Improved Glycemic Control in Poorly Controlled Patients with Type 1 Diabetes Using Real-Time Continuous Glucose Monitoring

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Intensive self-management with frequent self-monitoring of blood glucose (SMBG) is important in type 1 diabetes to achieve good metabolic control (1–3). Nevertheless, many patients still experience episodes of unrecognized hypo- and hyperglycemia (4). Novel technologies for continuous glucose monitoring (CGM) that provide information about glucose excursions are now available. Previous studies reported the benefits of retrospective evaluation of CGM data (5–11), but few assessed effects on glycemic control (5,12–14), and only one showed improvements compared with SMBG (14). We evaluated the effect of a new real-time glucose monitor on glycemic control in patients with poorly controlled type 1 diabetes. The device, Guardian RT (Medtronic MiniMed, Northridge, CA), allows users to see glucose readings and set hypo- and hyperglycemic alarms and provides trend information on changing glucose values.

RESEARCH DESIGN AND METHODS

— The study included 81 children (median age 14.4 years [range 8.0–18.9]) and 81 adults (age 39.1 years [19.0–59.5]) with stable type 1 diabetes. All had adhered to intensified insulin treatment (continuous subcutaneous insulin infusion, $n = 78$; multiple daily injection, $n = 84$) but had HbA_{1c} (A1C) levels ≥8.1%. Informed consent was obtained from patients regularly attending the eight participating centers.

Subjects were randomly assigned 1:1:1 for 3 months to Guardian RT continuously (arm 1) or biweekly for 3-day periods every 2 weeks (arm 2) or to continue conventional SMBG (control). Treatment adjustments made by physicians and patients were based on SMBG profiles in control subjects and on real-time glucose profiles in arms 1 and 2. Patients were instructed to perform confirmatory SMBG measurements before therapeutical interventions or corrective action if hypo- or hyperglycemic alarms or symptoms occurred. A1C was measured centrally after 1 and 3 months.

The Guardian RT continuously displays real-time interstitial glucose values and is calibrated prospectively using SMBG reference values. High/low alert thresholds were set at 50–80 mg/dl for hypoglycemia and 170–250 mg/dl for hyperglycemia with the upper alarm lowering to 200 mg/dl after the first 10 days. Settings could be readjusted during the study.

A repeated-measures ANOVA model was used to analyze changes from baseline across groups and visits (PROC MIXED using SAS, version 9.1). Fisher's least significant differences test was used to assess statistical significance ($P \leq 0.05$) between groups. Data were analyzed by intention-to-treat approach using last value carried forward for missing end points and adjusted for age-group (< or ≥19 years) as patients were randomized within age-groups.

RESULTS

— In total, 156 patients completed the evaluation. One discontinued before the start of intervention. Four discontinued arm 1, and one discontinued arm 2 due to difficulties with continuous sensor use and/or alarms.

Baseline values in arms 1 and 2 and the control arm for A1C were (means ± SD) 9.5 ± 1.1, 9.6 ± 1.2, and 9.7 ± 1.3%, respectively. Real-time CGM was associated with reductions from baseline in A1C in arm 1 versus control (Fig. 1) at 1 month (0.6 ± 0.8 vs. 0.2 ± 0.8%, $P = 0.008$) and 3 months (1.0 ± 1.1 vs. 0.4 ± 1.0%, $P = 0.003$). In arm 2 (1 month 0.4 ± 0.9%, 3 months 0.7 ± 1.3%), there was no difference versus control or arm 1. At 3 months, 50% of the patients in arm 1 had A1C reductions ≥1% (37% in arm 2 and 15% in control arm) and 26% had reductions ≥2% (9% in arm 2 and 4% in control arm).

Average baseline SMBG per day were 4.6 ± 1.4, 5.0 ± 1.5, and 5.1 ± 1.8, respectively. A mean reduction in SMBG per day from baseline was observed at 1 and 3 months in arm 1 (0.9 ± 1.8 and 1.4 ± 1.7, respectively) but was not statistically significant compared with arm 2 (0.5 ± 1.9 and 0.4 ± 2.1) or control subjects (0.5 ± 1.5 and 0.7 ± 1.8).

At 3 months, average total insulin dose per day was not significantly different from baseline in the three arms (about 0.8 units · kg^{-1} · day^{-1}). Almost all pa-

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Abbreviations: CGM, continuous glucose monitoring; SMBG, self-monitoring of 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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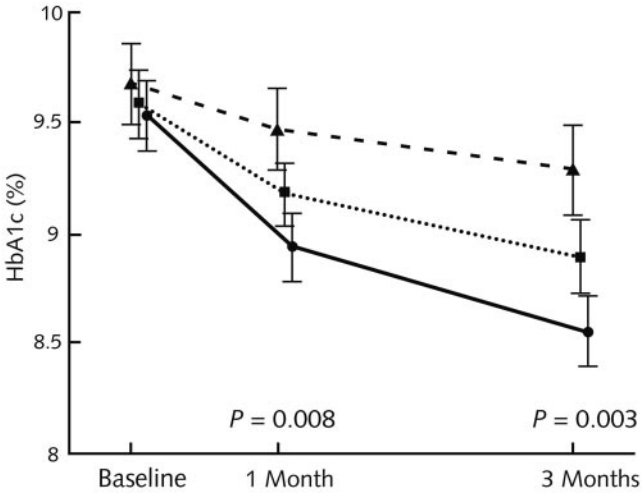

Figure 1—*Change from baseline at 1 and 3 months of AIC. Values are means ± SE.* P *values correspond to the difference in change from baseline between the continuous and control groups.* ●*, continuous group (arm 1);* ■*, biweekly group (arm 2);* ▲*, control group.*

tients (82% at 1 month and 95% at 3 months) in arms 1 and 2 reported making insulin, dietary, or lifestyle adjustments using the real-time information.

Severe hypoglycemia occurred once each in arms 1 and 2. The patient in arm 2 was not wearing the device at the time. The event during real-time CGM occurred despite a confirmatory low SMBG value and corrective carbohydrate intake.

CONCLUSIONS — This is the first randomized controlled trial to demonstrate a clinically meaningful reduction in A1C using real-time CGM in type 1 diabetic patients. One previous study (15) showed real-time CGM decreased time spent in hypo- and hyperglycemia but was too short (9 days) to assess A1C. Another controlled trial used real-time CGM for 1–2 days/week over 6 months and found no improvement in overall metabolic control (16). In the present study, real-time CGM gradually improved glycemic control over 3 months, resulting in a reduction in A1C by at least 1% in half the patients and at least 2% in one-quarter. This was achieved in a broad population of children and adults with type 1 diabetes and in a setting translatable into current clinical practice. Study patients had poor metabolic control, despite intensive insulin treatment and frequent SMBG. These patients are the main target group for improving glycemic control (17). Notably, the control subjects performed, on average, more than five SMBG per day at baseline, consistent with acknowledged recommendations (18) and with no significant within-group decrease throughout the trial. In addition, a within-group reduction in SMBG frequency was observed in arm 1, possibly because the patients became more confident at interpreting the real-time glucose readings and trend information.

In this study, the patients did not register specific information about their self-management of diabetes therapy on a daily basis. Therefore, we cannot delineate in detail the link between the use of real-time CGM and the improvement in glycemic control. However, despite no overall change in total daily dose of insulin, almost all patients using real-time CGM reported making treatment adjustments and/or changes to their lifestyle and food intake. Thus, intermittent corrective adjustments of insulin administration, such as the number of boluses or the basal-to–total dose ratio, and food intake adjustments based on the real-time glucose display and alarm functions may have been carried out on an individual basis. Evidently, further investigations are needed to better define treatment guidelines when using real-time CGM to optimize the improvement in glycemic control observed in this study. Moreover, other aspects of this new technique, such as long-term efficacy, clinical feasibility in patients with more satisfactory glycemic control, and effect on the incidence of hypoglycemia, need to be investigated. Our findings strongly indicate that the use of real-time CGM has considerable potential for the management of patients with diabetes.

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