg/dl (P value <0.001). In percentage it was -3.4%. Low-density lipoprotein cholesterol reduction was -19.87%. Our study is in contrast with the study of Allen KG et al<sup>15</sup> who observed more percentile changes in low density lipoprotein, high density lipoprotein cholesterol, and total serum cholesterol. Only change in triglycerides match with our study. They even observed 1% increase in HDL-C in placebo group but by psyllium treatment, HDL-C was decreased upto 0.3%. They did not mention the mechanisms by which psyllium decreased cholesterol. One mechanisms is that psyllium stimulate bile acid synthesis by  $\alpha$ -hydroxylase activity in hepatocytes. Agrawal AR et al<sup>16</sup> conducted placebo-controlled study and observed less increase in HDL-cholesterol and too much decrease levels of blood total cholesterol, LDL-cholesterol and triglycerides as compared to our study results. They observed 01.96% increase levels of HDL-C. Total cholesterol, LDL-cholesterol and triglycerides reduced -09.95%, -11.81%, and -03.73% respectively. This remarkable difference may be due to different sample size and change in duration of psyllium therapy.

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