DIA-2010-0190-Maurizi_1P
Type: original-article

DIABETES TECHNOLOGY & THERAPEUTICS
Volume 13, Number 4, 2011
© Mary Ann Liebert, Inc.
DOI: 10.1089/dia.2010.0190

A Novel Insulin Unit Calculator for the Management of Type 1 Diabetes

Anna Rita Maurizi, M.D., Angelo Lauria, M.D., Daria Maggi, M.D., Andrea Palermo, M.D.,
Elvira Fioriti, M.D., Silvia Manfrini, M.D., and Paolo Pozzilli, M.D.

Abstract

Background: Intensive insulin therapy is the gold standard therapy for type 1 diabetes (T1D) patients. To achieve optimal glycemic control, adjustments of insulin dose at mealtimes must be made taking into account several parameters: blood glucose levels, insulin/carbohydrate ratio, carbohydrate intake, and physical activity. Calsulin (Thorpe Products Ltd., Cambridge, UK) is a new tool for the administration of insulin dose before each meal. The aim of this study was to evaluate the efficacy of Calsulin on metabolic control in T1D patients undergoing intensive insulin therapy.

Subjects and Methods: Forty consecutive patients affected by T1D, 18–65 years old, with disease duration of >1 year, were randomized to Calsulin or to the control group. Hemoglobin A1c (HbA1c) was evaluated at entry into the study and at 3- and 6-month follow-ups. Paired *t* test (two tailed) and analysis of variance were used to evaluate differences in HbA1c at 3 and 6 months in the two groups.

Results: HbA1c at entry was 7.9 $\pm$ 1.0% (SD) in the Calsulin-treated group and 7.8 $\pm$ 1.6% (SD) in control patients (*P* not significant). Data showed a slight improvement in HbA1c levels at 3 months in the Calsulin-treated group (−0.61% vs. −0.14% difference, respectively; *P* not significant). At the 6-month follow-up, a significant reduction in HbA1c levels was observed in the Calsulin-treated group versus the control group (−0.85% vs. −0.07% difference, respectively; $P < 0.05$).

Conclusions: Calsulin is an acceptable and practical tool that makes the process of calculating insulin doses easy to use, and, most importantly, it improves metabolic control as shown by a significant reduction of HbA1c levels.

Introduction

Intensive insulin therapy, based on multiple daily injections and insulin pump therapy, is the gold standard treatment for type 1 diabetes (T1D). The rationale of intensive insulin therapy is to provide an adequate amount of basal insulin and short-acting insulin to reduce glycemic excursions. The effectiveness of intensive insulin therapy has been reported in the Diabetes Control and Complications Trial, showing that optimal glycemic control is directly related to the reduction of incidence and severity of diabetes complications.[1] Achieving treatment goals should be obtained by maintaining flexibility to fit individual lifestyle and without major variations in eating behaviors and physical activity. Diet, physical activity, and insulin dosage play a key role in the management of insulin treatment in T1D patients.

Diet, in particular carbohydrate (CHO) meal content, is the main determinant of a rise in postprandial blood glucose. Accordingly, an appropriate teaching and training program on CHO counting and specific instructions for the administration of insulin doses need to be implemented in patients with diabetes. In fact, CHO counting as a meal planning approach offers the flexibility of food choices and allows achieving treatment goals.[2–4] It has also been demonstrated that a sedentary lifestyle and lack of physical exercise are associated with poor blood glucose control.[5] Regardless of insulin therapy, physical activity helps decrease blood glucose levels and increase insulin sensitivity and peripheral glucose utilization, in addition to reducing cardiovascular risk factors and preventing obesity.[6]

For achieving treatment goals, the establishment of insulin dose at mealtimes must be made before each injection, while considering certain parameters, such as blood glucose levels, insulin/CHO ratio, CHO intake, and the intensity of physical exercise after injection. Calsulin, a simple tool recently developed by Thorpe Products Ltd. (Cambridge, UK) (see www.thorpe-products.com) (Fig. 1) calculates the premeal bolus that takes into account all of the above parameters in a matter of seconds, displaying the insulin units to be injected.

◀F1

Department of Endocrinology and Diabetes, University Campus Bio-Medico, Rome, Italy.

FIG. 1. The insulin units calculator Calsulin (Thorpe Products Ltd.).

The aim of the present study was to demonstrate the efficacy of Calsulin in improving glycemic control, as assessed by HbA1c in T1D patients using intensive insulin therapy.

Preliminary results of this study were presented at the 46th meeting of the European Association for the Study of Diabetes, held in Stockholm, Sweden, 2010.[7]

Subjects and Methods

T1D patients 18–65 years old attending the diabetes outpatient clinic at the University Campus Bio-Medico in Rome, Italy were asked to participate in the study. T1D was defined according to the American Diabetes Association classification, and all patients gave their consent to participate. Exclusion criteria were learning disabilities or the presence of chronic conditions potentially able to influence daily activities (visual or auditory disability, motor impairment for neurological or orthopedic problems). T1D patients affected by severe diabetes complications were also excluded.

In total, 40 consecutive T1D patients who agreed to participate in the study (26 men, 14 women) were randomized 1:1 to Calsulin or standard education for insulin treatment (control group). All subjects were followed up with visits every 3 months and telephone consultations according to standard procedures operating in our clinic. At enrollment all subjects were provided with a logbook and instructed to self-monitor glucose levels, to estimate meal CHO content, and to perform regular exercise, consisting of at least 2 h of physical exercising three times weekly. The target blood glucose, insulin/CHO ratio (I:C ratio), and insulin sensitivity factor (ISF) were determined for all patients, individually, by the physicians. The I:C ratio, defined as the amount of CHO (g) "covered" by 1 unit of insulin, was determined by the "500 rule." The ISF, defined as the estimated drop in blood glucose (in mg/dL) expected from the administration of 1 unit of insulin, was calculated by the "1,800 rule." During each clinical visit the hemoglobin A1c (HbA1c) level and frequency of hypoglycemic episodes were recorded for each patient, and adherence to the use of CHO counting was verified. Patients in the Calsulin group were trained on the use of Calsulin to administer the insulin dosage. Calsulin setup requires patients to enter four parameters: premeal blood glucose value, I:C ratio, g of CHO contained in the meal, and post-injection exercise. The potential physical activity, performed after injection, is quantified by a number from 0 to 5 on the numeric keypad, and each number, corresponding to the amount of physical exercise, represents the percentage that will be reduced from the total insulin dose calculated. Then, the instrument displays the premeal insulin units to be injected.

HbA1c (%), daily insulin requirement (IR), and body mass index (BMI) were evaluated at entry into the study and at 3- and 6-month follow-ups. The mean daily insulin requirement was expressed as units/kg/day, and BMI was calculated as the ratio of weight (in kg)/(height [in m])^2.

Sample size and statistical evaluation

Setting α (probability of type I error) equal to 0.05 and β (probability of type 2 error) equal to 80%, for a difference of HbA1c of 1% with 1% SD at the end of the study period, the required sample size was 34 patients for a two-sided test. To ensure the appropriate sample size, 40 patients were recruited to allow six dropouts.

Paired t test (two tailed) and analysis of variance were used to evaluate differences in HbA1c, IR, and BMI between the two groups. Data were expressed as mean $\pm$ SD values. A P value of < 0.05 was considered significant.

Results

The results of this study are shown in Table 1 and Figure 2. ◄T1◄F2 The comparison of baseline demographic and clinical features indicates that the two groups of patients did not differ in clinical and metabolic parameters. Level of physical activity was similar between the two groups, and no major differences were reported in socioeconomic status or level of education between the groups.

During the initial 3 months, there was a trend toward a decrease in HbA1c in the Calsulin-treated group versus the control group (7.3 ± 0.5% vs. 7.7 ± 1.0%, respectively; P not significant). At the 6-month follow-up, a significant reduction in HbA1c levels was observed in the Calsulin-treated group versus the control group (-0.85% vs. -0.07% difference, respectively; $P < 0.05$) (Fig. 2). There were no significant differences in IR (0.64 ± 0.24 vs. 0.58 ± 0.19, respectively; P not significant), BMI (23.9 ± 4.6 vs. 25.1 ± 6.1, respectively; P not significant), and frequency of hypoglycemic events between the two groups.

TABLE 1. DEMOGRAPHIC AND CLINICAL FEATURES OF TYPE 1 DIABETES PATIENTS PARTICIPATING IN THE STUDY

	Calsulin-treated	*Control patients*	P *value*
Number	20	20	
Male:female	13:7	13:7	
Age range (years)	34.5 ± 15	39.3 ± 13	
Duration of disease (years)	14.4 ± 10.8	13.4 ± 7	NS
BMI at baseline (kg/m^2)	23.7 ± 3.6	24.7 ± 6.1	NS
HbA1c (%)	7.9 ± 1.0	7.8 ± 1.6	NS
Daily insulin requirement at baseline (IU/kg/day)	0.64 ± 0.22	0.57 ± 0.21	NS

Data are mean $\pm$ SD values.

BMI, body mass index; HbA1c, hemoglobin A1c; NS, not significant.

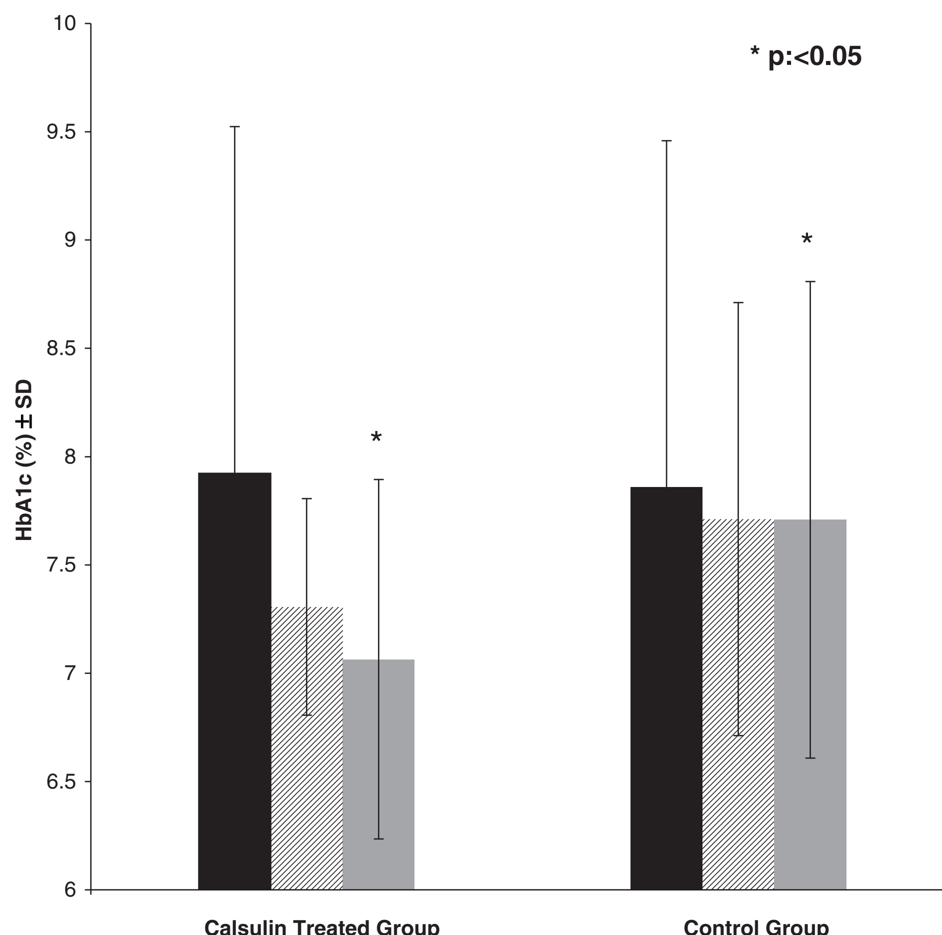

FIG. 2. Hemoglobin A1c (HbA1c) values at entry (time 0) and after 3- and 6-month follow-ups in the two groups of treated patients.

Discussion

To achieve treatment goals in diabetes, one crucial aspect is represented by the reduction of postprandial glycemic excursions. The metabolic control and the onset and progression of diabetes complications are related to both fasting and postprandial glycemia,[8] which results from the CHO content in each meal and of blood glucose levels before meals. Frequently, it is difficult to calculate the insulin dosage accurately using conventional bolus calculation methods. As reported in the study by Glaser et al.,[9] there is high frequency of error (50–64%) in calculating premeal insulin doses using conventional methods. Often, difficulties in performing dose calculations induce patients to administer fixed prandial insulin doses or to maintain an established amount of CHO in their meals.[10] However, a positive effect of correct premeal insulin doses has been also reported in the Diabetes Control and Complications Trial with better control for patients using CHO counting in the intensively treated group, showing a supplementary 0.56% reduction in HbA1c compared with those not using CHO counting.[11] To be effective, diabetes education must be implemented, not only on CHO counting but also on other features of the disease management, mainly specific algorithms to adjust insulin doses to achieve treatment goals. Therefore specific algorithms for insulin administration that take into account premeal blood glucose value and g of CHO contained in the meal should be used to reduce postprandial glycemic excursions and, moreover, to increase flexibility in meal planning, food choices, and physical activity. In the current study, we demonstrated that this simple pocket instrument, the same size of a small calculator, is an acceptable and practical tool to make the process of calculating the premeal insulin dosage very simple. Most importantly, it helps improve glycemic control, as shown by a significant reduction of HbA1c levels compared with standard methods used for calculating the required insulin doses. Finally, because Calsulin actively involves patients in decision-making for treating their own disease, it may improve to adherence and satisfaction with insulin therapy.

Acknowledgments

This study was supported by an educational grant of Thorpe Ltd. to Centro Internazionale Studi Diabete, Rome, Italy. Thorpe Ltd. had no role in the design of the study or management of data. The trial was designed by the investigators, and the manuscript was prepared independently of any input from the company.

Author Disclosure Statement

No competing financial interests exist.

References

1. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. The Diabetes Control and Complications Trial Research Group. N Engl J Med 1993;329:977–986.
2. Rabasa-Lhoret R, Garon J, Langelier H, Poisson D, Chiasson JL: Effect of meal carbohydrate content on insulin requirement in type 1 diabetic patient treated intensively with the basal bolus (ultralente-regular) insulin regimen: Diabetes Care 1999;22:667–673.
3. Kawamura T: The importance of carbohydrate counting in the treatment of children with diabetes. Pediatr Diabetes 2007;8:S57–S62.
4. American Diabetes Association: Nutrition recommendations and interventions for diabetes: a position statement of the American Diabetes Association. Diabetes Care 2008;31(Suppl 1): S61–SS78.
5. Margeirsdottir HD, Larsen JR, Brunborg C, Sandvik L, Dahl-Jørgensen K; Norwegian Study Group for Childhood Diabetes: Strong association between time watching television and blood glucose control in children and adolescents with type 1 diabetes. Diabetes Care 2007;30:1567–1570.
6. American Diabetes Association: Physical activity/exercise and diabetes mellitus. Diabetes Care 2003;26(Suppl 1):S73–S77.
7. Maurizi A, Palermo A, Beretta Anguissola G, Benevento D, Lauria A, Cipponeri E, Tuccinardi D, Manfrini S., Pozzilli P: A pocket instrument for calculating insulin need in the management of type 1 diabetes [abstract 970]. Diabetologia 2010;53(Suppl 1):S386–S387.
8. Ceriello A: Postprandial hyperglycemia and diabetes complications: is it time to treat? Diabetes 2005;54:1–7.
9. Glaser NS, Iden SB, Green-Burgeson D, Bennett C, Hood-Johnson K, Styne DM, Goodlin-Jones B: Benefits of an insulin dosage calculation device for adolescents with type 1 diabetes mellitus. J Pediatr Endocrinol Metab 2004;17:1641–1651.
10. Gross TM, Kayne D, King A, Rother C, Juth S: A bolus calculator is an effective means of controlling postprandial glycemia in patients on insulin pump therapy. Diabetes Technol Ther 2003;5:365–369.
11. Delahanty LM, Halford BN: The role of diet behaviours in achieving improved glycemic control in intensively treated patients in the Diabetes Control and Complications Trial. Diabetes Care 1993;16:1453–1458.

Address correspondence to:
Professor Paolo Pozzilli, M.D.
Department of Endocrinology and Diabetes
University Campus Bio-Medico
Via Alvaro del Portillo 21
00128, Rome, Italy

E-mail: p.pozzilli@unicampus.it