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A Bolus Calculator Is an Effective Means of Controlling Postprandial Glycemia in Patients on Insulin Pump Therapy

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ABSTRACT

Accurate bolus insulin doses require calculations based on (1) current blood glucose, (2) target blood glucose, (3) carbohydrate-to-insulin ratios, (4) total grams of carbohydrate in meals, and (5) insulin sensitivity factors. Patients may often forego these calculations for insulin doses based on empirical estimates. A bolus calculator (Medtronic MiniMed) uses these five parameters to generate a recommended bolus insulin dose. This study provides the evidence that a hand-held bolus calculator is effective in controlling postprandial blood glucose. Subjects (n = 49) with Type 1 diabetes and experienced with continuous subcutaneous insulin infusion therapy were randomized to begin one of two bolus dosing methods. After 7 days, subjects crossed over to the alternate method. Prior to entering the Bolus Calculator period, physicians established patients' bolus parameters and programmed them into a personal digital assistant (PDA). Subjects used the PDA to obtain recommended pre-meal insulin bolus doses. During the Standard Bolus period, significantly more correction boluses were administered to curtail postprandial hyperglycemia ($p = 0.008$) and more supplemental carbohydrate was consumed to raise low blood glucose ($p = 0.046$). Similar values were observed between the two bolus dosing methods in average deviation of 2-h postprandial blood glucose. Subjects reported that the bolus calculator was easy to use and that they were confident in the bolus doses suggested by the device. These results confirm that bolus insulin doses computed by a bolus calculator, compared with standard bolus techniques, achieve target postprandial blood glucose but with fewer correction boluses and supplemental carbohydrate. A bolus calculator, which can be integrated into insulin pump software, may help patients to more accurately meet prandial insulin dosage requirements, improve postprandial glycemic excursions, and achieve optimal glycemic control.

INTRODUCTION

INTENSIVE INSULIN THERAPY involves self-adjusting insulin doses according to the results of frequent blood glucose monitoring.[1] Accurate bolus insulin doses require calculations based on (1) target blood glucose, (2) current blood glucose, (3) carbohydrate-to-insulin ratios (CIR), (4) total grams of carbohydrate (CHO) in the meal, and (5) insulin sensitivity factors (ISF). Patients may diligently perform these calculations when beginning intensive

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therapy. However, adherence to these recommendations may become relaxed as patients gain familiarity with insulin dosing and begin to approximate pre-meal boluses by titrating insulin based on the "standard" or "usual" CHO content of their meals. This empirical method of determining pre-meal boluses promotes a rigid meal/insulin regiment and ultimately limits patients' ability to achieve optimal glycemic control.

Bolus calculator technology using a personal digital assistant (PDA) may make pre-meal bolus calculations more convenient and more accurate, and may help to improve patient adherence to the diabetes management regimen. A bolus calculator (Medtronic MiniMed) provides an enhanced method of insulin administration, by using these five parameters to generate a recommended bolus insulin dose. The user is only required to perform a pre-meal fingerstick and estimate the total CHO (g) in the meal. The patient then enters these two values into a PDA that has been preprogrammed with an individualized target blood glucose, ISF, and CIR. The bolus calculator then computes an appropriate dose recommendation. This algorithm could easily be integrated into insulin pump software.

The bolus calculator was designed to reduce postprandial glycemic excursions. Although postprandial excursions contribute to elevated hemoglobin A1c (HbA1c),[2–4] Boland et al.[5] were able to demonstrate prolonged postprandial hyperglycemia despite satisfactory HbA1c levels. These studies and others suggest targeting elevated postprandial blood glucose may improve overall glycemic control.[6–8] While others have described insulin dosing algorithms and evaluated the clinical effectiveness of more elaborate systems,[9,10] this study is the first evaluation of a small, hand-held calculator. The purpose of this study was to establish that a hand-held bolus calculator is as effective in controlling postprandial blood glucose as standard bolus estimation techniques.

MATERIALS AND METHODS

Subjects from two clinical sites, diagnosed with Type 1 diabetes, and on continuous subcutaneous insulin infusion (CSII) therapy using Medtronic MiniMed (Northridge, CA) insulin pumps for a minimum of 3 months were included in this study. Physicians at these sites were asked to identify potential subjects who were able to count CHO (g) in meals and deliver an appropriate pre-meal insulin bolus. Half of the subjects were randomized to the Bolus Calculator period (BC period) followed by the Standard Bolus period (SB period). The remaining subjects were randomized to the SB period followed by the BC period.

The study used a two-period, crossover repeated-measures design. Subjects in the SB period continued using their current insulin dosing method to determine pre-meal boluses. The target blood glucose, ISF, and CIR were determined for all subjects, individually, by the physician, using subjects' logbooks, at the start of their BC period in the study. The ISF was defined as the estimated drop in blood glucose (mg/dL) expected from the administration of 1 unit of insulin, and the CIR was defined as the number of CHO (g) covered by 1 unit of insulin. Subjects entering the BC period were trained on the use of the bolus calculator software. Subjects were required to enter their pre-meal blood glucose value (obtained from their home blood glucose meter) and the total CHO (g) in the meal into the bolus calculator in order to obtain a pre-meal bolus insulin dose. After 7 days, subjects crossed over to the alternate treatment period.

The bolus calculator software was implemented on a PDA platform for use by study participants. The software setup required each subject to input his or her (1) target blood glucose, (2) ISF, and (3) CIR. Subjects could create a profile of up to four separate ISF values and corresponding start times during the day. A similar profile of CIR values could also be created. The subjects initiated the bolus calculator by entering the current blood glucose and the total grams of CHO contained in the meal to be eaten. The recommended pre-meal bolus consisted of (1) the meal portion (calculated by dividing the total grams of CHO by the CIR) and, if the current blood glucose was higher than the target blood glucose, (2) a correction bolus (calculated by subtracting the target blood glucose from the current blood glucose and dividing by the ISF). The recommended bolus was then modified, if desired, and programmed manually into the insulin pump by the subject.

All subjects were instructed to test their blood glucose using their home meters. Subjects were asked to test blood glucose before meals, 2 h following meals, and at bedtime. All blood glucose values were recorded in logbooks, and subjects noted each administration of a correction bolus for blood glucose readings >200 mg/dL (or as needed) and supplemental CHO to correct blood glucose readings <65 mg/dL (or as needed). Hypoglycemia was defined as blood glucose <60 mg/dL, and hyperglycemia was defined as blood glucose >250 mg/dL. At the study's conclusion, all subjects were asked to complete an eight-item questionnaire that assessed satisfaction with the bolus calculator using a graphic rating mapped onto a 7-point Likert scale (rated 1 through 7) for analysis,[11] and to provide comments or suggestions regarding the bolus calculator.

The average deviation of the 2-h postprandial blood glucose from target was compared using analysis of variance. Frequency of correction boluses, supplemental CHO, and frequency of hypo- and hyperglycemia were compared using separate paired t tests. Results are presented as mean ± standard deviation or median (range) unless otherwise indicated. Significance was established at $p < 0.05$.

RESULTS

A total of 49 subjects (57% female; 43 ± 15 years old; diabetes duration, 22 ± 16 years) were enrolled in the study. The following parameters were entered into the bolus calculator setup. Target blood glucose was 112 ± 15 mg/dL, the ISF was 51 ± 19 mg/dL per unit of insulin, subjects entered a median of one (one to four) of the maximum of four separate daily ISF values, the CIR was 14 ± 5 CHO (g) per unit of insulin, and subjects entered a median of one (one to four) of the maximum of four separate daily CIR values. The majority of subjects ($n = 46$) were using Humalog, two subjects were using Velosulin, and one subject reported using "regular insulin."

Compared with the BC study period, significantly more correction boluses for hyperglycemia were administered because of insufficient pre-meal insulin bolus ($p = 0.008$) during the SB period, as shown in Table 1. In addition, significantly more supplemental CHO for hypoglycemia was consumed for overestimated pre-meal insulin bolus requirements ($p = 0.046$) during the SB period than during the BC period. There was no statistically significant difference between the two bolus dosing methods in average deviation of the 2-h postprandial blood glucose from target, also presented in Table 1. There were no statistically significant differences in the frequency of hypoglycemia and hyperglycemia between the two dosing methods, and no adverse events were reported in either period. Of the 1,076 uses of the bolus calculator, subjects decreased the recommended bolus dose 128 times (11.9%) with an average decrease of 1.3 ± 1.6 units of insulin. Subjects most often cited anticipated exercise or the prolonged effects of an earlier bolus dose as the rationale for reducing the pre-

TABLE 1. COMPARISON OF MEASURES OF POSTPRANDIAL GLYCEMIC CONTROL UNDER BOLUS CALCULATOR AND STANDARD BOLUS CONDITIONS

	Standard bolus (n = *49)*	*Bolus calculator* (n = *49)*	p *value*
Average deviation of 2-h postprandial blood glucose from target (mg/dL)	42.8 ± 74.5	42.5 ± 70.0	0.88
Number of correction boluses/week	13.5 ± 6.1	11.4 ± 5.8	0.008[a]
Frequency of supplemental CHO/week	4.6 ± 3.5	3.5 ± 2.8	0.046[a]
Hypoglycemic events/week	3.4 ± 3.1	3.1 ± 2.9	0.58
Hyperglycemic events/week	5.2 ± 3.6	5.0 ± 3.9	0.72

Data are mean ± standard deviation.
[a]Significant with $p < 0.05$.

meal bolus insulin dose recommended by the bolus calculator. Subjects increased the recommended bolus dose 61 times (5.7%) with an average increase of 0.8 ± 0.8 units of insulin that was often related to meal content.

Questionnaire responses (received from 48 subjects) are presented in Table 2, and indicated that subjects overwhelmingly felt that the bolus calculator was extremely easy to learn and use. They reported confidence using the device and, if it were available, would use it at all meals. In addition, subjects reported that the bolus calculator was an improvement over their current method in determining a meal bolus and that the benefit of using the device outweighed the extra time and effort involved in using it.

CONCLUSIONS

Postprandial hyperglycemia is a modifiable risk factor in diabetes management. Until recently, only two techniques were available to guide patients through self-adjusting pre-meal insulin bolus doses. Patients on intensive therapy regimens were required either to perform complex mental calculations based on current and target blood glucose, CIR, total CHO (g) in the meal, and ISF; or to administer a predetermined bolus insulin dose and follow a rigid calorie- and CHO-controlled diet. Compliance with either technique involves behavior modification that has been difficult to achieve and maintain in patients with diabetes.[12]

This study provides the first evidence that subjects' postprandial blood glucose is as well controlled using a bolus calculator as using standard bolus techniques. Importantly, subjects administered significantly fewer postprandial correction boluses and consumed significantly less supplemental CHO when using the bolus calculator. These findings suggest that pre-meal bolus doses recommended by a bolus calculator are no less accurate than those estimated by subjects with experience in CHO counting and delivering appropriate pre-meal insulin boluses.

It is generally easier to adjust an insulin dose than to change long-standing eating patterns.[13] However, in clinical practice it is often difficult for adults to estimate correct bolus doses, and may be especially difficult for children who often have ISF and CIR that result in doses of a fraction of an insulin unit. A bolus calculator aids patients in accurately adjusting pre-meal insulin boluses, and provides them with added flexibility in their meal times, food choices, and physical activity, allowing them to focus on

TABLE 2. MEDIAN AND RANGE OF SUBJECT RESPONSES TO A 7-POINT LIKERT SCALE (RATED 1 THROUGH 7) QUESTIONNAIRE ASSESSING PERCEIVED EASE AND USEFULNESS OF A BOLUS CALCULATOR

Questionnaire	*Median (range)*
1. For your meal boluses, was it easy/difficult to establish a bolus dose using the bolus calculator? (Extremely Difficult ↔ Extremely Easy)	7 (2–7)
2. What was your level of confidence with the bolus calculator's recommended bolus amounts? (Extremely Low ↔ Extremely High)	6 (1–7)
3. If the bolus calculator feature was in your MiniMed pump, how often would you use it? (No Meals ↔ All Meals)	7 (1–7)
4. Do you feel that using the bolus calculator improved your after meal blood glucose measurements? (Worsened ↔ Improved)	5.5 (2–7)
5. Was using the bolus calculator an improvement over your current method in determining a meal bolus? (Worse than Current ↔ Better than Current)	6 (2–7)[a]
6. How easy/difficult was it to learn how to use the bolus calculator? (Extremely Difficult ↔ Extremely Easy)	7 (4–7)
7. Did the benefit of using the bolus calculator exceed the extra effort/time to use it? (Effort Exceeds Benefit ↔ Benefit Exceeds Effort)	6 (2–7)
8. Would you be more likely to purchase a pump that included a bolus calculator? (Less Likely ↔ More Likely)	6 (1–7)

Forty-eight subjects completed the questionnaire.
[a]$n = 47$.

other aspects of the diabetes management regimen. Future bolus calculators should accommodate the nonlinear time action profiles of regular or fast-acting insulin that has previously been administered. The burden of bolus insulin dosing calculations may be shifted from the patient by equipping an insulin infusion pump with a bolus calculator that includes memory of residual insulin action profiles. Such a device may help patients to more accurately meet prandial insulin dosage requirements, improve postprandial glycemic excursions, and achieve optimal glycemic control.

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