Treatment of Type 2 (Non-Insulin-Dependent) Diabetic Patients with Diet Alone

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Summary. The effects of 3 months' diet therapy on glucose tolerance, plasma insulin response to oral glucose, fasting lipid levels and body weight were measured in 182 Type 2 (non-insulin-dependent) diabetic outpatients with fasting hyperglycaemia before treatment. Overall, there was a 25% improvement in glucose tolerance, a 58% increase in plasma insulin response during the glucose tolerance test, a 13.6% fall in fasting plasma triglyceride levels with no change in fasting cholesterol levels and a 5.1% fall in body weight. Of the 182 patients, 20% achieved normal glucose tolerance on diet alone for 3 months. These were mainly men of average age 63 years, who were 20% above their ideal body weight, and had milder glu-

cose intolerance and higher residual insulin response to glucose before treatment than the 16% of patients who remained poorly controlled. These latter patients were mainly older women, 9% above their ideal body weight and with more marked glucose intolerance and less insulin response to glucose. These results demonstrate the practical limitations of this type of anti-diabetic therapy, particularly if normal glucose tolerance is a desired therapeutic aim.

Key words: Type 2 diabetes, diet, glucose tolerance, insulin secretion, blood lipids, weight reduction.

With the publication of reviews from the American [1] and British [2] Diabetic Associations concerning the dietary care of diabetic patients, there is a resurgence of interest in this field of therapy. Coupled with this, it is becoming increasingly evident that wherever possible anti-diabetic therapy should return blood glucose levels to as near normal as possible if the development of diabetic vascular complications is to be ameliorated [3–5]. Therefore it seems important that the same critical analysis should be made of each form of anti-diabetic therapy, including diet.

In the majority of diabetic clinics, the practice is to commence therapy in Type 2 diabetic patients with diet alone for some months before considering further anti-diabetic therapy. Diets used restrict either calories (energy) or carbohydrate (usually of the exchange type), and in both the carbohydrate content is prescribed to give 40% total calorie intake. This paper examines the results of this therapy and some of the factors which might influence results.

Patients and Methods

Over a period of 3 years, 214 patients were referred from general practitioners and other hospital clinics with untreated diabetes. Of these pa-

tients, 32 (20 men and 12 women) failed, or were unable, to attend for follow-up due to age, immobility, intercurrent illness, mental infirmity or removal from Leeds.

All the 182 remaining patients (88 men, 94 women) completing 3 months' diet therapy suffered from untreated Type 2 diabetes. None was or had ever been known to be ketotic, nor had any received any prior dietary advice. No patient was receiving steroid therapy or the contraceptive pill, nor was any pregnant or suffering from any disease in which diabetes is a recognised complication, such as pancreatitis, thyrotoxicosis, etc.

A full clinical and family history and physical examination of each patient, including fundoscopy, was undertaken at the first visit. Body weight was expressed as a percentage of the ideal body weight for age, sex and height calculated from Kemsley's data [6].

Before treatment was commenced, an outpatient 50 g, 2-h glucose tolerance test was performed with venous whole blood glucose levels measured by a glucose analyser (model 23AM, Clandon Scientific, Yellow Springs, Ohio, USA). The interassay relative standard deviation for blood glucose levels was 1.5%. Plasma insulin levels were assayed during the glucose tolerance test by a double-antibody radioimmunoassay [7], all samples from one patient being measured in the same assay. The mean interassay relative standard deviation for plasma insulin assay was 8.3% ($n = 14$). Total areas under the glucose and insulin curves were measured and expressed as $\text{mmol} \cdot \text{l}^{-1} \cdot \text{h}^{-1}$ or $\text{mU} \cdot \text{l}^{-1} \cdot \text{h}^{-1}$. Fasting plasma triglyceride ('Technicon' N-78 a method) and total cholesterol ('Technicon' N-77 method) levels were measured after an overnight fast. Interassay relative standard deviation for triglyceride was 6.8% and for cholesterol 4.5% (in both, $n = 12$). During the glucose tolerance test all 182 patients studied had blood glucose levels $> 5.5 \text{ mmol/l}$ (fasting), $> 10.0 \text{ mmol/l}$ (1 h) and $> 6.6 \text{ mmol/l}$ (2 h).

Table 1. Clinical details of 182 Type 2 diabetic patients before various dietary treatments

Sex	Diet	No. of patients	Age (years)	Percentage ideal body weight	Blood glucose during GTT ^a (area under curve, mmol · l ⁻¹ · h ⁻¹)	Plasma insulin response during GTT (area under curve; mU · l ⁻¹ · h ⁻¹)	Fasting plasma cholesterol (mmol/l)	Fasting plasma triglyceride (mmol/l)
Male	All	88	62	112	31	31	5.6	2.20
Female	All	94	67 ^b	115	36 ^b	41	5.8	1.85
Male and female	Energy-restricted	81	65	121	34	41	5.6	2.01
Male and female	CHO-restricted	101	64	107 ^c	33	32	5.7	2.03
Female	4.2 MJ	18	65	135	37	55	5.8	1.94
	5.0 MJ	21	67	119	35	39	5.6	1.80
	6.3 MJ	9	69	111	33	60	5.0	1.83
	All	48	67	123	35	48	5.6	1.85
Male	5.0 MJ	13	64	127	32	34	6.2	2.44
	6.3 MJ	17	64	110	35	31	5.4	2.23
	All ^d	33	62	117	33	32	5.6	2.24
Female	100g CHO	5	69	115	32	55	6.7	1.86
	120g CHO	19	68	109	39	32	6.2	2.16
	150g CHO	22	66	102	34	29	5.7	1.62
	All	46	67	106	36	33	6.0	1.86
Male	120g CHO	9	66	115	26	35	5.5	2.64
	150g CHO	38	61	108	30	31	5.4	1.97
	180g CHO	6	61	97	30	25	5.7	1.65
	All ^e	55	61	108	30	31	5.5	2.18

^a GTT = glucose tolerance test ^b $p < 0.05$ (difference between males and females) ^c $p < 0.05$ (difference between calorie- and CHO-restricted diets) ^d Includes one patient on 4.2 MJ and two patients on 7.6 MJ diets ^e Includes two patients on 100-g CHO diet

Dietary Regimens

After the initial clinical assessment and glucose tolerance test, patients were allocated to a diet regimen chosen with regard to their physical activity, body weight and social position. Each diet was explained to the patient by a dietician and individual diet sheets given. Wherever possible meal patterns were preserved and wives of male patients were also interviewed by the dietician for explanation of diets. As a general policy mono- and di-saccharides were excluded from the diet but no firm advice was given concerning dietary fibre.

Two forms of dietary formulation were used: energy- (calorie) restrictive diets of 4.2 MJ/day (1000 kcal), 5.0 MJ/day (1200 kcal), 6.3 MJ/day (1500 kcal) or 7.6 MJ/day (1800 kcal); and carbohydrate- (CHO-) restricted diets of 100 g CHO, 120 g CHO, 150 g CHO and 180 g CHO/day in 10 g portions. The dietary prescribing policy in both diets was that 40% of calories in the diet were given as carbohydrate so that, for example, in a 6.3 MJ diet the CHO content was 150 g, and a 150 g CHO diet contained 6.3 MJ. However the presentation of the two types of diet was quite different, with the emphasis on specific prescribing of food intake in the energy-restricted diets, compared with 'exchange list' prescribing in the carbohydrate-restricted diets. Of the 88 men, 63% were prescribed CHO-restricted diets and of the 94 women 51% were prescribed energy-restricted diets.

After instruction in urine testing with Clinitest reagent tablets, all patients were asked to test daily before breakfast and record the result.

The clinical details of the patients are shown in Table 1. The men were significantly younger than the women and had less glucose intolerance at diagnosis. However, in 50 pairs of men and women matched for age, there was no significant difference in glucose tolerance.

The majority of patients (54%) presented with classical diabetic symptoms, including polyuria and polydipsia. Fourteen patients (all men) presented with no symptoms, glycosuria having been discovered

at a routine medical examination (such as for insurance, or for heavy goods vehicle licence). Forty-seven patients were found to have glycosuria while attending other hospital clinics and referred directly to the diabetic clinic. Thirteen patients (7%) were found to be suffering from diabetic retinopathy at diagnosis, and in four of these visual deterioration was the first symptom of the diabetes. However these variations in presentation made little difference to the measurements of each group except that the 13 patients with retinopathy were significantly lighter in weight and the group of 14 men without any symptoms had less glucose intolerance.

All patients were then seen monthly by the same doctor in an out-patient clinic in which they were weighed, urine charts were checked, symptoms were noted and any further examinations indicated were performed. Patients, with or without spouses, were also interviewed by the dietician to deal with any further dietary problems. After 3 months' therapy, the glucose tolerance test with plasma insulin and fasting plasma lipid levels was repeated while the patients were on their prescribed diet.

The results of therapy were analysed and compared using distribution-free statistical analysis [8], such as the Mann-Whitney 'U' test, Spearman rank correlation coefficient, Wilcoxon matched-pairs signed rank test and the χ^2 test.

Results

In the 182 patients treated with these diet regimens for 3 months, there was on average a 25.4% improvement in glucose tolerance, a 58.1% increase in plasma insulin response during the glucose tolerance test, a 5.1% fall in

Table 2. Effects of various dietary regimens for 3 months on weight loss, glucose tolerance, insulin response during glucose tolerance test (GTT) and fasting plasma lipid levels in 182 Type 2 diabetic patients

Sex	Diet	No. of patients	Percentage change on treatment in:				
			Weight	Blood glucose during GTT ^a (area under curve)	Plasma insulin response during GTT (area under curve)	Fasting plasma cholesterol	Fasting plasma triglyceride
Male	All	88	-4.9	-30	+ 55	-3	-20
Female	All	94	-5.3	-21 ^b	+ 61	+1	- 8 ^b
Male and female	Energy restricted	81	-6.5	-27	+ 59	+1	-12
Male and female	CHO restricted	101	-4.1 ^c	-24	+ 54	-2	-18
Female	4.2 MJ	18	-6.9	-26	+148	+7	-11
	5.0 MJ	21	-4.9	-22	+ 36	0	- 3
	6.3 MJ	9	-6.4	-15	+ 5	-1	+ 5
	All	48	-6.2	-22	+ 75	+3	- 9
Male	5.0 MJ	13	-9.2	-38	+ 51	-3	-29
	6.3 MJ	17	-5.3	-31	+ 36	-4	-23
	All ^d	33	-6.9	-33	+ 37	-3	-25
Female	100 g CHO	5	-7.2	-18	+ 41	-5	-14
	120 g CHO	19	-4.2	-19	+ 41	+1	-13
	150 g CHO	22	-3.5	-24	+ 53	+2	-14
	All	46	-4.5	-21	+ 46	+1	-14
Male	120 g CHO	9	-4.3	-20	+ 25	+3	-17
	150 g CHO	38	-3.6	-28	+ 82	-5	-16
	180 g CHO	6	-0.7	-16	- 8	+4	+ 2
	All ^e	55	-3.7	-26	+ 64	-3	-16

^a GTT: glucose tolerance test ^b $p < 0.05$ (difference between males and females) ^c $p < 0.05$ (difference between calorie and CHO) ^d includes one patient on 4.2 MJ and two patients on 7.6-MJ diets ^e includes two patients on 100-g CHO diets

body weight, a 0.9% fall in fasting plasma cholesterol levels and a 13.6% fall in fasting plasma triglyceride levels.

Table 2 shows the effect of each diet regimen on glucose tolerance, insulin response during the glucose tolerance test, fasting plasma lipids and body weight. Overall there were no significant differences when energy-restricted and CHO-restricted diets were compared except for a significantly greater weight loss on energy-restricted diets. However men as a whole had greater reductions in glucose tolerance and in fasting plasma triglyceride levels than did women. Both these effects were particularly marked in men given energy-restricted diets.

Table 3 shows the Spearman rank correlation coefficients between the percentage change in each of the following variables on the one hand, and the initial value of the same variable or change in other variables on the other hand: area under the glucose response curve, area under insulin response curve during the glucose tolerance test, fasting plasma lipid levels, and body weight. In men there were strong positive correlations between improvement in area under glucose response curve and both the reduction in body weight and fasting plasma triglyceride levels, particularly in men on CHO-restricted diets. In both men and women there was a strong negative correlation between the percentage changes in

area under the glucose and insulin response curves during the glucose tolerance test, particularly in women on energy-restricted diets.

However, there were negative correlations between initial values and changes after therapy for the following variables: insulin response curve, weight (in men only), plasma cholesterol and triglyceride levels, and (weakly) area under blood glucose curve.

Of the 182 patients studied, 37 became well-controlled in that the area under the glucose response curve after treatment became normal ($< 16 \text{ mmol} \cdot \text{l}^{-1} \cdot \text{h}^{-1}$). On the contrary, 29 patients were poorly-controlled as the area under their glucose response curves remained at least twice the upper limit of normal.

Those patients whose glucose tolerance became normal were mainly men, and were significantly heavier and had significantly less glucose intolerance before treatment than those patients who remained poorly controlled. On diet therapy the well-controlled patients lost more weight and showed a significantly greater fall in plasma triglyceride levels. Comparing the well- and poorly-controlled groups, there was no significant difference in the type of diet used (14 on energy-restricted and 23 on CHO-restricted diets in the well-controlled group and 10 and 19 respectively in the poorly-controlled group).

Table 3. Spearman rank correlation coefficients between percentage changes in the following variables after 3 months' dietary therapy and pre-treatment levels of the same, or post-treatment levels of other variables in 88 male and 94 female Type 2 diabetic patients: body weight, glucose tolerance, insulin response during glucose tolerance test (GTT) and fasting plasma lipid levels

Variables correlated			Males			Females		
Percentage change after therapy:			All (n = 88)	CHO-restricted (n = 83)	Energy-restricted (n = 33)	All (n = 94)	CHO-restricted (n = 46)	Energy-restricted (n = 48)
Area under GTT glucose response curve	versus	Pre-treatment area	-0.286 ^b	-0.223	-0.225	-0.263 ^a	-0.302 ^a	-0.182
		Weight change	+0.325 ^c	+0.354 ^b	+0.293	+0.102	-0.166	+0.350 ^a
		Plasma insulin response during GTT (area under curve) after treatment	-0.207	-0.014	-0.497 ^c	-0.372 ^c	-0.244	-0.538 ^c
		Plasma cholesterol after treatment	+0.146	+0.251	-0.049	+0.015	+0.015	-0.076
		Plasma triglyceride after treatment	+0.387	+0.441 ^c	+0.228	+0.063	-0.010	+0.083
Weight	versus	Pre-treatment weight	-0.502 ^c	-0.401 ^b	-0.473 ^b	-0.085	-0.035	+0.020
		Insulin response during GTT (area under curve) after treatment	+0.161	+0.246	+0.049	-0.049	+0.006	-0.124
		Plasma cholesterol after treatment	+0.157	+0.193	+0.091	+0.006	+0.016	+0.004
		Plasma triglyceride after treatment	+0.281	+0.192	+0.415 ^b	+0.080	+0.060	+0.108
Plasma insulin response during GTT (area under curve)	versus	Pre-treatment level	-0.416 ^c	-0.427 ^b	-0.450 ^b	-0.357 ^b	-0.451 ^b	-0.320 ^a
		Plasma cholesterol after treatment	-0.194	-0.378 ^b	+0.008	+0.081	-0.058	-0.116
		Plasma triglyceride after treatment	-0.066	-0.129	+0.044	-0.205	-0.138	-0.228
Plasma cholesterol	versus	Pre-treatment levels	-0.483 ^c	-0.418 ^b	-0.505 ^b	-0.305 ^b	-0.315 ^a	-0.301 ^a
		Plasma triglyceride after treatment	+0.219 ^a	+0.368 ^b	+0.092	+0.098	+0.067	+0.143
Plasma triglyceride	versus	Pre-treatment levels	-0.417 ^a	-0.523 ^c	-0.144	-0.326 ^b	-0.450 ^b	-0.279

^a p < 0.05 ^b p < 0.01 ^c p < 0.001

To assess the effect of weight loss on diabetic control, two groups of patients were compared: one group of 25 patients (14 men) who lost more than 10% of their initial weight on diet, and a second group of 30 patients (21 men) who lost no weight ($\pm 1\%$ of their initial weight). There were no significant differences between the groups in their pre-treatment details except that those who did not lose weight were lighter. However this was not due to this group having lost more weight before diagnosis. Those patients who lost weight on the diet showed a significantly greater improvement in glucose tolerance and a significantly greater fall in fasting plasma triglyceride levels, but no significant change in insulin response during the glucose tolerance test.

The effect of the patients' sex on their response to therapy was more difficult to assess because the women were significantly older and heavier. However, it was possible to match 29 pairs of men and women for age, obesity and type of diet prescribed. Improvement in glucose tolerance was then the same in men and women and the falls in plasma triglyceride levels were not signifi-

cantly different. This suggests that the sex of the patient has no absolute effect upon the response to diet therapy.

Comparing the effects of energy-restricted and CHO-restricted diets, patients on the former diets lost more weight despite the theoretical energy parity of the diets, but there were no significant differences in the percentage changes in the other measurements. However patients prescribed energy-restricted diets were heavier at diagnosis. If patients were matched for initial body weight and for CHO and energy content of their selected diets then there were no significant differences.

From the 182 patients in this study, it was possible to identify two groups with different responses in plasma insulin levels during a glucose tolerance test. A first group of 30 patients more than doubled their insulin response during a glucose tolerance test after dietary therapy, and a second group of 57 patients responded with a fall in plasma insulin levels (Table 4). These two groups had equal numbers of men and women and were comparable for age, weight and family history of diabetes. However, those patients in whom therapy pro-

Table 4. The pre-treatment clinical details and the response to 3 months' dietary therapy in two groups of Type 2 diabetic patients: group 1 showing a fall in insulin response during glucose tolerance test (GTT) on therapy, and group 2 showing an increase in insulin response of > 100%

	Pre-treatment details					Percentage change after treatment in:			
	Age (years)	Percentage ideal body weight	No family history	Blood glucose response GTT (area under curve) ($\text{mmol} \cdot \text{l}^{-1} \cdot \text{h}^{-1}$)	Plasma insulin response during GTT (area under curve) ($\text{mU} \cdot \text{l}^{-1} \cdot \text{h}^{-1}$)	Weight	Blood glucose area under glucose response curve	Plasma cholesterol	Plasma tri-glyceride
Group 1:	Patients with a fall in insulin secretion on treatment ($n = 57$, 28 male: 29 female)								
	64	115	75%	32	51	-5.4	-20	-1	-13
Group 2:	Patients with increase in insulin secretion > 100% ($n = 30$, 15 male, 15 female)								
	65	113	53%	37 ^a	19 ^b	-5.0	-37 ^c	-5	-18

^a < 0.01 ^b < 0.001 (Mann Whitney 'U' test)

duced a fall in plasma insulin levels had significantly less glucose intolerance and greater plasma insulin response during the pre-treatment glucose tolerance test. In this group, diet therapy produced a significantly smaller percentage fall in glucose tolerance but no difference in weight loss or plasma lipid changes compared with the group in whom diet therapy increased plasma insulin levels. Each group had similar types of diets prescribed and similar numbers of patients who achieved normal glucose tolerance.

After 3 months' diet therapy, 47% of patients on energy-restricted diets and 46% of those on CHO-restricted diets had detected no glycosuria on home urine testing; 16% and 21% respectively had occasional glycosuria and 37% and 34% respectively had regular glycosuria. As might be expected, those patients with regular glycosuria had significantly greater glucose intolerance after therapy. After dietary therapy, 61% patients had no diabetic symptoms, 23% had occasional symptoms and 17% still complained regularly of symptoms referable to their diabetes. Again those patients with symptoms had significantly greater glucose intolerance after treatment compared with those patients without symptoms.

Discussion

In a lecture given in 1972 reviewing the dietetic treatment of diabetes Pyke [9] ended by reminding his audience of the degree of ignorance that existed about the effects of such therapy. West [10] described in strong terms in his review of diet therapy the pitfalls and difficulties experienced by physician and patient alike in formulating and complying with dietary advice. The same point had been made earlier in Leeds by Tunbridge and Wetherill [11].

This present study made no particular point of stressing or measuring compliance except by the usual means of clinical practice. Indeed it was felt that the follow-up of these patients should not differ in any way from normal clinical practice, so as to avoid the criticism that the results were obtained from a small, selected popula-

tion of compliant patients undergoing intense diet control bearing little relationship to usual clinical practice. The results of diet therapy alone in these patients might be considered as being disappointing. However, two provisos should be borne in mind. First, patients with mild carbohydrate intolerance, such as those with normal fasting but raised 2-h blood glucose levels, were not included. Many of those patients would have been expected to respond to diet alone. Secondly a return to normal glucose tolerance may not be required to prevent the progression of diabetic vascular complications [12]. However, there seems no doubt that the results of diet therapy could be improved by a more intensive education programme as described by Hadden et al. [13], particularly with the use of domiciliary dietetic services.

This study followed the practice of prescribed diabetic diets to restrict either overall energy (calorie) intake or carbohydrate intake, and in both types of diet the carbohydrate content was maintained at 40% total calories. Thus the diets were theoretically similar. From the practical point of view energy-restricted diets are more difficult to manage in respect of patient compliance and involvement of dieticians' time and skill. However, this study has shown that, if improvement in glucose tolerance alone is required, then either an energy- or a CHO-restricted diet would be equally effective, but if weight loss is also required then an energy-restricted diet is more likely to be effective. This difference in weight-loss no doubt reflects the inadvertent intake of higher amounts of total calories on the CHO-restricted diets arising from the increased use of low-CHO foods, such as cheese. The lack of response in serum cholesterol levels presumably reflects the higher fat intake in both diets, and contrasts with the marked changes in fasting plasma triglyceride levels due to the restriction of carbohydrate to 40% of total calories.

This study measures the overall response to these diets as prescribed, in Type 2 diabetic patients. It is hoped that in the near future it will be possible to compare these results with those gained from similar patients given diets containing a higher percentage of carbohydrate and/or less-available sources of carbohydrate.

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