

## SINGLE BLIND PLACEBO CONTROLLED STUDY OF PSYLLIUM FIBRES TO REDUCE RISK OF MYOCARDIAL INFARCTION

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### ABSTRACT

**Background:** Recent research studies claim that myocardial infarction as a major cause of morbidity and mortality throughout the world. Among other risk and predisposing factors atherosclerosis is one of the major risk for myocardial infarction. Each 1% increase in the serum cholesterol concentration results in 2 to 3% increase in coronary heart disease risk. By lowering serum 'bad' lipids, and increasing 'good' lipid, i.e.; HDL – cholesterol, atherosclerosis may be prevented and so the prevention of myocardial infarction ensues. Research study was conducted to examine the effects of Psyllium fibres to decrease 'bad' cholesterol (LDL – C, Triglycerides, and Serum Total Cholesterol) and increase 'good' cholesterol (HDL – C) which prevent the risk of myocardial infarction (MI). It was single blind placebo controlled research study.

**Patients and Methods:** Forty already diagnosed primary hyperlipidaemic patients were selected from Cardiology OPD of Jinnah Hospital, Karachi, Pakistan. Exclusion criteria were patients suffering from hypothyroidism, renal dysfunction, any hepatic disease. Consent Proforma was designed and got the approval from "Research Ethical Committee of Jinnah Postgraduate Medical Centre, Karachi". After explaining the limitations, consent was obtained from all study participants before they were recruited to the study. They were divided in two groups, 20 patients were on Psyllium husk fibres, 10 gram daily in divided doses. And 20 patients were kept on placebo as control group. Lipid profile of all participants was estimated at day – 0 and at day – 90. All other vital functions of patients were also estimated and kept on record. They were advised to visit clinic fortnightly.

**Results:** When results were compiled at the end of this study, it was observed that two patients discontinued taking the drug, due to metallic taste of psyllium fibres. Psyllium decreased serum total cholesterol from  $228.27 \pm 4.89$  mg/dl to  $119.22 \pm 2.30$  mg/dl,  $159.72 \pm 5.70$  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 three months of treatment. 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. Results of all parameters of lipid profile were significant when paired 't' test was applied for statistical analysis.

**Conclusion:** We concluded from this study that psyllium is an effective agent to maintain lipid profile parameters at normal limits in hyperlipidaemic patients, and normal limits of all lipid parameters play major role in prevention of atherosclerosis and MI.

**Key Words:** Myocardial Infarction, Hyperlipidemia, Atherosclerosis, Psyllium fibres.

### INTRODUCTION

Excess of blood lipids except HDL – cholesterol are dangerous to health and human heart but elevation of LDL – cholesterol is particularly associated with risk of coronary artery disease.<sup>1</sup> Moderately raised triglycerides, VLDL or remnants in the presence of low LDL – Cholesterol may also be atherogenic.<sup>2</sup> Atherosclerosis, if not controlled and treated at early stage of its development may lead to myocardial infarction.<sup>3</sup> Prevention and treatment of hyperlipidaemia are the elimination or modification of risk factors, if possible, in conjunction with treat-

ment of the specific lipid disorder.<sup>4</sup> For treating primary hyperlipidaemia, statins, fibric acids, nicotinic acid, bile acid binding resins including psyllium husk fibres are main drug groups used. For many years psyllium husk has been used as an agent for gastrointestinal disturbances but it also has remarkable hypolipidaemic effects.<sup>5</sup> Like other bile acid binding resins, psyllium fibres have similar mode of action. It binds to bile acids and decreases their absorption from intestine. This in turn stimulates the hepatic synthesis of bile acid from cholesterol and thus reducing the total and LDL – cholesterol levels. It is

also likely to decrease the reabsorption of cholesterol from intestine by decreasing the micelle formation. LDL – Cholesterol concentrations increase by about 0.5 mg/dl, when psyllium is added to the treatment regimen of patients who are already receiving statins or nicotinic acid.<sup>6</sup> Various studies have proved remarkable effects on reducing risk of coronary artery disease by decreasing serum lipids which are responsible for development of atherogenesis.<sup>7</sup> In developed countries like UK and US, lipid Research Clinics have been established to conduct research, starting from counseling on diet, exercise, and change in sedentary life style to medication and cardiovascular – related therapeutics.<sup>8</sup>

### PATIENTS AND METHODS

As it was research study on humans, consent Proforma was formatted initially and got approval from 'Ethical Committee for Research, JPMC, Karachi, Pakistan. The study was conducted at 'LIPID RESEARCH CLINIC', Jinnah Hospital Karachi, Pakistan from January to July 2009. Forty patients of primary hyperlipidaemia were initially recruited to this study, referred from OPD of Jinnah Hospital, Karachi. Untreated primary hyperlipidaemic male and female patients, age range from 21 to 65 years, were randomly selected. Patients with diabetes mellitus, peptic ulcer, renal disease, hepatic disease, hypothyroidism and alcoholism were excluded from the study by laboratory investigations, history and clinical examination. Written consent was obtained from all participants. The study period consisted of 3 months with fortnightly follow up visits. The required information like name, age, sex, occupation, address, previous medication, date of follow up visit and laboratory investigations of each patient was recorded. Initially medical history and physical examination of all patients were carried out. All the base line assessments were taken on the day of inclusion (Day – 0) in the study and a similar assessment was taken on Day – 90. After fulfilling the inclusion criteria, patients were randomly divided into two groups, i.e. Drug – 1 (Psyllium husk 10 gm / day) and Drug – 2 (placebo capsules, containing equal amounts of partly grinded wheat) groups. Patients of drug – 1 group were advised to take psyllium fibres 10 gm daily in three divided doses after or before each meal. Patients of drug – 2 group were provided placebo capsules, i.e. one capsule, three times a day, after meal for 90 days. Patients were called every 2 weeks for follow up to check blood pressure, weight, pulse rate and general appearance of the individual. Serum total cholesterol and triglycerides were estimated by the enzymatic calorimetric method.<sup>9</sup> Serum LDL – Cholesterol was calculated by Friedwald formula (LDL – Cholesterol = Total Cholesterol – (Triglycerides / 5 + HDL – Choles-

terol).<sup>10</sup> Serum HDL – cholesterol was determined by direct method, at day – 0 and day – 90. Data were expressed as the mean  $\pm$  SD and "t" test was applied to determine statistical significance as the difference. A probability value of < 0.05 was the limit of significance.

### RESULTS

This study reveals that when used psyllium fibres in 18 hyperlipidaemic patients were employed for a period of 3 months, mean total serum cholesterol decreased from  $228.8 \pm 4.8$  mg/dl on day – 0 to  $199.2 \pm 2.3$  mg/dl on day – 90. This reduction in total cholesterol was highly significant ( $P < 0.001$ ) when levels on day – 0 and those on day – 90 were compared. The average percentage reduction in total cholesterol was –12.7%. Two of 20 patients, discontinued taking psyllium due to its metallic taste. The mean serum triglyceride level of 18 patients treated with psyllium fibres was  $169.2 \pm 9.9$  mg/dl on day – 0 which reduced to  $164.5 \pm 8.5$  mg/dl on day – 90. These differences were highly significant ( $P < 0.001$ ) when levels on day – 0 and those on day – 90 were compared statistically. The percentage change between day – 0 was –2.81. In 18 primary hyperlipidaemic patients, when started treatment with psyllium husk, their mean serum LDL – C level at day – 0 was  $159.7 \pm 5.7$  mg/dl. This level reduced to  $129.5 \pm 2.8$  mg/dl at day – 90.

Table 1: *Changes in lipid profile in psyllium husk group of patients (n = 18).*

Parameter	At Day – 0	At Day – 90	% Change
T – C	228.27 $\pm$ 4.89	199.22 $\pm$ 2.30	-12.72
TG	169.27 $\pm$ 9.92	164.50 $\pm$ 8.56	-2.81
LDL – C	159.72 $\pm$ 5.70	129.55 $\pm$ 2.81	-18.88
HDL – C	34.61 $\pm$ 1.85	36.77 $\pm$ 1.96	+6.24

Table 2: *Changes in lipid profile in of patients on placebo groups (n = 20).*

Parameter	At Day – 0	At Day – 90	% Change
T – C	215.95 $\pm$ 2.47	208.70 $\pm$ 5.38	-3.35
TG	148.45 $\pm$ 4.80	146.20 $\pm$ 4.20	-1.51
LDL – C	150.75 $\pm$ 2.67	148.80 $\pm$ 2.28	-1.29
HDL – C	35.50 $\pm$ 1.13	35.75 $\pm$ 1.07	+0.70

#### Key:

$\pm$  indicates standard error of mean; (-) indicates decrease in percentage; (+) indicates increase in percentage; T – C stands for total cholesterol; TG stands for triglycerides; LDL – C stands for low density lipoprotein cholesterol; HDL – C stands for high density lipoprotein cholesterol; All observations are measured in mg/dl; Figures in parentheses indicate number of patients

Table 3: Comparison of changes in lipid profile parameters between placebo and psyllium group of patients in 90 days of treatment.

Parameter	Baseline	Post Treatment	P – Value	Baseline	Post Treatment	P – Value	% Difference in Groups
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±9.92	<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

**Key:**

± indicates standard error of mean; T – C stands for total cholesterol; TG stands for triglycerides; LDL – C stands for low density lipoprotein cholesterol; HDL – C stands for high density lipoprotein cholesterol; P – value > 0.05 indicates non significant; P – value < 0.001 indicates highly significant

When compared between day – 0 to day 90, this change was highly significant ( $P < 0.001$ ). The percentage change was –18.88. In 18 patients treated with psyllium husk, the mean HDL – C at day – 0 was  $34.6 \pm 1.8$  mg/dl, which increased to  $36.7 \pm 1.9$  mg/dl on day – 90. The result was highly significant ( $P < 0.001$ ) when values were compared on day – 0 to day – 90. The percentage increase in HDL – C from day – 0 to day – 90 was +6.24. In placebo group serum total cholesterol reduced from  $215.95 \pm 2.47$  mg/dl to  $208.70 \pm 5.38$  mg/dl, triglycerides reduced from  $148.45 \pm 4.80$  mg/dl to  $146.20 \pm 4.20$  mg/dl, LDL – cholesterol reduced from  $150.75 \pm 2.67$  mg/dl to  $148.80 \pm 2.28$  mg/dl. HDL – cholesterol raised from  $35.50 \pm 1.13$  mg/dl to  $35.75 \pm 1.07$  mg/dl in three months of treatment period. All results of placebo group are non-significant when analysed statistically. Results of all parameters are shown in table 1, 2 and 3.

**DISCUSSION**

The statistical analysis proved that psyllium fibers reduced triglycerides 2.81%, LDL – cholesterol 18.88% and serum total cholesterol 12.72%. High density lipoprotein cholesterol was increased 6.24%.

These results match with the study of Van Rosendaal et al<sup>11</sup> who observed almost the same changes in lipid profile of 31 hyperlipidaemic patients, treated with 6 gram of psyllium thrice daily for ten weeks. Results also match with the study reported by Blackwood et al<sup>12</sup> in all parameters of lipid profile. In their study a change in high density lipoprotein cholesterol was higher than in the present study. This difference may be due to genetic variation in patients suffering from primary hyperlipidaemia. Different type of primary hyperlipidaemia could respond in different manners with different drug regimen and duration of the treatment. Results of the study also match with results of Jenkins et al,<sup>13</sup> in which 57 primary hyperlipidaemic patients were treated by psyllium husk fibers 12 gram daily in

divided doses for the period of 8 weeks. In their observation triglyceride reduction was –7.12%, LDL – C was reduce to –10.31%. HDL – cholesterol raised upto +5.11%. Another study conducted by McCrindle et al<sup>14</sup> on placebo controlled trials, reported male primary hyperlipidemic patients of either sex were treated with six gram psyllium husk fibers in divided doses, thrice daily for a period of three months. Results of the trial were very close to our results. In their results total – cholesterol reduction was 15.71%, triglycerides reduced from  $171.12 \pm 7.77$  mg/dl to  $161 \pm 3.23$  mg/dl ( $P$  value < 0.001) (3.7%). The low density lipoprotein cholesterol and very low density lipoprotein cholesterol reduction was –17.93% and –10.29%, respectively. The present study is in contrast with the study of Sanchez – Bayle et al<sup>15</sup> who observed more changes in serum total cholesterol. The (–19.11%) only change in low density lipoprotein cholesterol match with our study. They did not mention the mode of action of psyllium to reduce cholesterol. One of the agreed mechanisms is that psyllium stimulates bile acid synthesis through 7 $\alpha$  – hydroxylase activity. Another mode of action of psyllium fibers to reduce cholesterol is diversion of hepatic cholesterol synthesis to bile acid production. Effect of psyllium on absorption of cholesterol and fat appeared minimal but it is a small contribution to the cholesterol lowering effect. Other mode of action of psyllium to reduce cholesterol synthesis such as inhibition of hepatic cholesterol synthesis by propionate and secondary effects of slowing glucose absorption from gastrointestinal tract may also contribute. Results of study conducted by Stoy et al<sup>16</sup> are in contrast with our results. They used ispaghula fibers in twenty nine primary hyperlipidaemic patients of both genders, i.e; male and female with age range from twenty eight to sixty years for a period of one month. They used psyllium husk fibers 12 gram daily, in divided doses with step I diet. They observed that psyllium husk has reduced low density lipoprotein – cholesterol

19.99%, serum total cholesterol 19.00%, triglycerides 6.96%, and increased HDL – cholesterol 4.30%. These results are in contrast with our research work observations. The obvious reason for this contrast is step I diet, which was strictly followed by their patients recruited for this research. They were made to stay at Lipid Research Centre. Approach to conduct research work on nutrition and nutritional related works was to be monitored separately as already described<sup>16</sup> (at their Lipid Research Centre). Results of our study are in contrast with another study.<sup>17</sup> Where they observed remarkable increase in high density lipoprotein cholesterol and very low levels of plasma total low density lipoprotein cholesterol, and triglycerides. They observed 9.11% increase levels of HDL – C. Total cholesterol, LDL – C and triglycerides reduced – 21.23%, –19.90%, and –7.00% respectively. This difference may be due to a change in sample size and period of drug administration. In their study, sample size was 200 hyperlipidaemic patients who used psyllium fibers five gram twice daily for a period of eighteen months. Statistically recommended sample size of patients, design of research study, controlled directions for follow up, counselling on psyllium husk intake and a good compliance of the drug to be used may change the outcome of the results.

Finally It was **concluded** from this research study that use of psyllium fibres reduce the risk of development of atherosclerosis and myocardial infarction by reducing serum total cholesterol, low density lipoprotein cholesterol, triglycerides, and increasing high density lipoprotein cholesterol.

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