Effects of Carbohydrate Counting on Glucose Control and Quality of Life Over 24 Weeks in Adult Patients With Type 1 Diabetes on Continuous Subcutaneous Insulin Infusion

A randomized, prospective clinical trial (GIOCAR)

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OBJECTIVE—Few studies have assessed the efficacy of carbohydrate counting in type 1 diabetes, and none have validated its efficacy in patients who are treated with continuous subcutaneous insulin infusion (CSII). The aim of our study was to test the effect of carbohydrate counting on glycemic control and quality of life in adult patients with type 1 diabetes who are receiving CSII.

RESEARCH DESIGN AND METHODS—Sixty-one adult patients with type 1 diabetes treated with CSII were randomly assigned to either learning carbohydrate counting (intervention) or estimating pre-meal insulin dose in the usual empirical way (control). At baseline and 12 and 24 weeks, we measured HbA_{1c}, fasting plasma glucose, BMI, waist circumference, recorded daily insulin dose, and capillary glucose data, and administered the Diabetes-Specific Quality-of-Life Scale (DSQOLS) questionnaire.

RESULTS—Intention-to-treat analysis showed improvement of the DSQOLS score related to diet restrictions (week 24 – baseline difference, $P = 0.008$) and reduction of BMI ($P = 0.003$) and waist circumference ($P = 0.002$) in the intervention group compared with control subjects. No changes in HbA_{1c}, fasting plasma glucose, daily insulin dose, and hypoglycemic episodes (<2.8 mmol/L) were observed. Per-protocol analysis, including only patients who continuously used carbohydrate counting and CSII during the study, confirmed improvement of the DSQOLS score and reduction of BMI and waist circumference, and showed a significant reduction of HbA_{1c} (−0.35% vs. control subjects, $P = 0.05$).

CONCLUSIONS—Among adult patients with type 1 diabetes treated with CSII, carbohydrate counting is safe and improves quality of life, reduces BMI and waist circumference, and, in per-protocol analysis, reduces HbA_{1c}.

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Nutritional management is a cornerstone in the management of diabetes, and monitoring of carbohydrate intake, a major determinant of postprandial blood glucose, is a key strategy for achieving good glucose control (1–4).

Some studies have examined the contribution of quantity and type (i.e., simple vs. complex) of carbohydrates in patients with type 1 diabetes and showed that the daily insulin requirement is indeed associated with the amount rather than the type of daily carbohydrate intake (4–6).

Over the years, a number of methods have been proposed to help patients with diabetes to quantify the carbohydrate content of a meal in real life, for example, exchange lists, portion/servings, grams, glycemic index, and insulin:carbohydrate ratio (I:CHO) (7–9). Among these, the I:CHO is considered the most advanced counting technique, consisting of estimating the grams of carbohydrates in a meal and then calculating the pre-meal insulin dose based on this estimation and an insulin sensitivity measure (8). Carbohydrate counting was devised in the 1960s, but it has become widely used as part of intensive diabetes management after the Diabetes Control and Complications Trial (DCCT) (10,11).

Although carbohydrate counting is widely used by patients worldwide, few studies have validated its efficacy in type 1 diabetes (12,13), and none have validated its efficacy in adult patients receiving continuous subcutaneous insulin infusion (CSII). We designed the current study with the aim of testing the effect of carbohydrate counting on glucose control and quality of life over 24 weeks in adult patients with type 1 diabetes treated with CSII.

RESEARCH DESIGN AND METHODS

—The GIOCAR (contegGIOCARboidrati) was designed as a prospective, randomized, controlled, open-label clinical trial with a duration of 24 weeks. The study was approved by the Ethics Committee of the San Raffaele Scientific Institute in Milan and was registered at ClinicalTrials.gov (no. NCT01173991). After having received detailed information about the study and before any study procedure, participants signed a written informed consent.

We recruited adult patients with type 1 diabetes treated with CSII and followed

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at the CSII Outpatient Clinic of the San Raffaele Scientific Institute in Milan. We included patients with type 1 diabetes, aged 18–65 years, who had been treated with CSII for >3 months. Exclusion criteria were serum creatinine >124 μmol/L in women and >150 μmol/L in men, previous training in carbohydrate counting, celiac disease, pregnancy, severe comorbidities, and any disability preventing compliance with study procedures. Three diabetologists with experience in managing patients on CSII and trained in carbohydrate counting and one dietitian certified in carbohydrate counting conducted the study. We used the *Complete Guide to Carb Counting* (2nd ed.) (14) as a reference for carbohydrate counting. Learning carbohydrate counting involves several steps. The first step is keeping a food diary: complete food records include day of the week, meal time, amounts of food, carbohydrate grams for each food, total carbohydrate grams for the meal or snack, preprandial and postprandial (2 h after the start of the meal) blood glucose, short-acting insulin dose, and physical activity. The I:CHO tells how much insulin is needed to "cover" the amount of carbohydrates eaten and bring blood glucose level back to pre-meal target (14,15). This ratio is calculated on the basis of individual recorded diary data by dividing the total grams of carbohydrates of a meal by the number of units of short-acting insulin that were able to hold post-meal glucose excursions within 1.6 mmol/L. The sensitivity factor or correction factor is calculated by dividing 1,800 by the total daily insulin requirement (14,15) and corresponds to the glucose lowering obtained with one unit of short-acting insulin. By combining the I:CHO and sensitivity factor, patients are instructed to estimate the preprandial insulin dose, taking into consideration preprandial blood glucose and the amount of carbohydrates they plan to eat.

The primary outcome of the study was the change in HbA_{1c} at week 24. Secondary outcomes were the changes of the following variables at week 24: quality of life, assessed with the Diabetes-Specific Quality-of-Life Scale (DSQOLS) questionnaire (16), BMI and waist circumference, hypoglycemic events (capillary glucose 2.8 mmol/L), hypoglycemia and hyperglycemia risk indexes (low blood glucose index [LBGI] and high blood glucose index [HBGI]) (17), total daily insulin dose, and fasting plasma glucose. Participants were randomly assigned to two groups (group 1 intervention, group 2 control subjects) with a 1:1 ratio. An investigator without contact with study participants generated the treatment allocation sequence using a computerized random number generator (Stata, version 10.0; Stata Corp, College Station, TX). Because of the type of intervention, blinding was not possible. Patients were given the same glucose meter (OneTouch Ultra2; LifeScan Inc., Milpitas, CA) for self-monitoring of blood glucose during the study period and were asked to measure capillary glucose six times per day, according to American Diabetes Association Standards of Medical Care (4). Before randomization, all participants attended a group lesson with the dietitian about the recommended diet for patients with diabetes. After randomization, patients in group 1 (intervention) were trained on carbohydrate counting and bolus calculation in the first 12 weeks using the I:CHO and sensitivity factor during four to five individual sessions with the dietitian and a diabetologist, whereas patients in group 2 (control subjects) continued estimating their pre-meal insulin dose in an empirical way. HbA_{1c} and fasting plasma glucose were measured at baseline and after 12 and 24 weeks. At baseline and after 24 weeks, we measured BMI and waist circumference, recorded total daily insulin dose, and asked patients to complete a validated instrument for assessing diabetes-specific quality of life (DSQOLS) (16). Capillary glucose measurements were downloaded from the memory of glucose meters at 12 and 24 weeks at the time of the outpatient visits, and LBGI and HBGI were calculated as reported (17). Study data were recorded on a paper Case Report Form and then entered in a dedicated database maintained in Microsoft Office Access (Microsoft Corp., Redmond, WA), and de-identified datasets were extracted for statistical analyses. HbA_{1c} was measured using ion-exchange high-performance liquid chromatography (DCCT-certified method) (18), with a normal range of 3.5–6.0%.

Statistical analysis

The intention-to-treat (ITT) analysis included all randomized patients who concluded the trial, i.e., 56 patients (28 patients per group). The per-protocol (PP) analysis included 20 patients in the carbohydrate counting group and 27 patients in the control group. For this analysis, we excluded nine patients because of discontinuous use of carbohydrate counting (<75% of the meals) (six participants) or shift from CSII to multiple insulin injections for >7 consecutive days (two participants in the carbohydrate counting group, one participant in the control group).

Baseline characteristics of study participants in the two groups were compared using the χ^2 test, unpaired, two-tailed *t* test, or Mann–Whitney two-sample statistic as appropriate. Changes from baseline of DSQOLS scores, BMI and waist circumference, total daily insulin dose, fasting plasma glucose, LBGI, and HBGI in the two groups were compared using the unpaired, two-tailed *t* test or the Mann-Whitney two-sample statistic, as appropriate. HbA_{1c} levels and hypoglycemic events during the study in the two groups of participants were analyzed using mixed-effects models.

RESULTS—The clinical trial was carried out between October 2008 and July 2009. The flow diagram of the study is shown in Fig. 1. Of 67 patients assessed for eligibility, 61 were randomized and 56 concluded the study (28 in each group), with a dropout rate of 8.2%. Patients assigned to group 1 attended on average 4.4 (SD 1.13) individual training sessions on carbohydrate counting.

The baseline characteristics of study participants are shown in Table 1. The two groups were similar in age, sex, years of school completed, duration of diabetes, duration of CSII, type of insulin used, daily insulin requirement, and HbA_{1c} levels.

Metabolic control

In the ITT analysis, HbA_{1c} levels during the 24 weeks of the study were similar in the two groups ($P = 0.252$). However, the PP analysis showed significantly lower HbA_{1c} levels in the carbohydrate counting group than in control subjects (intervention group −0.4 vs. −0.05% in control subjects; Δ −0.35%, $P = 0.05$) (Fig. 2). BMI change was not a significant predictor of HbA_{1c}. No differences between groups were observed in total daily insulin dose, LBGI, HBGI, and fasting plasma glucose levels (data not shown).

Anthropometrics

The median changes in BMI and waist circumference for the two groups are shown in Table 2. Among patients in the carbohydrate counting group, we observed a significant reduction in BMI

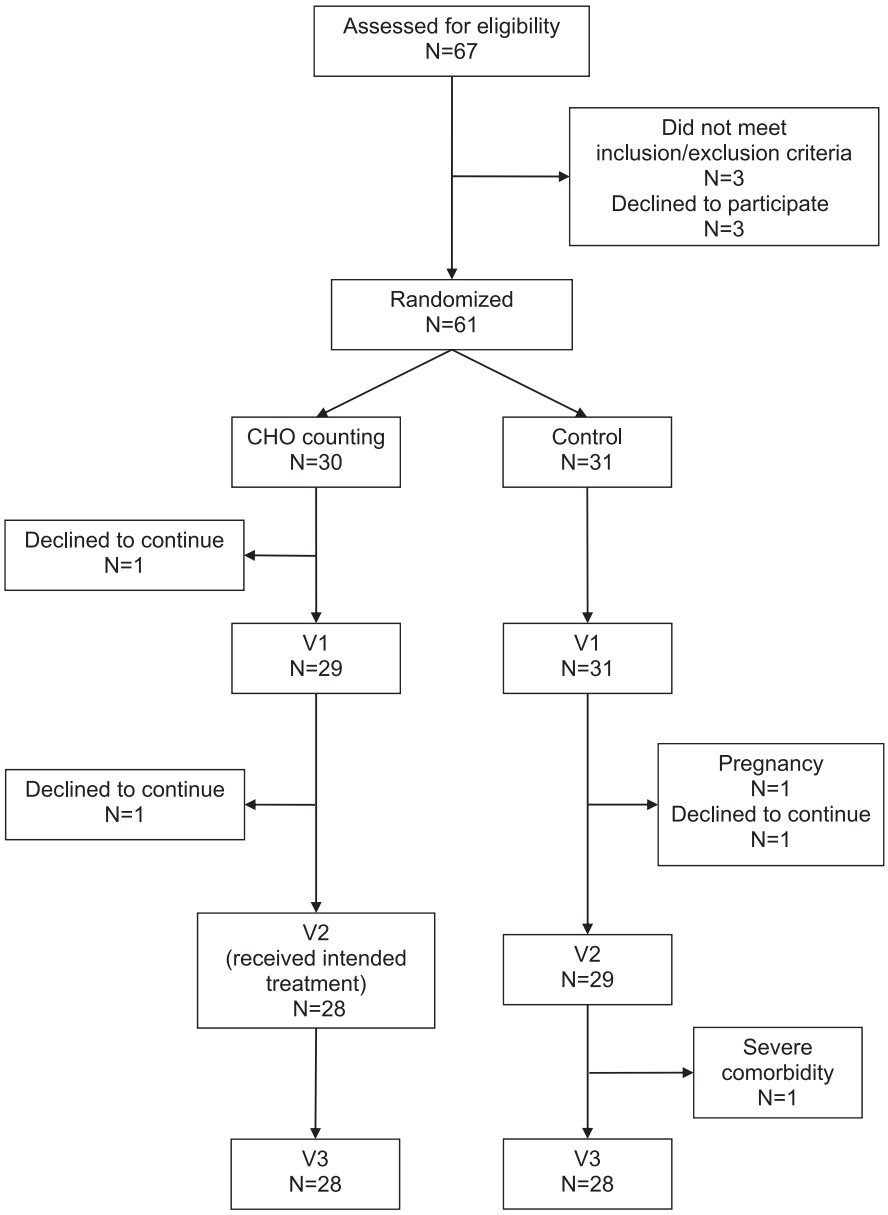

Figure 1—*Flow diagram for the GIOCAR trial.*

and waist circumference compared with control subjects. The significant difference in BMI and waist circumference persisted in the PP analysis (BMI: $P = 0.020$; waist circumference: $P = 0.007$).

Quality of life

The median changes in the score for the seven sections of the DSQOLS instrument between the two groups are shown in Table 2. Baseline scores were similar in the two groups of participants. At week 24, we observed a significant increase (meaning a better quality of life) in the scores related to diet restrictions among participants in the carbohydrate counting group compared with control subjects. The significant difference in the diet restrictions score between the two groups of participants persisted in the PP analysis ($P = 0.004$).

Adverse events

The frequency of hypoglycemic events (i.e., capillary glucose 2.8 mmol/L) was similar in the two groups in both the ITT and the PP analyses. No episodes of severe hypoglycemia requiring assistance from a third party were observed during the study. One patient in the control group was diagnosed with painful diabetic neuropathy during the study.

CONCLUSIONS—This study reports the results of the first randomized clinical trial testing the effects of carbohydrate counting in adult patients with type 1 diabetes treated with CSII. Carbohydrate counting improved the DSQOLS score related to diet restrictions and was associated with a modest, although significant, decrease in BMI and waist circumference. When patients who did not continuously use carbohydrate counting or CSII during the study were excluded from the analyses, carbohydrate counting was also associated with a significant reduction of HbA_{1c} not accompanied by an increase of hypoglycemic events.

Patients with type 1 diabetes must continuously match capillary glucose levels, food intake, and physical activity with the administration of the appropriate dose of exogenous insulin to maintain glucose levels within the recommended target (4). Dietary restrictions and the stress associated with the daily management of diabetes have a negative impact on the quality of life of these patients (19). Carbohydrate counting is a tool that helps patients to estimate in a systematic way the amount of the pre-meal insulin bolus to minimize the glucose increase after a meal, and if necessary, to correct an either inappropriately high or low pre-meal glucose level.

The improvement of the DSQOLS score related to diet restrictions that we observed in our study extends previous findings by Trento et al. (12) to patients with type 1 diabetes treated with CSII, although we did not observe an improvement in HbA_{1c} with carbohydrate counting in our ITT analysis, possibly because our study was relatively short (6 months) or not all participants trained in carbohydrate counting used it. However, when only patients who continuously used carbohydrate counting for the daily management of their diabetes were included in the analyses, we observed a significant improvement in HbA_{1c} (−0.35%) compared with control subjects. The fact that one of five participants who learned carbohydrate counting did not use it to estimate their meal boluses suggests that, although relatively simple, this method may be difficult to implement for a non-negligible proportion of patients with type 1 diabetes.

In our study, the observed improvement in metabolic control among patients using carbohydrate counting in the daily management of their diabetes was achieved without the increase of body weight, waist

Table 1—*Baseline characteristics of study participants by the allocated treatment group (ITT analysis)*

	Carbohydrate counting (n = 28)	Control subjects (n = 28)	P value
Female participants	13 (46.4%)	19 (67.9%)	0.105
Age (years)*	41.2 ± 10.0	39.8 ± 9.8	0.601
Years of school completed†	14 (10–18)	13 (13–15.5)	0.840
Duration of diabetes (years)*	21.9 ± 11.0	19.8 ± 11.7	0.490
Duration of pump therapy (years)†	2 (1–3)	2 (0–3.5)	0.796
Type of insulin			
Glulisine	14 (50.0%)	17 (60.7%)	0.340
Lispro	12 (42.9%)	7 (25.0%)	
Aspart	2 (7.1%)	4 (14.3%)	
Insulin requirement (IU/day)†			
Total	36 (24.5–49)	33 (28.5–39.5)	0.282
Basal	22.5 (15–26)	18.5 (14–22)	0.268
Boluses	15 (10.5–21.5)	12.5 (10–20.5)	0.522
BMI (kg/m^2)†	23.7 (21–25.2)	23.8 (20.8–26.8)	0.670
Waist circumference (cm)†	83 (78.5–91)	78 (74–85.5)	0.194
Glycated hemoglobin (%)*^	7.9 ± 0.9	8.1 ± 1.5	0.526

Categorical variables are presented as frequency with percent in parentheses. *Continuous variables with a normal distribution are presented as mean with SD in parentheses. †Continuous variables that do not have a normal distribution are presented as median with the interquartile range in parentheses. ^Normal range 3.5–6.0%.

circumference, or frequency of hypoglycemic events usually reported with intensive diabetes management (10,20). Indeed, in the carbohydrate counting group we unexpectedly observed a small, although significant, weight loss, for which we have no obvious explanation. At baseline, all randomized patients attended a group lesson with the dietitian about the recommended diet for patients with diabetes, with the only difference between the two groups being learning and using carbohydrate counting. A decrease in BMI with carbohydrate counting, although not significant, also was observed in the study by Trento et al. (21), in which the control group had similar exposure to the diabetes care team. We suggest that carbohydrate counting may provide users with some additional benefits that facilitate weight loss, most likely through improved nutrition or increased physical activity.

Our study has several strengths. First the sample size is at least as large as that of previously published research involving patients with type 1 diabetes who receive multiple daily injections. Second, patients were provided training in carbohydrate counting that is feasible in the setting of a diabetes clinic. On the other hand, our study has some limitations. First, patients in the intervention group had more contact with the diabetes care team during the teaching of carbohydrate counting, thus preventing us from ruling out that the intervention group lost weight and improved metabolic control secondary to the extra attention, rather than the use of carbohydrate counting. However, several evidences support a direct effect of carbohydrate counting on the improvement of glucose control: *1*) in our study a significant improvement in HbA_{1c} was observed only in the PP analysis, which included only those participants who indeed use carbohydrate counting to estimate their meal boluses; *2*) a similar decrease in HbA_{1c} after learning carbohydrate counting was observed in a study with a control group with similar exposure to the diabetes care team (21); and *3*) the study patients in the control group were long-term attendants of our CSII outpatient clinic, making it unlikely that a transient increase in contact with the diabetes care team could significantly affect their diet and diabetes management. Moreover, our study has a relatively short duration, not allowing the assessment of the effects of carbohydrate counting in the long-term, as it would be desirable for a lifetime intervention. Finally, we did not measure physical activity and food intake during the study, not allowing us to assess their contribution to weight loss and improved metabolic control.

In conclusion, our study shows that offering carbohydrate counting to patients with type 1 diabetes treated with

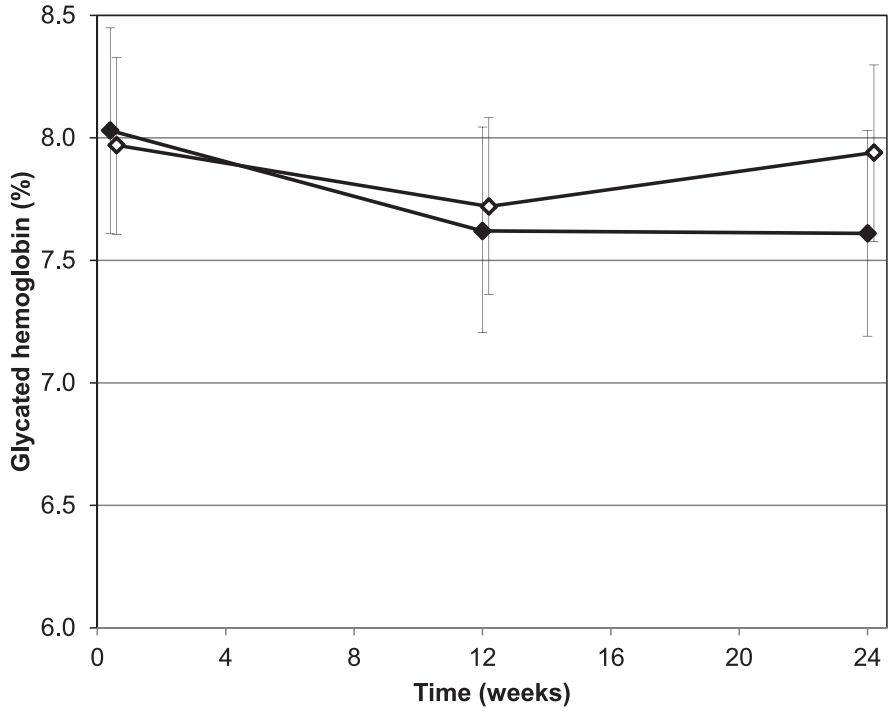

Figure 2—*PP analysis: HbA_{1c} levels (mean and 95% CI) in the two study groups during the GIOCAR trial. The carbohydrate counting group (◆) had significantly lower HbA_{1c} levels than the control group (◇) (P = 0.050).*

Table 2—*Changes from baseline at week 24 in DSQOLS scores, BMI, and waist circumference by the allocated treatment group (ITT analysis)*

	Carbohydrate counting (n = 28)	Control subjects (n = 28)	P value
DSQOLS scores			
Social relations	2 (−2.5 to 3.5)	0 (−1.5 to 5)	0.993
Leisure-time flexibility	−0.5 (−2 to 1)	0 (−2 to 3)	0.413
Physical complaints	2 (0–4.5)	2 (−0.5 to 5)	0.483
Worries about future	1 (−1 to 4)	0 (−1.5 to 3)	0.466
Diet restrictions	5.5 (0.5–8.5)	0 (−2 to 3.5)	0.008
Daily hassles	1.5 (−2.5 to 6)	2 (−1.5 to 3.5)	0.488
Fears about hypoglycemia	0.5 (−2 to 7.5)	1 (−5.5 to 5.5)	0.643
BMI (kg/m^2)	−0.32 (−0.65 to 0)	0.15 (0–0.40)	0.003
Waist circumference (cm)	−1 (−2 to 0)	0 (0–2)	0.002

Data are presented as median with the interquartile range in parentheses.

CSII improves quality of life related to diet restrictions and obtains a modest, although significant, decrease in BMI and waist circumference. A reduction of HbA_{1c}, not accompanied by an increase in hypoglycemic events, may be expected when patients continuously use carbohydrate counting in the daily management of their diabetes.

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A.L. conducted the study and had primary responsibility in patient care. A.M.B. contributed to patient care, data analysis, and article editing. G.P. was responsible for carbohydrate counting teaching and dietary education. V.D., A.C.U., and E.P. contributed to patient care and education. A.S. contributed to carbohydrate counting teaching and education. G.G. had primary responsibility in patient care. E.B. conceived and coordinated the study, and wrote the article. M.S. had primary responsibility in data analysis and wrote the article.

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