The Use of Insulin Pumps With Meal Bolus Alarms in Children With Type 1 Diabetes to Improve Glycemic Control

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OBJECTIVE — The aim of this study was to determine whether the use of meal bolus alarms would result in fewer missed meal boluses per week in youth with type 1 diabetes using continuous subcutaneous insulin infusion (CSII) therapy.

RESEARCH DESIGN AND METHODS — This was a randomized trial of 48 youth using CSII, who were in suboptimal glycemic control with HbA_{1c} (A1C) values ≥8.0%. Twenty-four subjects were randomized to use a Deltec Cozmo insulin pump with meal bolus alarms (experimental group), while the other 24 subjects continued use of their current insulin pumps (control group) without meal bolus alarms.

RESULTS — After 3 months of study, the number of missed meal boluses per week was significantly lower in the experimental group (from 4.9 ± 3.7 to 2.5 ± 2.5; $P = 0.0005$) but not significantly lower in the control group (from 4.3 ± 2.7 to 4.2 ± 3.9; $P = 0.7610$). Also after 3 months, the mean A1C value of the experimental group declined significantly (from 9.32 ± 1.12 to 8.86 ± 1.10; $P = 0.0430$). No significant decline in A1C was present for the control group (from 8.93 ± 1.04 to 8.67 ± 1.17; $P = 0.1940$). After 6 months of study, the significant decline in A1C from baseline in the experimental group was no longer present. Pooling of all available data from the control and experimental groups showed that at baseline and 3 and 6 months, the number of missed meal boluses per week was significantly correlated with A1C values.

CONCLUSIONS — While meal bolus alarms may have the potential to improve suboptimal glycemic control in youth using CSII, our results demonstrated that these alarms had only a transient, modest effect in doing so.

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Intensive diabetes management is now being advised for children with type 1 diabetes (1). This usually involves multiple daily injections of insulin or continuous subcutaneous insulin infusion (CSII; insulin pump) therapy. Unfortunately, even with CSII, ~30% of subjects remain in suboptimal glycemic control (2). The primary reason for suboptimal glycemic control in children using CSII was recently shown to be missed insulin meal boluses (3). The purpose of the current study was to determine whether the use of a pump with meal bolus alerts would result in reduced missed meal boluses and improved glycemic control.

RESEARCH DESIGN AND METHODS

— The first 48 subjects between the ages of 8 and 20 years, inclusive, who were using insulin pumps for at least 6 months and who had HbA_{1c} (A1C) values ≥8.0% were invited to participate. All subjects were patients who were routinely seen at the Barbara Davis Center for Childhood Diabetes (Denver, CO). A total of 23 male and 25 female subjects were enrolled in the study. Mean age of subjects was 15.2 ± 2.9 years. All subjects and parents signed consents approved by the Colorado Multiple Institutions Review Board and in compliance with the Health Insurance Portability and Accountability Act.

This was an investigator-initiated prospective, randomized, parallel-group pilot study following subjects during three clinic visits over 6 months. The visits were scheduled at baseline and 3 and 6 months. Randomization to the control or experimental group for each subject number (1–48) was performed before the start of enrollment using an SAS program. Upon enrollment, each subject opened a sealed envelope that contained the next sequential subject number and corresponding group assignment. Twenty-four youth were randomized to use the Deltec Cozmo insulin pump (Smiths Medical, St. Paul, MN) equipped with user-dependent alarms (experimental group). The alarms were set to sound or vibrate if a meal bolus was not delivered within the time range specified for each meal for each individual subject. Alarms were also set to remind participants to check blood glucose levels 2 h after correction boluses were taken and to alert the need to do a set change every 3 days. The subjects randomized to use the Deltec pump underwent a 1- to 2-h training session.

The 24 subjects randomized to be control subjects (and remain on their current insulin pump) underwent an advanced pump training session of similar length. Both groups were told about the importance of not missing food boluses and that they could phone us if they had questions. They were asked to return to the clinic for their routine appointments after 3 and 6 months. They did not have other required visits or contacts with the health care team. All 48 subjects were provided with Freestyle Flash meters (Abbott Diabetes Care, Chicago, IL) and sufficient blood glucose strips to do four or more self-monitored blood glucose (SMBG) tests per day.

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Abbreviations: CSII, continuous subcutaneous insulin infusion; SMBG, self-monitored blood glucose.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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Table 1—*Baseline demographics*

	Experimental group	Control group	*P* value
Age (years)	15.6 ± 2.5	14.9 ± 3.3	0.4273
Duration of type 1 diabetes (years)	8.83 ± 3.04	8.07 ± 3.95	0.4607
Duration of CSII (years)	3.64 ± 1.22	2.99 ± 1.52	0.1099
Male:female	12:11	10:14	NA

Data are means ± SD.

A subject questionnaire, as described previously (3), was administered initially and at 3 and 6 months. Pump and blood glucose meter downloads were evaluated for number of missed meal boluses and percentage of SMBG values "in-range" initially and at 3 and 6 months. The counting of missed boluses with the subject and health care provider using the pump download was done after both did initial estimates (the subject on the questionnaire and the care provider by comparing SMBG and pump bolus downloads). Parents, when present, were usually helpful in reminding subjects when they had or had not eaten. Eating only two meals (brunch and dinner), for example, was common on weekends (and thus no missed meal bolus was counted for these periods). As previously described (3), the apparent missed meal boluses were verified with the patient and family. Only meal boluses mutually agreed to having been missed were counted as missed boluses. The A1C levels were measured at each visit using the DCA 2000 analyzer (Bayer Diagnostics, Elkhart, IN). A1C values obtained from the DCA 2000 have been shown to be accurate and to correlate well with those obtained from a central laboratory using a cation-exchange high-performance liquid chromatography method (4).

Statistical analysis

Due to the skewed distribution of A1C values, a log-10 transformation was used for all analyses. Repeated-measures analysis was performed using SAS Proc Mixed. Preplanned contrasts were performed to test within- and between-group differences in A1C, missed boluses per week, physician and subject estimates of missed boluses, weight, frequency of blood glucose testing, and percent of SMBG results within target range. Results were considered significant at $\alpha < 0.05$ for a two-sided test. Pearson correlation coefficients and linear regression were used to explore the relationship between missed boluses and glycemic control at baseline and 3 and 6 months.

RESULTS — The mean age, duration of type 1 diabetes, and duration of CSII use were similar in the control and experimental groups (Table 1). One experimental group subject who initially agreed to participate did not come for pump training or further participation, so data are reported for 47 subjects. A total of 44 of 47 subjects were using "smart" pumps that did automatic food and correction bolus calculations.

The experimental and control groups were similar at baseline in A1C values (9.32 ± 1.12 vs. 8.93 ± 1.04%, respectively; $P = 0.1507$) and in number of missed meal boluses per week (4.9 ± 3.7 vs. 4.3 ± 2.7, $P = 0.5770$). Mixed-model repeated measures demonstrated no treatment effect or treatment and time interaction on A1C; however, preplanned contrasts suggested that mean A1C values in the experimental group improved slightly, but significantly, from 9.32 ± 1.12 to 8.86 ± 1.10%; $P = 0.0430$ at 3 months (Table 2). A similar significant decrease did not occur for the control group. The number of missed meal boluses per week in the experimental group decreased significantly from 4.9 ± 3.7 to 2.5 ± 2.5 ($P = 0.0005$) at 3 months. A similar significant decrease did not occur for the control group. Mixed-model repeated measures indicated a significant interaction between treatment and time on the number of missed boluses ($P = 0.0434$); however, preplanned contrasts showed no significant difference in the number of missed meal boluses between groups at 3 months ($P = 0.1159$). The percent of glucose readings "in range" did not increase significantly from baseline to 3 months (or 6 months) in either the experimental or control group (Table 2).

Twenty-two subjects in the experimental group and 23 in the control group completed 6 months of study. At 6 months, the experimental group no longer had a significant reduction in A1C values (Table 2). In fact, a preplanned contrast of the two groups at month 6 for A1C was marginally significant ($P = 0.0463$), without adjustment for multiple contrasts, favoring the control group. This suggests that A1C values in the experimental group (9.41 ± 1.16%) were slightly worse than for the control group (8.78 ± 1.17%) by the end of the study. The number of missed meal boluses was not significantly different between the experimental (3.3 ± 3.6) and control (3.6 ± 3.5) groups at 6 months ($P = 0.8585$) (Table 2). However, the number of missed boluses was still decreased significantly from baseline to 6 months in the experimental group ($P = 0.0150$) but not in the control group ($P = 0.1727$). One person in the experimental group had an episode of ketoacidosis (the only severe adverse event in either group) before the

Table 2—*Parameters related to glycemic control*

	Experimental group			Control group		
	Baseline	3 months	6 months	Baseline	3 months	6 months
A1C (%)	9.32 ± 1.12	8.86 ± 1.10*	9.41 ± 1.16†	8.93 ± 1.04	8.67 ± 1.17	8.78 ± 1.17†
Number of missed meal boluses per week (7 days)	4.9 ± 3.7	2.5 ± 2.5*	3.3 ± 3.6*	4.3 ± 2.7	4.2 ± 3.9	3.6 ± 3.5
SMBG (% in range)	31.8 ± 15.1	35.4 ± 11.3	30.4 ± 10.6	31.0 ± 11.1	34.4 ± 11.6	34.0 ± 11.7
Mean difference in physician and subject estimates of missed boluses per week	1.29 ± 3.44	0.348 ± 4.57	1.05 ± 4.08*	0.667 ± 2.51	1.79 ± 3.24	−0.167 ± 3.99*

Data are means ± SD. *$P < 0.05$ for within-group difference from baseline. †$P < 0.05$ for preplanned contrast at 6 months.

6-month visit, and his A1C was 4.0 percentage points higher at 6 months compared with 3 months.

There were no significant differences between male and female subjects in A1C values or in number of missed boluses at any time point (data not shown). There were no significant differences in weight or in weight gain between the experimental and control groups at any time (data not shown). After pooling data from all subjects, there was a slight correlation between BMI and number of missed meal boluses per week at visit 0 ($r = 0.31$, $P = 0.0334$). However, no such correlation was present at 3 or 6 months ($r = 0.18$, $P = 0.2246$ and $r = 0.21$, $P = 0.1601$, respectively). There were also no significant differences between or within groups with respect to frequency of blood glucose testing per day (data not shown).

The 10 experimental group patients who improved in A1C (>0.5%) at 3 months showed a mean decline in missed meal boluses of 2.6 ± 2.4 per week and a mean decline in A1C of 1.3 ± 0.67% from baseline to 3 months. Six subjects had reduced A1C values (≥0.5%) from baseline to 6 months (mean decrease 1.3 ± 0.45%). At 6 months, these six subjects had a mean decline in missed meal boluses (compared with baseline) of 1.8 ± 1.8 per week. At baseline and 3 and 6 months, there were positive correlations, using the data from all 47 subjects, between the number of missed boluses and the A1C values ($r = 0.60$, $P < 0.0001$; $r = 0.64$, $P < 0.0001$; and $r = 0.58$, $P < 0.0001$ for the three time periods, respectively). Linear regression showed that at 3 months, there was a 0.92% increase in A1C for every four meal boluses missed. At 6 months, there was a 0.98% increase in A1C for every four meal boluses missed.

The mean differences between the physician and subject estimates of missed meal boluses were not significantly different between groups at any time point. However, both groups experienced a significant decrease in the discrepancy between physician and subject estimates between baseline and 6 months (experimental group: $P = 0.0259$; control group: $P = 0.0007$) (Table 2).

CONCLUSIONS— This is the first report of the use of insulin pump alarms in children or adults with type 1 diabetes to attempt to improve glycemic control. The experimental group showed a significant reduction in A1C values at 3 months as fewer meal boluses were missed. However, the intervention did not result in a durable improvement in diabetes control, nor did these subjects achieve the 2005 American Diabetes Association A1C target goals (1). The patients in this study were included because they had baseline A1C levels >8.0%. While A1C values in this range are neither optimal nor desirable, they are similar to previously reported mean values. The baseline A1C in the conventionally treated adolescent cohort of the Diabetes Control and Complications Trial was 9.76 ± 0.12% (6).

In the present study, ranges for eating times were set for the experimental group, and if a bolus was not taken by the end of this time interval, the pump was set to either alarm audibly (elected by 70% of subjects) or to vibrate (30% of subjects). A disadvantage of the use of alarms at the end of time ranges was the likely taking of the food bolus after the meal rather than before the meal for some subjects, which results in an A1C value ~0.7% higher (3). However, even though the bolus may have been given late in some of the experimental group subjects, the alerts resulted in significant decreases in the number of missed meal boluses per week at 3 and 6 months.

We had previously reported an estimate of a 1.0% increase in A1C for every four missed meal boluses per week (3). Data obtained from the present study at both the 3 and 6 month time points further confirm this estimate.

It is not known why the significant decrease in A1C found after 3 months was lost after 6 months. The number of missed meal boluses increased by a mean of 0.8 per subject per week between 3 and 6 months. This increase could have been intentional, as controlling or losing weight through missed or altered insulin boluses is common in adolescent female patients (6). While this may have been a factor, the number of missed boluses was similar between male and female subjects in the current study. Additionally, while there was a slight correlation between number of missed boluses and BMI at baseline, no such correlation was present at any subsequent study time point. Thus, it is more likely that the novelty of being reminded to bolus in the experimental group had diminished and the subjects again focused less attention on their bolusing habits.

In addition to alarms for missed meal boluses, the initial study protocol called for the setting of alarms to remind subjects to recheck SMBG values 2 h after bolus corrections for high SMBG levels. At the 3-month time point, some initial study subjects reported that they tended to ignore all the alarms (both missed meal bolus and postcorrection bolus alarms) as they felt the alarms were occurring too frequently. In response to this, some subjects chose to turn off the postcorrection bolus alarms by 3 months. For standardization purposes, and to prevent other study subjects from ignoring all the alarms, the investigators turned off the postcorrection bolus alarms in all subjects at their 3-month visit. While this decision was made in an effort to increase compliance with the primary alarm of interest (the missed meal bolus alarm), the loss in A1C improvement at 6 months may have been due to the absence of these postcorrection bolus alarms.

It should be noted that if meal boluses are being missed, it is likely that snack boluses are also omitted. Unfortunately, we could not quantify this parameter with any accuracy. Most youth do not enter snack information into their meter or pump, and their memory of snacks is poor.

In summary, the use of meal bolus alarms in the insulin pump did result in fewer missed meal boluses and initial improvement in A1C values. However, the improvement was not sustained in the long term. The data obtained from this study indicates that technology, per se, may not solve behavioral problems, such as omission of insulin boluses, in children and adolescents with suboptimal diabetes control. Future research is needed to explore additional techniques that may sustain the effects initially observed in this study.

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