

The Effect of Psyllium Fibre supplement on Lipid Profile In Patients with Non-Insulin-Dependant Diabetes Mellitus (NIDDM)*

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INTRODUCTION

Dietary fibre is widely recognized to have beneficial effect in-patients with NIDDM. In particular, water-soluble fibre has been associated with improved glycaemic control and lowering of blood lipid (1). These effects are not due to increased insulin secretion but probably due to increased secretion of VIP and GIP, increased cholesterol binding in the gut and increased intestinal transit time (2). The American Diabetes Association has currently recommended a daily intake of 40g of soluble fibre (3).

When foods of known glycaemic index are combined together in a meal, their glycaemic profile changes and the differences between foods of high and low glycaemic index tend to disappear (4). It is therefore quite possible that the addition of fibre to a meal or snack will improve its glycaemic profile.

Most studies on fibre supplements have been of short duration (2). A pilot study done in the Diabetes Clinic of the Ramakrishna Mission Seva Pratishthan (RKMSPP) showed a beneficial effect of fibre on glucose profiles (manuscript under preparation). We have now carried out a long-term study to see whether prolonged fibre use conferred additional cardioprotective benefits that did not show up in short term studies.

Diabetics have a two to four times higher risk of cardiovascular mortality compared to non-diabetic controls, (5). One potentially correctable cause for this is hyperlipidaemia. The commonest lipid abnormality in NIDDM is hypertriglyceridaemia, accompanied usually by a modest rise of LDL and low HDL levels (6, 7). However, hypertriglyceridaemia improves with improvement of diabetic control and is not a major independent risk factor. On the other hand, lowering the LDL and raising the HDL level have been shown to confer considerable protection on non-diabetic subjects, (8). There is every reason to believe that the effects in NIDDM patients will be equally cardioprotective.

Psyllium fibre (isabgul) has been shown to

improve lipid and glucose profiles (9). A water soluble preparation (Naturolax) has recently become available and we have used it in our study.

MATERIAL

Patients with stable NIDDM were recruited from the Diabetes Clinic of the Ramakrishna Mission Seva Pratishthan. Eligible subjects were required to have not more than 10% variation of their fasting or post prandial blood glucose levels over the past six months (10). They had to be free from major cardiovascular, renal or gastro-intestinal disease. Patients with known hyperlipidaemia were excluded. The study protocol, was approved by the local Review Committee. Fifteen subjects, 11 male and 4 females, mean age 55.8 years, ultimately completed the study. Seven healthy non-diabetic persons, 5 male, 2 female, mean age 46 years, were studied as controls.

Psyllium fibre was made available as 'Naturolax', manufactured by Infar Ltd.

Data were calculated a mean \pm SEM. Students 't' test was employed to compare data and the level of significance was set at $p = 0.05$.

METHODS

On Day 1 the subjects presented in the fasting state. They had a thorough clinical examination, ECG and urinalysis. Blood from an antecubital vein was obtained for the measurement of glucose, urea, creatinine, total cholesterol, LDL and HDL cholesterol, triglyceride, liver function tests and a routine haemogram. Serum was prepared from the blood sample and stored at 4°C till it was analysed later on the same day. The subjects took 7.5g of psyllium fibre, twice daily, 15 min. before breakfast and the evening meal. They were seen at monthly intervals and encouraged to attend the Diabetes Clinic between visits if they so wished. On day 90, the entire procedure of Day 1 was repeated. The first 6 diabetic subjects had Oral Glucose Tolerance Tests (OGTT's) done on Days 1 and 90 using 75g of glucose with blood sampling being done at 0, 15, 30, 45, 60, 90, and 120 minutes.

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No alteration in diet or treatment was advised during the study. A dietary history based on patient recall was taken on Days 1 and 90.

Three major lipoprotein classes, HDL, LDL, and VLDL were separated utilising the selective precipitation technique of Ononogba and Lewis (11) and Warnick and Albers (12), and quantitatively estimated by measuring the cholesterol content of the fractions, utilising the method of Zlatkis et al (13) as modified by Nath and Nath et al (14). Triglyceride was measured by the method of Nori and Frings (15).

RESULTS

All the subjects and controls completed the study. None reported any side effect or any alteration in bowel habits. All the safety parameters, like ECG, blood biochemistry remained unchanged. The fasting glucose values fell in the NIDDM subjects (Table 1). This was reflected in the improved glucose profiles on OGTT's done on the first 6 subjects (Fig. 1). The area under the curve (AUC) dropped from 349 ± 136 to 272 ± 85 ($p = n. s.$). This improvement was felt to be due to increased patient interest and more frequent clinic visits, and could not be attributed to fibre alone. Hence further OGTT'S were not done.



Table 1 Fasting blood glucose levels (FBG) before and after psyllium fibre.			
	FBG (mg/dl) Before fibre	FBG (mg/dl) After fibre	P
NIDDM(n=15)	114 ± 11.8	103 ± 1.8	n.s.
Control (n=7)	73 ± 3.5	71 ± 4.1	n.s.

Table 2 Total Cholesterol (TC) and triglyceride (TG) level (mg/dl) before and after psyllium fibre						
	TC			TG		
	Before	After	P	Before	After	P
NIDDM (n=15)	230 ± 11	197 ± 6	0.02	121 ± 25	97 ± 13	n.s.
Control (n=17)	192 ± 5	180 ± 8	0.02	104 ± 8	88 ± 10	n.s.

In the diabetic subjects total cholesterol dropped from 230 ± 11 mg/dl to 197 ± 6 mg/dl ($p = 0.02$). In the controls total cholesterol dropped from 192 ± 5 mg/dl to 180 ± 8 mg/dl ($p = 0.02$) (Table 2). Comparison between subjects and controls showed that pre-treatment total cholesterol was significantly higher in the subjects ($p = 0.01$); however, the post treatment values were not different between subjects and controls.

LDL cholesterol dropped from 129 ± 9 mg/dl to 95 ± 6 mg/dl ($p < 0.01$) in the diabetic subjects and from 106 ± 7 mg/dl to 92 ± 7 mg/dl in controls ($p < 0.01$). LDL cholesterol was higher in the pre-treatment subjects ($p = 0.04$) compared to control, but the post treatment values were not different. (Table 3) HDL cholesterol rose from 76 ± 5 mg/dl to 82 ± 5 mg/dl ($p = n. s.$) in the diabetic subjects and from 65 ± 5 mg/dl to 66 ± 7 mg/dl in controls ($p = n. s.$) (Table 3).

Table 3 HDL cholesterol (HDL-C), LDL Cholesterol (LDL-C) and HDL:LDL ratio before and after psyllium fibre									
	HDL-C			LDL-C			HDL:LDL		
	Before	After	P	Before	After	P	Before	After	P
NIDDM (n=15)	76 ± 5	82 ± 5	n.s	129 ± 9	95 ± 6	<0.01	0.65 ± .08	0.96 ± .12	<0.1
Control (n=17)	65 ± 5	66 ± 7	n.s.	106 ± 7	92 ± 7	<0.01	0.61 ±.08	0.76 ± .13	n.s

Comparison between diabetic subjects and controls showed no difference when the pre-treatment and post-treatment HDL-cholesterol values were compared.

DISCUSSION:

The beneficial effects of soluble dietary fibre on the lipid profile are well documented (9, 16). In most studies subjects had to consume over 100 gm. of fibre each day to achieve a significant fall in total cholesterol or LDL cholesterol levels. High doses of fibre lack universal acceptance for easily understood reasons. We found that psyllium fibre in a dose as low as 7.5gm twice daily had an appreciable impact on lipid profiles. The finding has since been validated many times in the authors' clinical experience. At this dose, there were no side effects and no effects on bowel function. The fibre supplement was fully acceptable and culturally appropriate in our setting.

The mechanism by which lipid profiles were altered remains elusive, however, it is widely felt that psyllium fibre acts as a bile salt sequestrant in the gut, and this hampers the enterohepatic circulation of cholesterol (10). Definite proof is still lacking.

In the case of oat bran, it has been suggested that fibre acts simply by displacing high cholesterol foods from the diet without any intrinsic lipid lowering effects (17). The subjects in the study that came to this conclusion had to ingest 100gm of fibre or placebo daily. Automatically, their intake of high fat foods was reduced. A similar displacement mechanism is unlikely in the case of psyllium fibre, because the dose used was very small. The diabetic subjects and controls were asked to continue with their usual diet. A dietary history based on patient recall was taken on Days 1 and 90. These showed that diets were similar for all participants and that they had not undertaken any dietary manipulation on their own during the course of the study.

It is of note that the pre-treatment total cholesterol was higher in the diabetic subjects compared with controls. This was perhaps due to the fact that dyslipidaemia, NIDDM, obesity, hypertension tended to cluster together (7, 18). The largest impact of psyllium fibre was on LDL-cholesterol and to a lesser extent on total cholesterol. Triglycerides and HDL-cholesterol were not

Triglycerides fell from 121 ± 25 mg/dl to 97 ± 13 mg/dl ($p = n. s.$), in the diabetic subjects. In controls, triglycerides fell from 104 ± 8 mg/dl to 88 ± 10 mg/dl ($p = n. s.$) When the diabetic subjects were compared with controls, there were no differences in the triglyceride levels (Table 2). affected. Non-diabetic controls benefitted in a manner similar to the NIDDM subjects. The difference in LDL-cholesterol and total cholesterol between diabetic subjects and controls tended to disappear at the end of the study.

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REFERENCES:

1. Munoz JM. Fibre and diabetes. *Diabetes Care*. 1984; 7: 297-300.
2. Simpson HCR, Lousley S., Geekie M, et al. A high carbohydrate leguminous fibre diet improves all aspects of diabetic control. *Lancet*. 1981; 1: 1-5.
3. American Diabetes Association: Nutritional recommendations and principles for individuals with diabetes mellitus. *Diabetes Care*. 1987; 10: 126-132.
4. Nuttal FQ, Mooradian AD, DeMarais R, et al. The glycemic effect of different meals approximately isocaloric and similar in protein, carbohydrate and fat content as calculated using ADA exchange lists. *Diabetes Care*. 1983; 6: 432-435
5. Garcia MJ, McNamara PM, Gordon T, et al. Morbidity and mortality in diabetics in the Framingham population. Sixteen-year follow-up study. *Diabetes*. 1974; 23: 105-111.
6. Kissebah AH, Alfarsi S, Evans DJ, Adams P.W. Integrated regulation of very low-density lipoprotein triglyceride and apolipoprotein-B kinetics in non-insulin dependent diabetes mellitus. *Diabetes*. 1982; 31: 217-225.
7. Kissebah AH, Alfarsi S, Evans DJ, Adams P.W. Plasma low-density lipoprotein transport

- kinetics in non-insulin dependent diabetes mellitus. *J. Clin Invest.* 1983; 71: 655-667.
8. Lipid Research Clinics Program: The lipid research clinics coronary primary prevention trial results. I. Reduction of incidence of coronary heart disease. II. The relationship of reduction in incidence of coronary heart disease to cholesterol lowering. *J. Am. Med Assoc.* 1984; 251: 315-374.
 9. Platt R. Oat bran mania. *Diabetes forecast.* December 1989; 18-21.
 10. Sen Aditi, Nath RL, Bandyopadhyaya RA. A study on the determination of true sugar in blood by ortho-toluidine method under local conditions. *J Inst. Chemists (India)* 1982; 54: 250-254.
 11. Ononogba IC, Lewis B. Lipoprotein fractionation by a precipitation method – a simple quantitative procedure. *Clin. Chem. Acta* 1976; 71: 307-402.
 12. Warnick GR, Albers JJ. A comprehensive evaluation of the heparin-manganese iron precipitation procedure of estimating high-density lipoprotein cholesterol. *J. Lipid Res.* 1973; 19: 65-76.
 13. Zlatkis A, Zak B, Boyle GJA. New method for the direct determination of serum cholesterol. *J. Lab. Clin Med* 1953; 486-492.
 14. Nath RL, Nath RK. *Practical biochemistry in clinical medicine.* 2nd Ed., 1990, p. 112-118; Academic Publishers, Calcutta.
 15. Nori P, Frings S, Christopher S. Improved method of determination of triglyceride in serum. *Clin Chem* 1973; 19: 1201-1202.
 16. Bell LP, Hectorne K, Raynolds H, Balm TK, Hunnim-Hame DB. Cholesterol lowering effects of psyllium hydrophilic mucilloid adjunct therapy to a prudent diet for patients with mild to moderate hyper-cholesterolemia. *JAMA* 1989; 261: 3419-3423.
 17. Swain JF, Rouse IL, Curley CB, Sacks FM. Comparison of the effects of oat bran and low fiber wheat on serum lipoprotein levels and blood pressure. *N Engl J Med* 1990; 322: 147-152.
 18. Reaven GR. Role of insulin resistance in human disease. *Diabetes* 1988; 37: 1595-1607.