TRIAL OF LOW GLYCEMIC DIET AND ACARBOSE THERAPY FOR CONTROL OF POST-PRANDIAL HYPERGLYCEMIA IN TYPE 2 DIABETES MELLITUS: PRELIMINARY REPORT.

J M Ghosh

ABSTRACT

Several trials have shown low glycemic index (G.I.) foods have beneficial effects in control of hyperglycemia especially in type 2 diabetes mellitus (T2DM) where first phase insulin secretion by beta cells of pancreas is defective. Substantially reducing high G.I. starchy rice and wheat preparations in daily diet and replacing them by low G.I. and popular Bengal gram and pulses as staples, helped ensure satiety and adequate calories. Combined with acarbose, the modified diet resulted in significant decline in post-prandial blood glucose during six months follow-up of T2DM cases, large majority of which were cases of secondary failure with oral hypoglycemic agents (OHA). It is suggested that before adding Insulin in cases of OHA failure, adequate trial of low G.I. diet and acarbose should be routinely tried.

KEY WORDS: Type 2 diabetes mellitus; Glycemic index; Acarbose.

INTRODUCTION

Several trials (1-3) have shown beneficial effects of low glycemic index diets in the control of postprandial hyperglycemia in type 2 diabetes mellitus (T2DM). Viswanathan et al (4) in 1981 and Dilwary et al (5) in 1987 showed the same using Indian foods. In T2DM, the usual diet modification is to stop intake of sugar and potatoes, stop or reduce rice intake and replace by wheat products. However both boiled rice and wheat flour preparations e.g. bread, *chapattis* have the same high glycemic indices (G.I.) i.e.72.

First phase insulin secretion by the β–cells of pancreas is defective in T2DM and in impaired glucose tolerance (IGT). Both rice and wheat preparations, with high G.I. as the principal sources of calories, logically appear unsuitable especially in cases of secondary failure with oral hypoglycemic agents (OHA) e.g. sulfonylureas and metformin.

Majority of Indian T2DM's have normal or less than normal bodyweight. Quantitatively reducing rice and wheat products (and stoppage of potatoes) generally result in lower calorie intake relative to subjects' activity status [30 calorie/kg bodyweight being the recommendation of Indian Diabetes 2000 guidelines (6)]. It also causes less satiety, loss of weight and frequent failure of compliance.

While modifying diet in T2DM due importance should be given to the G.I. of popular and staple food items not only to provide adequate calories, proteins, fiber etc. but also prevent post-prandial hyperglycemia. Pulses which are grown almost exclusively in south Asia are popular complex carbohydrates having in general relatively low G.I. and containing substantial protein and fibre. Bengal gram (*cicer arietinum*) or *channa dal* contain 64% carbohydrates with G.I. 33 to 42, protein 22%, fiber 13.6gm/100gm and gives 327 kcal/100gm (7). Other pulses e.g. *urad*, *moong*, *masur*, *matar* and legumes contain carbohydrates with similar G.I., protein, fibre and calorie content. Therefore these are ideally suited as staples in Indian T2DM's provided these could quantitatively replace rice and wheat products in daily diet as the main energy sources. To do so, pulses need to be acceptably cooked in the form of *chapatties* or *parathas* which these patients are habituated to take during principal meals instead of wheat and rice preparations. This will ensure adequate calories, satiety and at the same time control post-prandial hyperglycemia.

B9 Collins Path, Bidhannagar, Durgapur – 713212, email: ghoshjm@sancharnet.in

A trial was undertaken using preparations of *chattoo* / *bason* (flour of roasted / unroasted bengal gram) as staples in a diet menu plan, quantitatively replacing wheat and rice in principal meals along with an alpha-glucosidase inhibitor as anti-diabetic drug, for T2DM cases, most of whom had secondary OHA failure.

MATERIALS AND METHODS

During the year 2003-04, 56 T2DM cases, 41 males and 15 females, whose average post prandial blood glucose (PPBS) was more than 140 mg%, were included in the trial. At least three available PPBS reports, during past one year were used to calculate the average. Five of them (Patient 1, 18, 27, 31 and 45) were recently diagnosed T2DM cases with duration less than one year. They were not taking any anti-diabetic drugs before inclusion in the trial. The rest 51 cases were having T2DM for more than one year. They were under professional supervision and follow-up, taking usually two OHA's e.g. sulfonylurea and metformin. None of these cases had taken insulin or acarbose before trial.

Average age of the patients was 54 years, average weight was 58 kg, duration of T2DM varied between 2 months to 40 years. !8 patients had hypertension, 6 had neuropathy, 2 patients each had nephropathy and retinopathy and 2 were diagnosed to have ischemic heart disease by conventional methods.

Diet Before Inclusion in Trial

5 new cases of T2DM were on unrestricted diet. The rest 51, were more or less on 1540 kcal diet. Sample menu and diet is shown in Table 1 and 2. The estimate was based on recall. As per the Indian Diabetes 2000 diet guidelines (6) these patients should have been on a diet of more than 1700cal, @ 30cal/ kg. They were having 830 kcal (275gm) of high G.I. (i.e.72) wheat preparations and only 40 kcal dal and 185 kcal milk/ non-veg items as low G.I. items (Table-2). Protein content of this diet was about 26.5gm/day and fat about 9% which were far below the same guidelines i.e. 0.8gm/kg protein and 20-25% of total calories as fat.

Table - 1 Sample of Pre-treatment Diet Menu - 1500 kcal (approx).

Time	Item	Servings	Ingre-dients	Amt.	Kcal.
Morning tea	Tea	1cup	milk	30ml	40
	Biscuits	2 nos	w.f.*	15gm	75
B'fast	Chapatties/ bread -	2 nos	w.f.*	70gm	170
	Veg curry	1k	v.#	50gm	90
Lunch	Chapatties	3 nos	w.f.*	105gm	255
	Dal-	1k	Pulses$	25 gm	40
	Veg curry-	1 k	v.#	100gm	90
	Non-veg	1 piece	f/c/e ♠	50gm	100
	Curd (Vegetarian)	¾ cup	milk	120gm	-do-
Evening tea	Tea	1 cup	milk	20ml	40
	Biscuits/ puffed rice	2 nos / 1k	w.f *./ rice	15gm	75
Dinner	chapatties-	3 nos	w.f.*	70gm	255
	Veg curry-	1 cup	v.#	100gm	90
	Milk-	1 cup			85
			Oil	15gm	135
			Total calories -		**1540**

*c- cup =125ml; k – katori =200ml; *w.f. – wheat flour;♥ - bg.fl - Bengal gram flour (besan or chattoo); ♠ fish / chicken / egg; # v – all vegetable except potato; $ Pulses – Dals e.g. masur, chana, urad, arhar, matar Calorie contents of menus calculated on the basis of National Institute of Nutrition, Hyderabad publications [8].*

Table-2: Pre-treatment Diet (Summary) :-

Items	gm/cup/k	kcal
Tea	2 cups	80
Wheat flour	275gm	830
Dal (pulses)	25gm	40
Veg except potatoes	250gm	270
Curd or	3/4 cup	100
Fish/meat/egg -	1 piece	-do-
Milk	1cup	85
Oil	15gm	135
Total calories -		1540

Trial Diet

In designing 1800 kcal low glycemic diet (sample shown in Tables 3 and 4), high glycemic wheat flour items in the pre-treatment diet (Table-1) were reduced to about 110 kcal of boiled rice and 100 kcal wheat flour and were replaced by 780 kcal (225gm) of Bengal gram flour preparations; quantity of dal was increased from 25gm (40 kcal) to 75gm (120 kcal) (Table-4). All these low glycemic (G.I.-35) items constituted more than 60% of total calories, protein content of which was 99gm/day. In this way, to satisfy energy (30kcal/ kg) and satiety requirements, about 300 additional kcal could be provided in trial diet.

To make at least three *chappatis*, 100gm (20 teaspoonful) of *chattoo*, 5 tsp of atta and one tsp oil were dry-mixed thoroughly, kneaded well with sprinkling of water to make soft dough balls, before rolling and baking; frying in little oil or ghee and this made three acceptable *parathas*. Adding spices to the dough or fillings for *paratha* rolls helped acceptability. *Parathas* (*besan-ka-pura or chilla*) (8, 9) could also be fried from batter of 100 gm *besan* by adding a pinch of salt. Fermenting the batter helped making tastier preparations. For variety, soaked and fried whole Bengal gram, legumes e.g. peas, beans during breakfast were encouraged, in place of *chapattis* or *parathas*. Dry fried Bengal gram, peanuts, dry *besan* preparations e.g. *gathias, bhujias* with tea were allowed as snacks in place of biscuits, puffed rice etc.

Initially the changes in diet caused problems in acceptance due to the unfamiliarity especially in cooking techniques but the same could be sorted out by the initiatives of the spouses who came forward with their own innovations, while being rigid in not increasing the quantities of rice and wheat products especially as snacks. Overall, the trial diet with variations had satisfactory compliance at follow-up for 6 months.

Table 3: Sample of 1800 kcal (approx).**Diet Menus During Treatment**

Time	Item	Servings	Ingre-dients	Amt.	Kcal.
6 am	Tea	1 cup	Milk	60 ml	40
8 am	Chapatties/	3nos	♥bg.fl	100gm	350
B'fast	paratha		+w.f.*	+25gm	+50 =400
	Veg curry	½ k	v.#	50gm	45
1 pm	Rice (boiled)	100g	Rice	35gm(dry)	110
(lunch)	*Dal	2 k	Pulses $	50 gm	80
	Vegetables curry	1k	v.#	100gm	90
	Non-veg -	1 piece	f/c/e ♠	50gm	100
	Curd				
	(vegetarian)	¾ cup	milk	120gm	-do-
4 pm	Tea	1 cup	Milk	60 ml	40
	Pakodas		♥bg.fl	25gm	80
6 pm	Fruits (seasonal)-	one			100
9 pm	Roti /	3nos	♥bg.fl.	100gm	350
	paratha		+w.f.*	+25g	+50 =400
	*Dal -	1k	Pulses$	25 gm	40
	Vegetables-	1/2k	v.#	50gm	45
	Curd (if veg)	3/4 c	Milk	120 gm	80
	Non-veg -	One piece	f/c/e ♠	50gm	-do-
			Oil	20 gm	175
			Total Calories		**1825**

*c- cup =125ml; k – katori =200ml; *w.f. – wheat flour; ♥ - bg.fl -Bengal gram flour (besan or chattoo); ♠ fish / chicken / egg; # v –all vegetable except potato; $ Pulses – Dals e.g. masur, chana, urad, arhar, matar*

Calorie contents of menus calculated on the basis of National Institute of Nutrition, Hyderabad publications [8].

Table 4: Summary of 1800 kcal Diet

Items	gm/cup/k	kcal
Tea	2 cups	80
Rice(boiled)	100gm	110
Wheat flour	50gm	100
Dal (pulses)	75gm	120
Bengal gram flour	225gm	780
Vegetables except potatoes	200gm	180
Curd or f/c/e	1 ½ c 1 pce	180
Fruits	one	100
Oil	20gm	175
	Total:	**1825**

Drug

All 56 patients were put on acarbose, usually 50 mg three times a day to start with, with three principal meals. The dose was decreased to 25mg three times a day when PPBS came down to satisfactory levels.

Counseling and Follow Up

Before inclusion in the trial each patients were counseled on the following points:-

a) On causes and effects of hyperglycemia especially in causation of complications and the imperative need for monthly post-prandial blood sugar tests to monitor results of treatment;

b) On the potentiality of starchy preparations e.g. wheat, rice and potato to cause high post-prandial rise of blood sugar; therefore the need to quantitatively replace these by *chappatis* or *parathas* made of *chattoo* or *besan* and increasing intake of *dal* in the principal meals for adequate calories and satiety at the same time prevent post-prandial surge of blood sugar;

c) Detailed instructions regarding methods of cooking *chapattis* or *parathas* from flour of bengal gram (*chattoo* or *besan*) were given particularly to the spouses;

d) Reiterating the need to chew (or grind the same, if edentulous) acarbose tablets, 25 or 50 mg 3 times a day with each principal meal especially before giving blood samples for glucose estimation;

At each visit during follow-up, careful enquiries were made regarding their continued adherence to the changed diet by recall. Any problems in the preparations and

acceptability thereof were discussed including any suggestions regarding changes in cooking while no change in quantities of rice and wheat products were reiterated.

RESULTS

Results of at least three or more monthly samples of PPBS during six months of trial were recorded and averaged (Table-5). Overall mean decline (Table-6) in PPBS was 85.3mgm% (4.7mmol/l). Table-5a showed the decline was significant ($p < 0.001$).

Amongst 5 new cases (Table-5) one had insignificant decline in PPBS of 10mgm%, but in 4 others average reductions were 33, 100, 120.5 and 344 mg % which were considered satisfactory.

Of the 51 old cases, 24 had uncontrolled T2DM for 1 to 5yrs and 27 for more than 5 years, all of whom apparently were having secondary failure with OHA. In these cases average PPBS declined to <140mg% in 20 cases and between 140 to 200mg% in 24 cases. In 7 cases PPBS remained more than 200mg%. Overall, goal of reducing post-prandial hyperglycemia to <200mg% could be achieved in 48 out of 56 patients included in the trial i.e. in 85.7% of cases.

Table 5: **Blood Glucose Response to Trial Diet and Acarbose**

Pt no.	Age kg	Wt (months)	Duration *BG Start	avg #BG	avg End	BG Decline
*1	55	57	2	197	164	33
2	74	54	480	200	112.5	87.5
3	60	47	84	163	141.5	21.5
4	64	42	312	231	226	5
5	60	54	180	198	126	72
6	51	70	12	226	150	76
7	60	70	96	145	106.5	38.5
8	70	59	180	324	122	202
9	38	58	84	221.5	103	118.5
10	49	61	48	212	269	-57
11	51	73	12	226	165	61
12	58	51	120	270	212.5	57.5
13	65	46	7	186.5	192	-5.5
14	59	56.5	180	280	138	142
15	55	58	36	181	195	-14
16	50	44	72	279	102	177
17	55	62	180	144	227	-83
*18	45	61	6	220	210	10
19	42	70	18	182.5	115	67.5
20	65	55	24	219.5	130	89.5
21	47	64	84	269	141	128
22	45	50	15	262.5	157	105.5
23	40	41	144	268	199.5	68.5
24	41	56	30	198	142.5	55.5
25	65	53	192	300	255	45
26	56	70	96	255	157.5	97.5
*27	68	61	4	282.5	162	120.5
28	66	46	36	186	156	30
29	52	60	24	232	108	124
30	50	66	96	179	126	53
*31	71	65	6	461	117	344
32	50	46	84	560	236	324
33	56	50	36	191	115	76
34	60	63	48	273	172	101
35	53	55	228	200	175	25
36	50	70	84	225	144.5	80.5
37	31	74	24	223	94	129
38	78	58	420	282	191.5	90.5
39	48	63	180	179	83	96
40	56	53.5	48	237	152	85
41	81	47	264	185	144.8	40.25
42	58	51	24	315	160	155
43	55	33	36	347	150	197
44	29	58	12	201.5	152	49.5
*45	62	58	5	210	110	100
46	44	56	48	204.5	134	70.5
47	51	76	84	226	169	57
48	61	72	70	238	227	11
49	49	56	56	199	157	42
50	40	61	62.5	243.5	104	139.5
51	63	57	58	243	143	100
52	54	78	78	350	130	220
53	34	70	70	202.5	158	44.5
54	46	55	55	269.5	118	151.5
55	34	51	51	225	153	72
56	60	60	60	217.5	138	79.5
				TOTAL		4806.75

mean (x)	mean (y)	$\sum(x-y)^2$	$\{\sum(x-y)\}^2$	$\sum d^2$	s.d.	s.e.	t	df = n-1	p value
240.11	**154.27**	**727467.31**	**23104845.56**	**314880.78**	**10.20**	**1.38**	**62.39**	**55**	**<0.001**

Table 6: Blood Glucose Response Before (BT) and After (AT) Trial, Graded as per Duration of Diabetes.

	<1YR	1-10YRS	>10YRS	Overall
Average BT ± S.D.	259.5mg ± 104.3	239.4mg ± 69.6	232.6mg ± 56.5	
Average AT ± S.D.	159.2mg ± 39.7	149.6mg ± 38.1	166.7mg ± 53.6	
Mean Decline	100.3 mg%	89.8mg%	65.9mg%	85.3mg%

DISCUSSION

Onset and progression of micro and macro-vascular complications in diabetes are closely related to duration and severity of hyperglycemia especially in post-prandial state. These complications are due to 1) glycation of proteins e.g. hemoglobin, ApoB 100, collagen etc, of lipids and nucleic acids, 2) initiation of the polyol pathway by the enzyme aldose reductase leading to oxidative stress and 3) activation of protein kinase-C causing endothelial dysfunction.

Therefore early detection and tight control of hyperglycemia are *sine qua non* for prevention of complications of diabetes and to halt their progression at early stage, as shown by DCCT and other trials. To achieve control, modification of diet, life style and exercise remain the foremost steps besides use of OHA in early cases. Of late, addition of Insulin is advocated in combination with OHA's when hyperglycemia cannot be controlled otherwise. This study emphasizes the need for trial of low G.I. foods and acarbose before resorting to Insulin treatment.

The weakest point in this trial is our inability to monitor HbA_1c values both before and during the trial due to resource and availability constraints which is not surprising as one study (10) found only 7.6% diagnosed Indian diabetics could have HbA_1c tested. However using the conversion table (11) the mean PPBS before the trial (Table 5) being 240.11 mg, the mean A_1c level may be estimated at 9%. During the trial, PPBS (Table-5) declined to 154.27mg i.e. HbA_1c below 7%, the target of the American Diabetic Association (ADA).

In this context it is pertinent to highlight the large glycemic load of Indian diet due to rice and wheat products contents compared to those in N. America :-

	Carbohydrates	Rice/Wheat	Protein	Fat
Indian	63-67%	61– 62%	18 - 26%	11-15%
N. American	45-65%	130gm/day	20 - 35%	10-35%

Low glycemic diet has not been found to be of consistent benefit by the ADA (12). It is presumably because quantity of high G.I. carbohydrates in diet of N. Americans are already low in contrast to the same in Indian diabetic diet which when changed to low glycemic yet popular menu plan not only controlled post-prandial hyperglycemia but also satisfied satiety and supplemented protein and fiber.

The reasons why acarbose only was not used were that dosage of the drug would have to be higher with the type of diet at Table-1, cost of which would have been prohibitive and caused more gastro-intestinal side effects. In the series of Rabasa-Loret et al (13) of T2DM cases with secondary failure of OHA, average reduction of PPBS was 2.82 mmol/l after addition of acarbose with no change in diet; good control could be achieved in one-third of cases. In this trial on T2DM cases treated with low glycemic diet and acarbose 50mg tid reducing to maintenance 25mg t.i.d dosage, average decline in PPBS was 4.7 mmol/l overall and in 85% of cases. Thus the low glycemic diet appeared to have enhanced the decline in PPBS in larger number of cases with lower dosage of acarbose.

However long term beneficial effects or otherwise can only be proved by trial in other centers, on larger number of cases and a decade of follow-up.

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