Missed Insulin Meal Boluses and Elevated Hemoglobin A_{1c} Levels in Children Receiving Insulin Pump Therapy

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ABSTRACT. ***Objective.*** **To identify possible causes of suboptimal glycemic control (ascertained by hemoglobin A_{1c} [HbA_{1c}] level) in youths using insulin pump therapy.**

Methods. **Forty-eight youths who were receiving insulin pump therapy for ≥6 months, and who were using insulin pumps and blood glucose meters with data that could be downloaded at our facility, are included in this cross-sectional study. Possible causes of suboptimal glycemic control were evaluated by using 4 information sources: 1) insulin pump data downloads; 2) glucose meter data downloads; 3) patient/family questionnaire about insulin bolusing habits, eating habits, exercise, and blood glucose testing habits; and 4) a physician questionnaire. Physicians completed the questionnaire during the patient interview after reviewing the downloaded information and discussing these results with the patient/family.**

Results. **The mean (± standard deviation) age of participants was 15.3 (±3.0) years (range: 7–20 years), and the mean (± standard deviation) duration of type 1 diabetes and continuous subcutaneous insulin infusion was 8.2 (±4.0) and 1.9 (±1.0) years, respectively. Patients who missed <1 bolus per week had a mean (95% confidence interval) HbA_{1c} level of 8.0% (7.7, 8.3), whereas those who missed ≥1 mealtime boluses per week had a mean HbA_{1c} level (95% confidence interval) of 8.8% (8.6, 9.1). No significant relationships were found between HbA_{1c} levels in males and females, the amount of exercise per week, or bolusing before insulin pump disconnection for exercise. Although not significant, a trend was found for those who missed <1 bolus per week to perform more blood glucose tests per day and for those who bolused before a meal rather than after to have lower HbA_{1c} levels. Significant correlations were found between HbA_{1c} levels and the number of missed mealtime boluses per week (r = .414) and mean blood glucose levels (r = .70).**

Conclusion. **Missed mealtime insulin boluses seem to be the major cause of suboptimal glycemic control in youths with diabetes receiving continuous subcutaneous insulin infusion therapy.** ***Pediatrics*** **2004;113:e221–e224. URL: http://www.pediatrics.org/cgi/content/full/113/3/e221;** ***type 1 diabetes, insulin pump, children, hemoglobin A_{1c}, missed meal bolus, continuous subcutaneous insulin infusion, CSII.***

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ABBREVIATIONS. DCCT, Diabetes Control and Complications Trial; CSII, continuous subcutaneous insulin infusion; HbA_{1c}, hemoglobin A_{1c}; CI, confidence interval; BMI, body mass index.

Intensive diabetes management was shown in the Diabetes Control and Complications Trial (DCCT) to reduce the risk for the eye, kidney, and nerve complications of diabetes.[1] In the DCCT, the intensive management included ≥3 insulin injections per day or continuous subcutaneous insulin infusion (CSII) (insulin pump) therapy. The mean hemoglobin A_{1c} (HbA_{1c}) level of the intensively treated patients was 7.1% for adults[1] and 8.1% for adolescents.[2] In a previous report from a general pediatric diabetes clinic, 39% of children changing to insulin pump therapy showed improvement in HbA_{1c} levels (a decrease ≥0.5%), although 64% either showed improvement (of at least a 1.0% decrease of HbA_{1c} levels) or maintained a HbA_{1c} level <8%.[3] Unfortunately, 20% showed a worsening of their HbA_{1c} level from a mean of 7.8% to 8.8%. The clinical impression was that missed insulin boluses were a major reason for worsening glycemic control, although insulin pump data downloads were not available to confirm the impression. The purpose of the current study was to identify possible causes of suboptimal glycemic control in youths using insulin pump therapy.

METHODS

The first 48 youths seen at our clinic who were using insulin pumps and glucose meters with data that could be downloaded were included in this study. All participants were receiving insulin pump therapy for at least 6 months before inclusion and had attended pump training classes. All had received training on counting carbohydrates for the calculation of mealtime insulin boluses and agreed to perform at least 4 blood glucose tests per day before initiating insulin pump therapy. In addition, all participants were using Medtronic MiniMed (Northridge, CA) insulin pumps, because this was the only type of pump with data that could be downloaded at our facility at the time. A variety of glucose meters were used in this study, all of which had data that could be downloaded at our facility. Before inclusion, participants were required to sign a consent/assent form and complete a questionnaire approved by the Colorado Multiple Institutional Review Board. Parents of youths <18 years of age also signed the consent form.

A questionnaire was developed to identify possible reasons for suboptimal glycemic control in youths using insulin pumps, including missed mealtime insulin boluses, timing of meal boluses in relation to meals, pump disconnection and bolus for exercise, and number of blood glucose tests performed per day. Participants were asked to answer as accurately and honestly as possible and were told that they would not be criticized for their responses. Younger children (≤12 years old) completed the questionnaire with the assistance of their parents, whereas older children were encouraged to complete the questionnaire on their own. Participants (and families) were questioned about their insulin bolus administration habits and parameters and frequency of home blood glucose monitoring. Pump data downloads used in this study were analyzed over the 4 weeks before the clinic visit. Physicians estimated boluses missed per week (from the downloads) after interviewing the participant, taking into account the sleeping and eating habits of each participant for the time period, and then reported the result as a 1-week average. Occasions on which a participant did not bolus because hypoglycemia was experienced at mealtime or no carbohydrate was consumed were not counted as a missed bolus. Blood glucose data downloads were analyzed for the 30 days before the clinic visit. Responses on the patient questionnaire pertaining to boluses missed per week and blood glucose tests done per day were compared with physician estimates based on the downloaded data and the patient interview.

The HbA_{1c} levels were determined by using the DCA 2000 Analyzer (Bayer Diagnostics, Elkhart, IN) with a nondiabetic range of 3.2% to 6.2%. This method of HbA_{1c} analysis has been shown to be accurate in our laboratory.[4] HbA_{1c} level at the time of study inclusion was used for analyses.

Statistical analyses were performed by using Microsoft (Seattle, WA) Excel 2000 for Windows and analyzed later by using SAS/STAT, Version 8e (SAS Institute, Inc, Cary, NC) statistical package for Windows.

RESULTS

The mean age (± standard deviation) of the participants was 15.3 (±3.0) years (range: 7–20 years), with a mean duration of diabetes of 8.2 (±4.0) years and time of insulin pump usage of 1.9 (±1.0) years (Table 1). There were 23 females and 25 males, and all patients were non-Hispanic white. The mean (95% confidence interval [CI[) HbA_{1c} level at the time of study was 8.5% (8.3, 8.7), with little variation among genders or age groups (Table 1).

Seventeen patients (35%) missed <1 mealtime bolus per week, and 31 patients (65%) missed ≥1 mealtime boluses per week. The mean (95% CI) HbA_{1c} level for the 17 patients was 8.0% (7.7, 8.3), compared with 8.8% (8.6, 9.1) for the 31 patients ($P = .0001$). The mean (95% CI) number of physician-estimated missed mealtime boluses per week was 2.1 (1.5, 2.7), whereas self-reporting revealed 1.3 (0.93, 1.73) missed mealtime boluses per week ($P = .052$) (Fig 1). All age groups underestimated the number of missed meal boluses, with the greatest underestimation in the 13- to 15-year age group (1.3 per week underestimation). This group also had the highest mean HbA_{1c} level (8.8%) of the 4 age groups. There was no difference in the number of missed boluses by gender ($P = .41$). There was no correlation between missed boluses and body mass index (BMI) or between HbA_{1c} level and BMI.

Fifty-two percent of participants said they disconnected their pump for exercise. There were no significant differences in HbA_{1c} values in relation to disconnecting or not disconnecting from the pump for exercise ($P = .223$) or bolusing before disconnecting from the pump for exercise ($P = .58$). There was also no correlation between the duration of time the participants reported being disconnected from their pumps and their HbA_{1c} values. The possible effect of timing of insulin boluses on HbA_{1c} levels was examined: 21% of participants reported taking their meal boluses before meals, 58% reported taking their meal boluses after meals, and 21% reported dividing their bolus before and after the meal. The timing of insulin boluses in relation to meals (before only versus after only), although not significant, showed a trend for those who bolused before a meal to have lower HbA_{1c} levels ($P = .052$).

The only factor found to correlate significantly with the HbA_{1c} level was the number of missed mealtime insulin boluses ($r = .41$; $P = .003$; Fig 1). The most frequently reported reason for missing boluses was "forgetting" (67%). Other participants admitted to a fear of hypoglycemia (6%) as the reason for missed boluses, as well as inconvenience of the pump location (2%) and being too busy (8%).

Participants reported performing a mean (95% CI) of 4.7 (4.1, 5.3) blood glucose tests per day, although meter printouts revealed a mean of 3.6 (3.0, 4.2) tests per day ($P = .017$). The frequency of blood glucose testing did not significantly correlate with HbA_{1c} levels in this study ($P = .25$). However, mean blood glucose levels did correlate with HbA_{1c} levels ($r = .7$; $P < .0001$).

DISCUSSION

This is the first report of using insulin pump data downloads to evaluate diabetes management in youths using insulin pumps. In this group of patients, downloading of insulin pump data revealed that the major cause of suboptimal glycemic control was missed meal insulin boluses. The only other factor that correlated with HbA_{1c} values was the mean blood glucose level. Exercise, insulin pump disconnection, number of blood glucose tests done per day, BMI, and gender did not correlate with HbA_{1c} levels. Although we focused on meal bolusing, it is likely that participants who missed meal boluses also missed boluses with snacks.

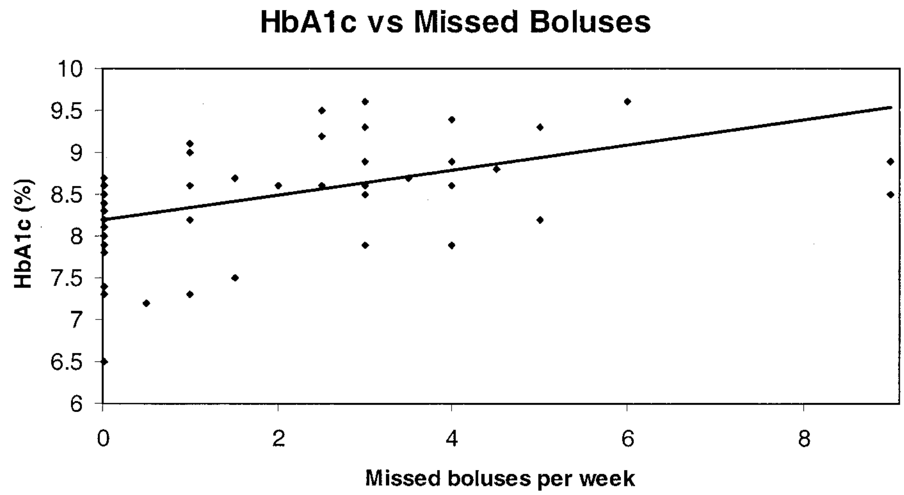
In the past, intermediate-acting insulins (neutral protamine Hagedorn or Lente) were used to provide some insulin activity to cover the noon meal or an

TABLE 1. Clinical Parameters by Age Group

	Age Group				
	<13 y ($n = 12$)	13–15 y ($n = 12$)	16–17 y ($n = 18$)	18–20 y ($n = 6$)	Total ($n = 48$)
Duration of diabetes, y*	6.2 (±3.4)	7.9 (±3.5)	8.7 (±3.8)	11.1 (±4.6)	8.2 (±4.0)
Duration of of CSII therapy*	1.7 (±1.2)	1.6 (±0.62)	2.3 (±0.95)	1.5 (±1.0)	1.9 (±1.0)
Missed boluses per wk†	2.0 (0, 9)	2.4 (0, 5)	1.9 (0, 6)	2.0 (0, 9)	2.1 (0, 9)
HbA_{1c}, %‡	8.4 (7.9, 8.9)	8.8 (8.3, 9.2)	8.5 (8.1, 8.9)	8.2 (7.8, 9.0)	8.5 (8.3, 8.7)

* Results represent the mean (± standard deviation).
† Results represent the mean (minimum, maximum).
‡ Results represent the mean (95% CI).

Fig 1. HbA_{1c} levels correlated with the number of missed meal insulin boluses per day (r = .4).



afternoon snack. This was not ideal, because the peaks in activity seldom coincided with the postprandial glucose load; however, it was better than no short-acting insulin bolus to cover food. Recently, it became common for youths to use insulin pumps or insulin glargine (Lantus) as the source of their basal insulin. The resultant basal activity from either therapy is very flat, and there is no insulin coverage for food intake unless a short-acting insulin bolus is taken. The time of day when blood glucose levels are the highest is after food intake, which is generally 1 to 2 hours after eating; thus, there needs to be adequate insulin coverage for this time period. It is thus not surprising that missed mealtime insulin boluses, as described in this report, are the major cause of elevated HbA_{1c} levels in youths receiving insulin pump therapy. It is also likely that a major reason for the lower HbA_{1c} levels in adults compared with children (including in the DCCT) relates to the greater vigilance of adults in giving insulin boluses whenever food is eaten as well as fewer snacks generally consumed by adults.

Figure 2 represents a pump printout for a teenage male (seen after the completion of this study) with an HbA_{1c} level of 10.0% who had been using a pump for 4 years and previously had been more compliant and in better glycemic control. The deterioration of his glucose control and compliance in giving boluses was temporally related to serious emotional stress in the family. He stated that he had been missing 2 mealtime boluses per week, although after reviewing his logbook diary with him, he admitted to missing ~7 meal boluses per week (the Xs in Fig 2 represent times he admitted to missing boluses). Similarly,

Logbook Diary

Units: mg/dL	Over Night 12:00 AM - 06:59 AM		Morning 07:00 AM - 10:59 AM		Afternoon 11:00 AM - 02:59 PM		Evening 03:00 PM - 06:59 PM		Bed Time 07:00 PM - 11:59 PM	
Date	BG	Bolus	BG	Bolus	BG	Bolus	BG	Bolus	BG	Bolus
26-Jun-03				07:32A 3.0U		11:46A 0.5U		X		11:34P 6.0U
25-Jun-03				09:51A 2.1U				X		
24-Jun-03						01:22P 7.5U		X		
23-Jun-03		02:58A 3.5U						03:25P 5.0U		08:16P 4.5U
22-Jun-03		03:31A 4.0U				X		03:30P 3.0U		08:59P 4.2U 09:35P 3.6U 10:21P 4.7U
21-Jun-03						X		04:19P 6.0U		
20-Jun-03		01:26A 6.0U				X				07:31P 2.7U 10:34P 6.0U 11:05P 3.0U
19-Jun-03		12:28A 4.5U 01:58A 4.0U				11:30A 5.0U		X		09:18P 1.3U 10:40P 4.5U

Fig 2. Computer download of MiniMed 508 insulin pump data. Blanks for boluses at the usual times of meals and the blood glucose records were reviewed with the patient/family. Missed mealtime boluses (represented by an X) were counted only if the patient and family agreed that a meal had likely been eaten and a bolus not administered. Blood glucose records were not entered into the logbook feature of the insulin pump. U indicates units of insulin administered.

there were ~7 missed meal boluses in his other weekly downloads.

Because the most common reason given by participants for missing boluses was "forgetting," a reminder feature such as an alarm on pumps might address this problem. Of ~6 insulin pump manufacturers, 2 recently developed insulin pumps with alarms to help remember boluses. Our current research is being directed at determining the benefit of alarms. Participants could also wear a wristwatch that is set to alarm at usual meal times. Friends and family are often helpful in reminding those using insulin pumps to bolus at meals. Some doctors have also tried greatly increasing basal rates at mealtimes for patients who eat on a regular schedule to alleviate the need to bolus. Unfortunately, this does not work for patients who vary their meal schedule or who vary the carbohydrate content of their meals.

The question of how to best choose youths who will succeed in CSII therapy remains. Youths who miss shots, do not have close parental support, have difficulty remembering other life responsibilities, or have certain medical problems (psychological problems, attention-deficit disorder, etc) are going to be less likely to do well on CSII therapy. We have often suggested to such youths that they delay pump therapy until they are older, possibly making the switch before beginning college (when they are more mature and likely to remember to bolus). Perhaps the best prepump "test" would be to treat youths with Lantus insulin as a basal insulin and Humalog or NovoLog insulin before food intake.[5] Youths on this type of insulin regimen, who are fastidious about giving premeal, short-acting insulin, will generally have HbA_{1c} levels <8% and probably would be successful using insulin pump therapy.

Controlling or losing weight through inadequate or missed insulin boluses could have been a factor for some participants, although this was not addressed in our study. These unhealthy weight-control/disordered eating practices are not uncommon in the adolescent population. One study of 70 adolescent females and 73 adolescent males with the same mean age as the participants in this study (15.3 years) and a similar race/ethnicity did address this issue.[6] Eighteen percent of the young women (12 of 66) reported either missing insulin doses (10.3%) or decreasing the amount of insulin taken (7.4%) to lose weight; only 1 male reported similar behaviors. Higher levels of weight dissatisfaction and disordered eating habits correlated with higher BMI values. In the present study, there was no correlation of missed insulin boluses with BMI values, and males and females had a similar incidence of missed boluses.

A patient-education book states that it was a "clinical impression" that missing 1 meal bolus per week resulted in a half-point rise in HbA_{1c} level over a 3-month period.[7] The current data (Fig 1) show that 2 missed boluses resulted in a half-point rise, and 4 missed boluses per week resulted in a full-point rise in HbA_{1c} level. However, the current data were from objective pump data downloads, whereas the "clinical impression" was from patient self-reporting, shown here to be underestimated by ~50%.

CONCLUSIONS

Missed mealtime insulin boluses represent a major reason for suboptimal glycemic control in some youths with type 1 diabetes receiving insulin pump therapy. Future studies should address the issue of how best to help youths who do use insulin pumps to remember to bolus and how to identify youths and families ready for insulin pump therapy and those who should delay or even reconsider starting an insulin pump.

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