ORIGINAL ARTICLE

New Slant on Hyperlipidemia

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ABSTRACT

Research study was conducted to examine the effects of psyllium on different types of lipids in primary hyperlipidemic patients. It was conducted in JPMC Karachi, Pakistan, from December 2008 to June 2009. Forty hyperlipidemic patients were included, in research. Out of these 40, twenty patients were on placebo as control/compare group, and twenty were on psyllium, 10 grams daily for the period of three months. Exclusion criteria was patients with hypothyroidism, alcoholism, renal and hepatic disease. Serum 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 ± SD and "t" test was applied to determine statistical significance of results. P value lesser than 0.05 was the limit of significance. When results compiled it was observed that two patients discontinued to take drug given, due to metallic test of psyllium husk. Psyllium decreased serum total cholesterol from 228.27±4.89 mg/dl to 199.22 ± 2.30 mg/dl, triglycerides from 169.27± 9.92 mg/dl to 164.5±8.56 mg/dl, LDL-Cholesterol from 159.72 ± 5.70 to 129.55± 2.81 mg/dl, and increased serum HDL-Cholesterol from 34.61±1.85 to 36.77±1.96 mg/dl in three months of treatment. Results of all parameters were significant when paired 't' test was applied for result analysis. At end of the research work we concluded that psyllium is very effective agent to maintain lipid profile parameters at normal limits in hyperlipidemic patients.

Key words: Blood lipids, low density lipoproteins, high density lipoproteins, cholesterol, resins.

INTRODUCTION

Recent research in medical sciences has explored on and explained morbidity and mortality rate due to lipid disorders. Hyperlipidemia is one of these disorders, which has changed older viewpoint on nutrition and lipids used in junk foods, daily caloric usage of energy and its biochemical and pharmacological effects on human body[1]. Cholesterol can't dissolve in the blood. It has to be transported to and from the cells by carriers called lipoproteins[2]. Types of serum lipids, along with triglycerides and Lp(a) cholesterol, make up human total -cholesterol count, which can be determined by lipid profile in routine medical investigations[3]. Together with other biochemical substances, low density lipoproteins can form plaque, a thick, hard deposit that can narrow the arteries and make them less flexible. This condition is known as atherosclerosis[4]. Most of our knowledge about atherosclerosis at young ages is derived from necropsy studies, which have inherent limitations. Detailed, in vivo data on atherosclerosis in young individuals are limited. Intravascular ultrasonography provides a unique opportunity for in vivo characterization of early atherosclerosis in a clinically relevant context[5]. Although patients with coronary artery disease typically become symptomatic after age 40 years, necropsy studies have demonstrated that atherosclerotic changes in the vessel wall begin early in life6. Characterization of coronary disease through postmortem examination of young subjects has important limitations, however, particularly the presence of non physiological conditions (arteries not pressure-distended) and fixation artifacts.Few in vivo data have documented the extent and severity of atherosclerosis in young, healthy subjects.[7] This atherosclerotic condition, even asymptomatic could be prevented only by lowering abnormally high bad cholesterol and by increasing high density cholesterol. Total serum cholesterol and triglycerides reduction is plus point in patients suffering from hyperlipidemia[5,8]. There are various drug groups which are used in treatment of hyperlipidemia; i.e. statins, niacin, fibrates, and bile acid binding resins including psyllium hydrophilic mucilloid. Psyllium fibers bind with bile acids in gastrointestinal tract and excrete them out of the body. This excretion of bile acids from body reduce bile acid pool in liver, so cholesterol is used in hepatocytes to synthesize bile acids, reducing over all concentration of cholesterol in blood[6-9].

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PATIENTS AND METHODS

The research was conducted at department of Pharmacology and therapeutics, Basic Medical Sciences Institute, Jinnah Postgraduate Medical Centre, Karachi, from December 2008 to June 2009. Forty patients of primary hyperlipidemia were initially enrolled in this study, selected from ward and OPD of National Institute of Cardiovascular Diseases, Karachi. Newly diagnosed and untreated primary hyperlipidemic male and female patients , age range from 17 to 70 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 such as name, age, sex, occupation, address, previous medication, date of follow up visit and laboratory investigations, etc of each patient was recorded on a Performa. Initially a detailed 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 of research design. After fulfilling the inclusion criteria patients were randomly 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 (ISPAGHULA) 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, TID, 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. Drug compliance to the regimen was monitored by interview and counseling at each clinical visit.

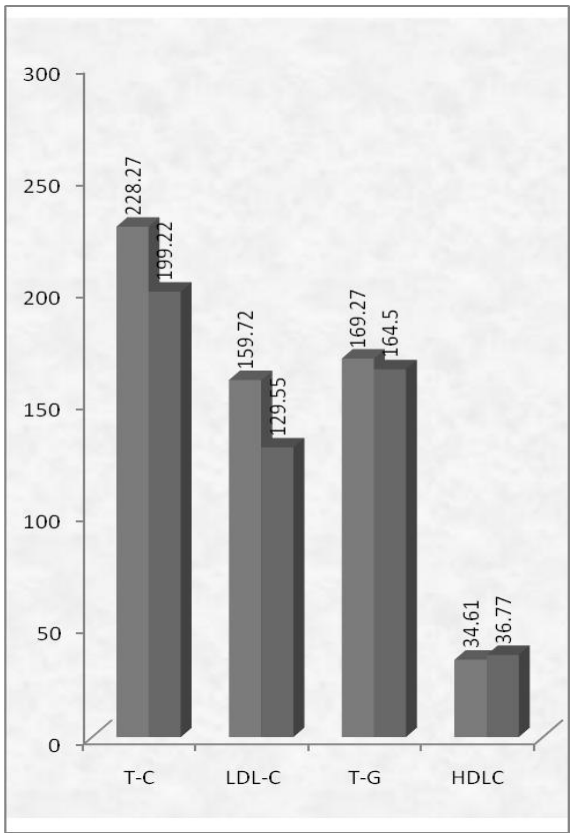
Serum total cholesterol and triglycerides were estimated by the enzymatic calorimetric Method.

Serum LDL-Cholesterol was calculated by Friedwald formula (LDL-Cholesterol = Total Cholesterol-(Triglycerides/5 +HDL-Cholesterol). Serum HDL-cholesterol was determined by direct method, at day-0 and day-90. Data were expressed as the mean ± SD and "t" test was applied to determine statistical significance as the difference. A probability value of <0.05 was the limit of significance.

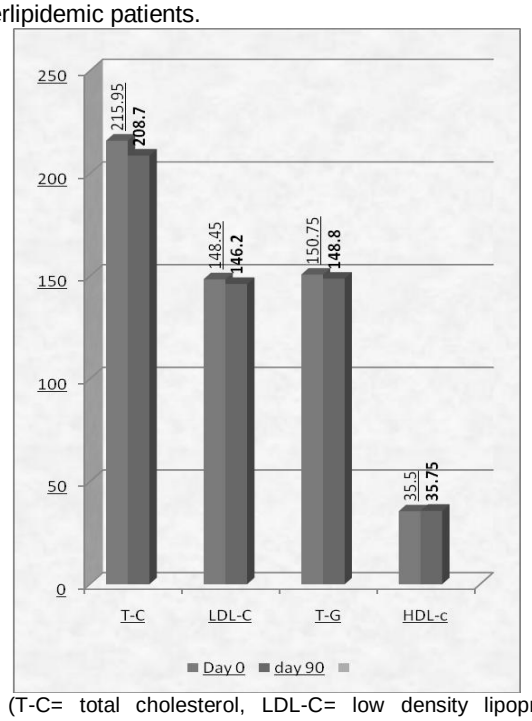
RESULTS

In 18 hyperlipidemic patients when 10 grams of psyllium fibers were used for 90 days, mean 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) when levels on day-0 and those on day-90 were compared. The average percentage reduction in total cholesterol was −12.7%. The mean serum triglycerides level of 18 patients treated with psyllium husk was 169.2±9.9 mg/dl on day-0 which reduced to 164.5±8.5 mg/dl on day-90. The mean value differences were highly significant (P <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. In 18 primary hyperlipidemic patients, when started treatment with psyllium husk, their mean serum LDL-C level at day-0 was 159.7±5.7 mg/dl. This level reduced to 129.5±2.8 mg/dl at day-90. When compared between day-0 to day-90, this change was highly significant (<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±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-C from day-0 to day-90 was +6.24(Graph 1, 2 and 3).

Graph 1: Effect of psyllium on lipid profile of 18 primary hyperlipidemic patients.

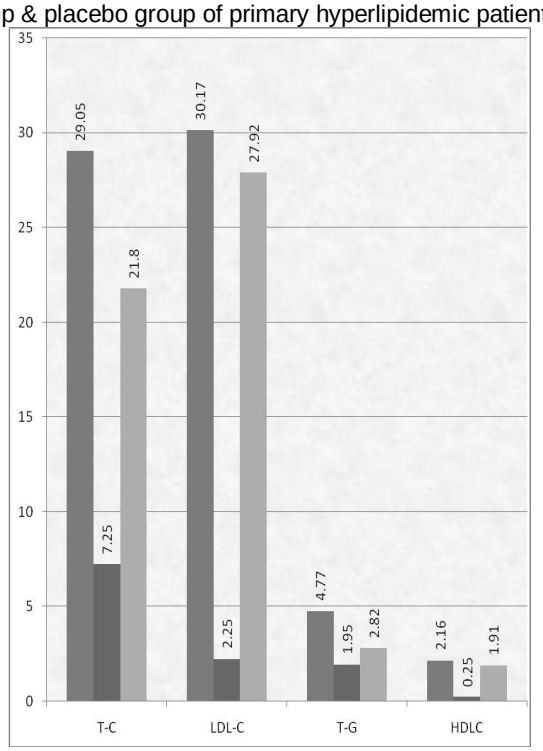


Graph 2: Effect of placebo on lipid profile of 20 primary hyperlipidemic patients.



Key: (T-C= total cholesterol, LDL-C= low density lipoprotein cholesterol, T-G= triglycerides, HDL-C= high density lipoprotein)

Graph 3: Comparison of effect on lipid profile in psyllium group & placebo group of primary hyperlipidemic patients.



Key: (T-C=Total Cholesterol, LDL-C=Low Density Lipoprotein Cholesterol, T-G=Triglycerides, HDL-C=High Density Lipoprotein Cholesterol . Blue (1st) bar shows effect of drug on specific parameter in percentage, red (2nd) bar shows effect of placebo in percentage and green (3rd) bar shows difference between two groups in percentage)

DISCUSSION

Treatment of hyperlipidemic patients with 10 grams of psyllium husk daily for the period of three months decreased serum total cholesterol 12.7%, triglycerides 2.81%, LDL-C 18.88% and HDL-C 6.24%. Results of all parameters (TC, TG, LDL-C and HDL-C) are highly significant (<0.001), when analyzed statistically. Our findings match with the study of Segawa K et al[9] who observed same changes in 49 hyperlipidemic patients, treated with three grams of psyllium thrice daily for the period of 6 months. In their study LDL-cholesterol reduced 17.98% and HDL-cholesterol increased 8.11%. Serum total cholesterol and triglycerides were not estimated by them. These findings also match with the study of Fagerber S[10] in lipid profile of 31 primary and secondary hyperlipidemic patients of age range from 30 to 70 years, when treated with 10 grams of psyllium fibers for three months. They observed 4.11% reduction in triglycerides, 21.17% reduction in low density lipoprotein cholesterol, 14,01% decrease in total serum cholesterol. HDL-cholesterol increased 6.91%. Results of our study also match with results of Frati-Munari AC[11], in which 37 primary hyperlipidemic patients were treated by psyllium fibers nine grams daily in divided doses for the period of six months. In his observation triglyceride reduction was 3.77%, LDL-C was reduced up to 21.91%. HDL-cholesterol increased 5.94%. Total serum cholesterol estimation was not included in his research work. Another placebo-based double blind study was conducted by Gupta RR et al[12] in which 21 primary hyperlipidemic patients of either sex were treated with 9 gram psyllium fibers in divided doses, thrice daily for the period of 105 days. Results of the trial almost match with our results. In their results total-cholesterol reduction was 12.1%, triglycerides reduced from 161.12±7.77 mg/dl to 155±2.12 mg/dl (P value <0.001). In percentage it was −2.9%. Observed LDL-C and VLDL-C reduction was −18.01% and −12.31%, respectively. Results of our study do not match with research work results of Jenkins DJ et al[13] who used eight grams psyllium fibers daily in 103 hyperlipidemic patients of both sex, male and female for the period of 9 months. They observed much more increase in HDL-Cholesterol and very less decreased levels of plasma total cholesterol, LDL-Cholesterol and triglycerides. They observed 10.73% increase levels of HDL-C. Total cholesterol, LDL-C and triglycerides reduced 19.23%, 31.90%, and 7.93% respectively. This difference may be due to large sample size and long period of drug used in their study. Our study results are in contrast with the results of study conducted by Roberts DCK et al[14] who observed less percentile decrease in serum total

cholesterol and triglycerides. Change in LDL-cholesterol match with our study, i.e. 17.66% in 26 hyperlipidemic patients when treated with four grams of psyllium fibers, thrice daily for the period of 7 months. HDL-cholesterol increased 9.54%, which is higher than our observations. Decrease in triglyceride was 8.11% and in serum total cholesterol it was 20.00%. They even observed 1% increase in HDL-cholesterol in placebo group. They did not mention the mechanisms by which psyllium increased HDL-cholesterol in placebo group. Results of study conducted by Sprecher DL et al[15] are also contradictory to our results, who observed 9.99% decrease in low density lipoprotein cholesterol and 2.19% increase in HDL-cholesterol, when 6 grams of psyllium was used in 9 primary hyperlipidemic patients for 5 weeks. The obvious reason for these differences are small sample size and dose of psyllium fibers used in their study.

REFERENCES

1. D. Steinberg. Earlier Intervention in the Management of Hypercholesterolemia What Are We Waiting For? J. Am. Coll. Cardiol. 2010; 56(8): 627 - 629.
2. J. S. Forrester. Redefining Normal Low-Density Lipoprotein Cholesterol A Strategy to Unseat Coronary Disease as the Nation's Leading Killer. J. Am. Coll. Cardiol. 2010; 56(8): 630 - 636.
3. E. M. Tuzcu, O. Bayturan, and S. Kapadia. Coronary intravascular ultrasound: a closer view**.** Heart 2010; 96(16): 1318 - 1324.
4. M. Philippova, Y. Suter, S. Toggweiler, A. W. Schoenenberger, M. B. Joshi, E. Kyriakakis, P. Erne, and T. J. Resink. T-cadherin is present on endothelial microparticles and is elevated in plasma in early atherosclerosis**.** Eur. Heart J. 2010; (2010) ehq206v1.
5. A.E. Donald, M. Charakida, E. Falaschetti, D. A. Lawlor, J. P. Halcox, J. Golding, A. D. Hingorani, G. D. Smith, and J. E. Deanfield. Determinants of vascular phenotype in a large childhood population: the Avon Longitudinal Study of Parents and Children (ALSPAC)**.** Eur. Heart J. 2010; 31(12): 1502 - 1510.
6. A.Myredal, W. Osika, Li Ming Gan, P. Friberg, and M. Johansson. Increased intima thickness of the radial artery in patients with coronary heart disease**.** Vascular Medicine, 2010; 15(1): 33 - 37.
7. G. D. Giannoglou, K. C. Koskinas, D. N. Tziakas, A. G. Ziakas, A. P. Antoniadis, I. K. Tentes, and G. E. Parcharidis. Total Cholesterol Content of Erythrocyte Membranes and Coronary Atherosclerosis: An Intravascular Ultrasound Pilot Study**.** Angiology 2009; 60(6): 676 - 682.
8. S. Amirbekian, R. C. Long Jr., M. A. Consolini, J. Suo, N. J. Willett, S. W. Fielden, D. P. Giddens, W. R. Taylor, and J. N. Oshinski. In vivo assessment of blood flow patterns in abdominal aorta of mice with MRI: implications for AAA localization**.** Am J Physiol Heart Circ Physiol 2009; 297(4): H1290 - H1295.
9. Segawa K, Kataoka T, Fukuo Y. Cholesterol-Lowering Effects of Psyllium Seed Associated with Urea Metabolism. Biol Pharm Bull. 1998;21:184–187
10. Fagerberg S. The effects of a bulk laxative (Metamucil) on fasting blood glucose, serum, lipids and other variables in constipated patients with non-insulin dependent adult diabetes. Curr Ther Res. 1982;31:166–172.
11. Frati-Munari AC, Fernandez-Harp JA, Becerril M, Chavez-Negrete A, Banales-Ham M. Decrease in serum lipids, glycemia and bodyweight by plantago psyllium in obese and diabetic patients. Arch Invest Med (Mex) 1983;14:259–268
12. Gupta RR, Agrawal CG, Singh GP, Ghatak A. Lipid-lowering efficacy of psyllium hydrophilic mucilloid in non insulin dependent diabetes mellitus with hyperlipidaemia. Indian J Med Res. 1994;100:237–241.
13. Jenkins DJ, Kendall CW, Vuksan V, Vidgen E, Parker T, Faulkner D, Mehling CC, Garsetti M, Testolin G, Cunnane SC, Ryan MA, Corey PN. Soluble fibre intake at a dose approved by the US Food and Drug administration for a claim of health benefits: serum lipid risk factors for cardiovascular disease assessed in a randomized controlled crossover trial. Am J Clin Nutr. 2002;75:834–9.
14. Roberts DCK, Truswell AS, Bencke A, Dewar HM, Farmakalidis E. The cholesterol-lowering effect of a breakfast cereal containing psyllium fibre. Med J Aust. 1994;161:660–664.
15. Sprecher DL, Harris BV, Goldberg AC, Anderson EC, Bayuk LM, Russell BS, Crone DS, Quinn C, Bateman J, Kuzmak BR. Efficacy of Psyllium in Reducing Serum Cholesterol Levels in Hypercholesterolemic Patients on High-or Low-Fat Diets. Ann Intern Med. 1993;119:545–554.