Feasibility of 10-Day Use of a Continuous Glucose-Monitoring System in Adults With Type 1 Diabetes

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OBJECTIVE — The purpose of this pilot study was to evaluate the feasibility of 10-day use of a transcutaneous, real-time, continuous glucose-monitoring (CGM) system. All previous reports using different CGM systems were for 3-, 5-, or 7-day use.

RESEARCH DESIGN AND METHODS — On day 1, subjects received the CGM device (SEVEN System) and underwent training on proper use. Subjects returned to the clinic on days 2, 7, and 10 for in-clinic sessions. On days 2 and 7, half the subjects performed fingersticks every 15 min and the other half had Yellow Springs Instruments (YSI) samples drawn every 15 min. On day 10, all subjects participated in an 8-h in-clinic session with YSI and fingerstick testing.

RESULTS — The median absolute relative difference for CGM versus YSI was 12.6, 11.3, and 14.5% on days 2, 7, and 10, respectively ($P = 0.63$). CGM performed better on day 10 when compared with self-monitoring of blood glucose as compared with YSI.

CONCLUSIONS — This is the first study to document 10-day use of a 7-day CGM system.

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Improvement in metabolic control, as measured by reduction in A1C levels, has been shown to decrease the incidence and progression of both micro- and macrovascular diabetes complications (1–5). Hypoglycemia is the main limiting factor in achieving target A1C values for subjects with type 1 diabetes (6), and self-monitoring of blood glucose (SMBG) is an integral part of intensive diabetes management (7). Recent availability of continuous glucose-monitoring (CGM) devices has allowed patients to view real-time glucose values and glucose trends and receive alarms/alerts of impending hypo- or hyperglycemia (8–12).

RESEARCH DESIGN AND METHODS

— The protocol was approved by the institutional review board, and 30 adult subjects (20 female) with type 1 diabetes gave written informed consent to participate. Mean ± SD age and duration of diabetes were 35.3 ± 7.8 years and 22.3 ± 8.4 years, respectively. Sixteen subjects were using multiple daily injections, and 14 were on insulin pumps.

All subjects came to the clinic on day 1 for sensor insertions and training. Sensor replacements were allowed within 72 h of the initial insertion. Two patients required replacement sensors within 72 h due to dislodgement of the sensor. In instances where the sensor shut off prematurely, subjects were allowed to "restart" the same initial sensor; one patient had to restart the sensor within 8 h.

On day 2, all 30 subjects also participated in a 6-h in-clinic session. Half the subjects performed comparative SMBG fingersticks once every 15 min; the other half underwent peripheral venous catheterization for Yellow Springs Instruments (YSI) samples every 15 min. On day 7, 28 patients returned for another 6-h in-clinic session. The subjects who performed SMBG fingersticks on day 2 now underwent peripheral venous catheterization, and those who previously underwent peripheral venous catheterization performed SMBG fingersticks. At the end of the session, subjects stayed for an extra 2 h to restart and calibrate the sensors for extended use. At home, patients were asked to do similar fingersticks to assure accuracy of the sensors. On day 10, 24 patients returned for an 8-h in-clinic session, during which all patients underwent peripheral venous catheterization and had YSI samples drawn every 15 min. Two patients had sensors that failed prematurely between 72 and 96 h, and four other patients could not attend the in-clinic session on day 10 because of schedule conflicts and/or bad weather in Denver, Colorado. All patients also performed SMBG every 15 min on day 10. At the end of the session, all sensors were removed and sensor insertion site assessments were made for any skin irritation/infections.

The SEVEN sensor unit consists of an applicator, a sensor probe, and transmitter housing as previously described (11,12). After initial calibration at 2 h, patients were instructed to upload at least one SMBG value every 12 h when glucose values were stable. Once calibrated, the receiver displayed glucose values that were updated at 5-min intervals. The high glucose alert was set at 200 mg/dl, and the low glucose alert was set at 80 mg/dl. Data from all receivers were downloaded on day 10 for analyses.

Statistical analysis methods

Categorical variables such as patient diabetes history and baseline characteristics are summarized using *n* values and percentages. The Kruskal-Wallis nonparametric test was used to compare CGM system accuracy at different times during sensor wear. Analyses were performed using SAS software (version 9.1.3; SAS Institute, Cary, NC).

RESULTS

— Of the 1,050 paired points in reference to the YSI measure-

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Table 1—*Differences in glucose values (mg/dl) from CGM in reference to YSI and SMBG*

	No. of paired data points	Absolute difference (mg/dl)*		Relative difference (%)†		Absolute relative difference (%)*	
		Mean ± SD	Median	Mean ± SD	Median	Mean ± SD	Median
YSI in-clinic days 2, 7, and 10§				5.0 ± 27.3	1.4		
Overall	905	25.2 ± 25.4	17.3			17.9 ± 21.2	12.9
Day‖				−0.1 ± 18.3	−1.2		
2	271	23.6 ± 21.1	16.5	4.5 ± 20.5	1.7	14.4 ± 11.3	12.6
7	227	21.2 ± 21.0	16.0	8.7 ± 34.3	1.6	15.7 ± 14.0	11.3
10	407	28.4 ± 29.7	18.8	5.0 ± 27.3	1.4	21.6 ± 27.9	14.5
P		0.08		0.02		0.63	
SMBG in-clinic days 2, 7, and 10¶							
Overall	1,130			−0.9 ± 26.3	−4.9	17.7 ± 19.5	13.3
Day‖		24.8 ± 25.3	17.0				
2	379	23.0 ± 22.5	16.0	0.2 ± 21.4	−1.9	15.6 ± 14.5	12.8
7	317	20.9 ± 25.1	15.5	−2.7 ± 21.3	−6.4	15.7 ± 14.6	12.5
10	434					20.9 ± 25.1	15.5
P		0.03		0.002		0.002	

Data are mean ± SD or median unless otherwise indicated. *Calculated as absolute value of (sensor − YSI) where, for each paired point, sensor = time-matched continuously measured glucose value and YSI = SMBG values. †Calculated as (sensor − YSI)/YSI. ‡Calculated as the absolute value of (sensor − YSI)/YSI. ‖From the time of sensor insertion (in 24-h increments). *P* values calculated by the χ^2 Kruskal-Wallis test from median values. §Percent of points within 20% of reference = 70.8%; percent of points within 30% of reference = 87.6%. ¶Percent of points within 20% of reference = 73.4%; percent of points within 30% of reference = 88.7%.

ments collected, 1,017 were between 40 and 400 mg/dl (range of glucose values used in this study) and were analyzed prospectively for various statistics using sensor glucose values as displayed to subjects in real time. Sensor performance was stable across 10 days of sensor wear (Table 1). There is no appreciable difference in the overall accuracy results; see Table 1 for correlation coefficient, absolute difference, and absolute relative difference including all the paired data points (Kruskal-Wallis $P > 0.05$), with minor changes in the relative difference (Kruskal-Wallis $P = 0.02$). Median (interquartile range) of absolute difference to YSI measurement was 11.8 ± 20.9 mg/dl (<70 mg/dl) in the hypoglycemic, 13.5 ± 19.5 (70–180 mg/dl) in the euglycemic, and 30.5 ± 54 mg/dl (>180 mg/dl) in the hyperglycemic ranges. Median (interquartile range) of absolute relative difference to YSI measurement was 22.0 ± 37.9% (<70 mg/dl) in the hypoglycemic, 11.8 ± 17.8% (70–180 mg/dl) in the euglycemic, and 12.8 ± 14.6% (>180 mg/dl) in the hyperglycemic ranges. The hypoglycemic alert used in this study was set at 80 mg/dl (considered clinically inadequate). This low alert detected hypoglycemia (<80 mg/dl) with 61% sensitivity, 91% specificity, and a positive predictive value of 90%. In comparison with SMBG, the CGM system performed slightly better on day 10 in absolute difference (median 15.5 mg/dl, $P = 0.03$; Table 1). However, absolute relative difference was slightly higher on day 10 when compared with SMBG.

The sensor performance was stable throughout 10 days of use at home when data were compared with SMBG values. More than 90% of paired glucose readings fell within the clinically relevant Clarke error grid zones A and B, as reported previously, with 3- and 7-day use of sensors (supplemental Fig. 1*A* and *B*, available in an online appendix at http://dx.doi.org/10.2337/dc08-1745).

There were no sensor insertion site infections. Over the 10-day duration of this study, there were seven incidences of sensor insertion site effects and two instances of mild erythema with sensor adhesives, and one patient reported mild bruising at the sensor site.

CONCLUSIONS

This is the first report on the use of transcutaneous CGM that lasts for 10 days. The SEVEN system, when used for 10 days (currently approved for 7 days), was safe (off-label) and well tolerated with no skin reactions. The mean absolute relative difference for CGM versus YSI was 12.6, 11.3, and 14.5% on days 2, 7, and 10, respectively, and did not differ over the study duration ($P = 0.63$). The sensor performance was stable for 10 days when compared with SMBG values. Most CGM devices had reported similar sensitivity levels for detecting hypoglycemia, and these need levels to be improved in future CGM devices. The longer use of a sensor may result in better compliance and health outcomes and will be cost-effective due to an extra 3-day use of a 7-day sensor. Increased sensor use has been correlated with better A1C reductions in recent clinical trials (10–15). This is the first study to document that longer sensor usage (10 days) is feasible, safe, and practical. Long-term impact of 10-day use of SEVEN on A1C and hypoglycemia needs to be evaluated.

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