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ORIGINAL ARTICLE

Effect of a low-calorie high nutritional value formula on weight loss in type 2 diabetes mellitus

Patrizio Tatti · Patrizia di Mauro · Marisa Neri · Giuseppe Pipicelli · Vikkie A. Mussad

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Abstract We treated 96 obese diabetic subjects (BMI 33–44 kg/m^2) with a "package of interventions" including therapeutic education, regular follow-up at 15-day intervals and a hypocaloric diet of 60% of their daily needs, 20% at breakfast and 40% at each meal. At the beginning of the observation and after 3 and 6 months we checked certain baseline characteristics. All the subjects performed self blood glucose measurement (SMBG) 3 or 5 times a day and kept a log. After the first 3 months of observation (Phase 1) 18 were lost to follow-up and 40 who obtained a weight loss >5% of their initial BW continued on their diet (G–). The remaining 38 substituted a nutritionally rich hypocaloric meal (Glucerna® SR) for 206 calories of one of the main meals (G+). During the following three months (Phase 2) all were treated with the package of interventions. The subjects treated with Glucerna® SR had a more consistent weight loss and a more remarkable improvement of the parameters under evaluation, with greater statistical significance. With the logistic regression analysis the residual variance not explained by the weight loss was greater for the G+ group, which implies the existence of an additional beneficial effect of the formula used. Of great relevance is the observation that the G+ group had a reduction of the standard deviation of the SMBG data, thus suggesting a greater stability of the BG values in this group.

Keywords Weight loss · Nutritional formula · Obesity · Metabolic disorders

Introduction

The prevalence of obesity is increasing worldwide and due to a close relationship with altered carbohydrate (CHO) metabolism and other metabolic disorders, it is probably responsible for the increased prevalence of diabetes and the so-called "metabolic syndrome".

Weight loss of as little as 5–7% is important to help improve glycaemic control and metabolic risk factors [1–4]. Unfortunately, it is extremely difficult to obtain a consistent and durable weight loss in these subjects, even with an intensive management programme [5]. To complicate matters further, diabetics and obese subjects often present with subtle deficits of vitamins and/or other nutrients [6]. Thus, simply cutting the calories may paradoxically aggravate this condition or precipitate a borderline insufficiency state.

Dr. Mussad provided information on the product and helped with the English translation and other perspectives, but had no input on the study inception, design, data analysis or conclusions.

P. Tatti (✉) · P. di Mauro · M. Neri
UOCA di Endocrinologia e Diabetologia
ASL RMH, Rome, Italy
e-mail: info@patriziotatti.it

G. Pipicelli
UOC Diabetologia e Dietologia, ASP Catanzaro
Catanzaro, Italy

V.A. Mussad
Abbott Nutrition
Abbot Laboratories
Columbus, OH, USA

In our Metabolic Unit we adopted a routine protocol including the use of a low-calorie low-glycaemic index nutrient-enriched diabetes-specific meal replacement (Glucerna® SR). Meal replacements have been shown to help calorie control [7–9]. This paper evaluates the usefulness of this diabetes-specific formula in subjects unsuccessful at weight loss in the context of an intensive management programme.

Hypothesis

We hypothesised that the substitution of one of the main meals with a low-calorie diabetes-specific meal replacement could improve the weight loss without interfering negatively with the nutritional status of the obese type 2 diabetic subjects.

Research design and methods

Subjects

During 2006, we prospectively enrolled 96 consecutive obese type 2 diabetic subjects into our clinic programme for weight loss subjects for this open-label clinical trial. Subjects were recruited if their BMI was >30, had type 2 diabetes mellitus and did not have any serious concomitant disease other than diabetes. Exclusion criteria were secondary causes of obesity including endocrine disorders (hypothyroidism, hypercortisolism), congenital disorders, history of diet failures (>3 attempts), psychological disturbance or the use of drugs affecting body weight, including insulin or glitazones. The subjects gave their informed consent to the anonymous use of their data.

Intervention

A structured intervention programme has been developed and is in use at the hospital's Department of Endocrinology and Metabolism at the Diabetes and Endocrinology Unit, ASL RMH. The intervention consists of a structured package including group discussion, a session of weight control and analysis of any failure, 30 min of therapeutic diet education, a brief period of walking with medical supervision while patients wear a step counter to monitor physical exercise and cooking lessons (see Fig. 1). The sessions were scheduled at 15-day intervals and led by the professional dietician and a physician of the unit.

All the participating subjects were started on a diet with an energy content of 60% of their daily caloric needs calculated from the basal metabolic rate (BMR) as obtained with an impedenziometric analysis (Akern BIA 101) increased to accommodate the additional caloric expenditure related to the daily activity. The caloric content of the diet was subdivided as 20% at breakfast and the remainder split evenly at the main meals. The composition of the diet was 55% CHO, mostly complex, 27% fat, mainly unsaturated, and 18% protein. After 3 months the diet of all the subjects was recalculated on the basis of the new body weight obtained.

The protocol is illustrated in Figure 2. The study consisted in a first phase of 3 months of diet alone plus the structured package of interventions. At the end of this period we added a diabetes-specific meal replacement as a substitute for the main meal for those who could not lose at least >5% of their initial weight (the rationale being the data supporting that weight loss of at least 5–7% can improve metabolic parameters, even when ideal body weight is not achieved [1–4]). Subsequently, the two groups are designated as follows: G– denoting the group that continued without the meal replacement and G+ denoting the group that continued with the meal replacement.

Fig. 1 Example of a practical teaching session

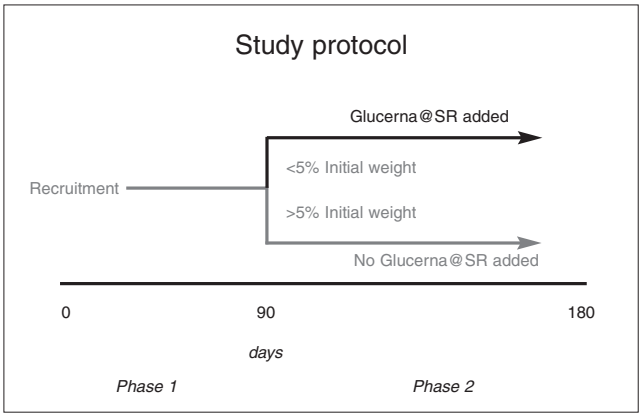

Fig. 2 Study protocol

The follow-up was continued for a further 3 months. Twenty-eight subjects who failed to attend the 15-day interval follow-up >3 times were considered as drop-outs. The follow-up was continued for a further 3 months with the same package of intervention for both groups.

Meal replacement

To facilitate adherence to the dietary plan, the subjects were provided a low glycaemic (glycaemic index = 19), diabetes-specific nutritional meal replacement (Glucerna® SR, Abbott Nutrition, Zwolle, the Netherlands/Chicago, IL) to substitute for the same amount of calories at the main meal. The nutritional meal provided 206 calories per 230 ml, with 9 g protein (20% kcal), 6 g fat (33% kcal) from monounsaturate-rich sources, 25 g (47% kcal) low glycaemic carbohydrate blend, and 24 vitamins and minerals. To improve the satiety-inducing effect, we suggested to blend and stir the formula with a low-calorie frozen yoghurt; this resulted in a larger quantity of nearly 1 l of a semisolid low-calorie (250–270 kcal) cream, which could be eaten slowly with a spoon.

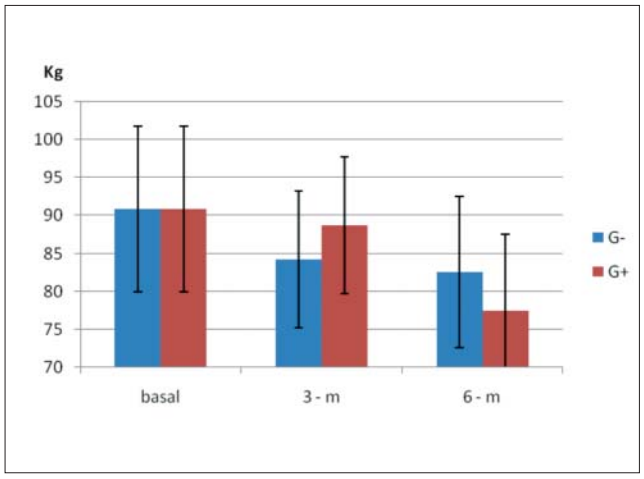

Fig. 3 Weight variation

Assessments

Major study assessments were carried out at baseline, and after 12 and 24 weeks. Body weight and height at baseline were assessed with subjects wearing undergarments in the morning before lunch. The performance of the scale was regularly checked at bimonthly intervals according to the ISO rules.

Blood samples were collected via venipuncture after overnight fast. Subjects were instructed to withhold medications, with the exception of drugs for diabetes, antihypertensives and aspirin or thyroid. The day before the blood sampling plasma glucose, insulin, iron, iron-binding capacity, haemogram, protein electrophoresis and lipids were assessed by the Central Laboratory of the Hospital. HbA1c was evaluated with HPLC. Blood pressure was checked at each visit using a mercury sphygmomanometer. All the subject made 2–5 point Home Self Blood Glucose Measurement (SMBG). The data were downloaded directly from the monitors to the computer to avoid errors/cheating and the standard deviation was calculated. Adherence to the diet and to the treatment was assessed by direct questioning, logbooks and retrieving and counting the tetrapaks of the formula.

Statistical analysis

The data were evaluated after logarithmic transformation with the student's *t*-test for paired data, with the SPSS 13 program for differences between the first and the second 3-month period within each group (G+ and G–), and were further evaluated with the multiple logistic regression with the body weight as the dependent variable. The data were analysed to compare the data at the end of the first trimester *vs.* the end of the study with the outcome analysis using the last weight carried forward and with the ITT analysis (Tables 1 and 2). The baseline (beginning of the first trimester) and the final data (end of the study) for each subgroup (G+ *vs.* G–) are in Figure 3 and Table 3.

Table 1 Outcome analysis: end of phase 1 *vs.* end of phase 2

	G–			G+		
	End of phase 1	End of phase 2	*p*	End of phase 1	End of phase 2	*p*
n	40	36		38	29	
kg	84.4 ± 7.1[a]	82.5 ± 8.6	0.013[a]	88.7 ± 9.6	77.5 ± 10	0.000[a]
HbA1c	7.5 ± 1.2	7 ± 1.5	0.022[a]	8 ± 1.65	6.7 ± 0.88	0.000[a]
Col	222 ± 38[a]	218 ± 34	0.040[a]	219 ± 37	204 ± 31	0.000[a]
TG	141 ± 71[a]	123 ± 51	0.003[a]	140 ± 84	103 ± 56	0.000[a]
HDL	53 ± 15[a]	55 ± 7.24	0.033[a]	54 ± 12	58 ± 9.4	0.000[a]
PAS	144 ± 20	141 ± 17	0.038[a]	144 ± 23	136 ± 19	0.000[a]
PAD	83.5 ± 11	82.9 ± 9.6	0.719[a]	84.7 ± 9.7	78.3 ± 9.3	0.000[a]

[a]Data logarithmically transformed for analysis

Table 2 ITT analysis. End of phase 1 *vs.* end of phase 2

	G–			G+		
	End of phase 1	End of phase 2	*p*	End of phase 1	End of phase 2	*p*
n	40	40		38	38	
kg	84.4 ± 7.17[a]	82.6 ± 8.4	0.018[a]	88.9 ± 11	77.7 ± 9.17	0.000[a]
HbA1c	7.5 ± 1.2	7.2 ± 1.4	0.087	8 ± 1.65	6.9 ± 1	0.000
Col	222 ± 38[a]	219 ± 38	0.040[a]	219 ± 37	208 ± 33	0.000[a]
TG	141 ± 71[a]	121 ± 51	0.003[a]	140 ± 84	109 ± 55	0.000[a]
HDL	53 ± 15[a]	56 ± 8	0.034[a]	54 ± 12	58 ± 11	0.000[a]
sBP	144 ± 22	141 ± 17	0.400[a]	144 ± 23	139 ± 20.9	0.000[a]
dBP	83 ± 11	83.5 ± 9.3	0.719[a]	85.5 ± 9	80.6 ± 9.9	0.000[a]
SD of MBG[b]		167	171	165	88	

[a]Data logarithmically transformed for analysis
[b]SD of MBG, standard deviation of the mean BG obtained by home self-monitoring

Table 3 Statistical evaluation of the outcome results (independent samples) at the end of phase 2 for G+ *vs.* G– group

	G–	G+	*p*
n	36	29	
kg	82.5 ± 8.6[a]	77.5 ± 10[a]	0.027
HbA1c	7 ± 1.5[a]	6.7 ± 0.88[a]	0.057
Col	218 ± 34[a]	204 ± 31[a]	0.117
TG	123 ± 51[a]	103 ± 56[a]	0.066
HDL	55 ± 7.24[a]	58 ± 9.4[a]	0.242
PAS	141 ± 17[a]	136 ± 19[a]	0.348
PAD	82.9 ± 9.6[a]	78.3 ± 9.3[a]	0.051

[a]Data logarithmically transformed for analysis

Table 4 Baseline characteristics of subjects at baseline (*n* = 96)

Variable	Mean ± SEM
Age	52 ± 8
Sex (M/F)	59/34
Duration of disease (years)	7 ± 5
BMI (kg/m^2)	33 ± 5
Number on metformin/sulfa drugs/glinides/metformin+glinides	75/0/6/3
% on diet alone	14
Number of hypertensives on ACE-I or ARBS or CCB	62
Other drugs	GI drugs

Results

Table 4 shows the baseline characteristics of the 96 individuals enrolled.

Regarding the retention rate, four subjects withdrew spontaneously prior to study completion (*n* = 3 in the intervention group; *n* = 1 in the reference group). The reasons for withdrawal included interference of the dietary programme with work schedule (*n* = 2); change of job (*n* = 1) and gastrointestinal problems associated with the fibre intake (*n* = 1).

Of the initial 96 subjects enrolled, 18 were considered "dropped" within the third month because they failed to attend the follow-up sessions >3 times.

Of the remaining 78, forty subjects lost >5% of their initial BW (data in Table 3), and continued their diet adjusted for the reduced BMR. This group was conventionally defined as non-Glucerna users (G–). The other 38 who lost <5% of the initial BW were switched to the low-calorie diet with the substitution of the meal with Glucerna (Table 3), and were conventionally defined G+.

During the second phase of the observation (months 3–6) 4 subjects in the G– group and 9 in the G+ group dropped out. The final subgroups were thus G– = 36 and G+ = 29. The statistical results in Tables 1 and 2 represent the difference between the first and the second phase for each group. All the differences present at the beginning of the third month were in the opposite direction to the final outcome. The data were evaluated both with the outcome (Table 1) and with the ITT analysis using the last weight carried forward (Table 2). The *p* values for the difference between the first and the second phase are of greater statis-

tical and biological significance in group G+ for all the variables studied. The diastolic blood pressure difference did not reach statistical significance in the G+ group. The standard deviation of the SMBG was reduced by 50% in the G+ group but did not change in the G– group. We also evaluated the different outcome at the end of phase 2 for G– *vs.* G+ with the *t*-test for independent samples (Table 3 and Fig. 2). However the results are of limited statistical significance given the non-randomisation of the study design.

Discussion

The results of this study show that patients who are resistant to traditional weight loss methods can be successful when diabetes-specific meal replacements are added to their treatment plan.

As is evident from the Tables, the subjects treated with Glucerna® SR had a significant reduction in body weight. More importantly, the use of Glucerna® SR in the G+ group reversed the lower weight loss observed during the first 3 months following the diet intervention without the meal replacement. This is in contrast with our previous experience showing that in patients ($n > 100$) without the use of meal replacements, weight loss tends to slow down after 3 months (unpublished data). As apparent from the Table, there was also a reduction in the values of HbA1c, cholesterol, triglycerides, HDL cholesterol and blood pressure. There was a reduction of the same parameters also in both groups, but the magnitude of the reduction in G– was lower and correspondingly the *p* value was lower. While the (near) normalisation of many biochemical variables is the rule with weight loss [8–10], the logistic regression analysis demonstrates that a large residual variation is unaccounted for by the weight change in the G+ group, thus suggesting a favourable effect of Glucerna® SR beyond the weight reduction. The weight loss was independent of the blood glucose status, as in the literature [1, 7]. Another important observation is the 50% reduction of the standard deviation of the mean blood glucose in the G+ group, which is proof of a consistent reduction in the blood glucose variability [11].

The use of a low-calorie, high nutritional value food is an attractive option for any overweight subject who must undergo a prolonged period of weight loss. Diabetes-specific nutritional products are designed to deliver quality nutrition in a portion-and-calorie-controlled manner, and at the same time minimise postprandial glucose response [12]. We think that in our subjects better nutrition with Glucerna® SR may have led to greater well being, thus contributing to limited appetite. Furthermore the high fibre content, slow CHO absorption and presentation in a prepackaged formula may have contributed to a sense of fullness, facilitating compliance to the weight loss intervention [5].

The present data were obtained after a meal replacement intervention protracted for 3 months, which is a rather short time for treating obesity. We are planning a much longer follow-up to confirm these results. However, in our view the metabolic improvement obtained has great clinical relevance.

Conflict of interest The authors declare that they have no conflict of interest related to the publication of this manuscript.

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