Sustained Benefit of Continuous Glucose Monitoring on A1C, Glucose Profiles, and Hypoglycemia in Adults With Type 1 Diabetes

OBJECTIVE — To evaluate long-term effects of continuous glucose monitoring (CGM) in intensively treated adults with type 1 diabetes.

RESEARCH DESIGN AND METHODS — We studied 83 of 86 individuals ≥25 years of age with type 1 diabetes who used CGM as part of a 6-month randomized clinical trial in a subsequent 6-month extension study.

RESULTS — After 12 months, median CGM use was 6.8 days per week. Mean change in A1C level from baseline to 12 months was −0.4 ± 0.6% (P < 0.001) in subjects with baseline A1C ≥7.0%. A1C remained stable at 6.4% in those with baseline A1C <7.0%. The incidence rate of severe hypoglycemia was 21.8 and 7.1 events per 100 person-years in the first and last 6 months, respectively. Time per day with glucose levels in the range of 71–180 mg/dl increased significantly (P = 0.02) from baseline to 12 months.

CONCLUSIONS — In intensively treated adults with type 1 diabetes, CGM use and benefit can be sustained for 12 months.

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In a 6-month randomized trial of intensively treated individuals with type 1 diabetes and baseline A1C ≥7.0%, adults ≥25 years of age benefited from use of continuous glucose monitoring (CGM) compared with adults using conventional blood glucose monitoring (1). In a contemporaneous parallel study of individuals with type 1 diabetes who had A1C levels <7.0%, those in the CGM group had a reduction in biochemical hypoglycemia compared with those in the control group while maintaining A1C levels in the target range (2). This report describes the 12-month follow-up of adult subjects in the two randomized trials' CGM groups.
Table 1—Clinical features and metabolic control measures

|                      | Overall | Baseline A1C ≥7.0% | Baseline A1C <7.0% |
|----------------------|---------|--------------------|--------------------|
|                      | n       | Baseline†          | Month 6           | Month 12          | Baseline†          | Month 6           | Month 12          | p*               |
| Body weight (kg)     | 83      | 77 ±15             | 78 ±16            | 79 ±15            | 83                  | 79 ±16            | 80 ±17            | 81 ±17           | 75 ±13            | 75 ±13            | 76 ±13            | <0.001            |
| Daily insulin dose   | 49      | 0.5 ± 0.1          | 0.5 ± 0.2         | 0.5 ± 0.1         | 49                  | 0.5 ± 0.2          | 0.6 ± 0.2         | 0.6 ± 0.2         | 0.5 ± 0.1          | 0.5 ± 0.1          | 0.5 ± 0.1          | 0.72              |
| Blood glucose meters | 7.0     | 2.4 ± 3.1          | 5.7 ± 2.1         | 6.5 ± 2.3         | 7.0                 | 5.7 ± 2.3          | 5.5 ± 2.0         | 7.6 ± 2.4         | 7.3 ± 3.9          | 6.0 ± 2.2          | 6.0 ± 2.2          | <0.001            |
| A1C (%)              | 7.0     | 7.1 ± 0.8          | 6.8 ± 0.6         | 6.9 ± 0.7         | 7.0                 | 7.6 ± 0.5          | 7.1 ± 0.5         | 7.2 ± 0.5         | 6.4 ± 0.5          | 6.3 ± 0.5          | 6.4 ± 0.6          | <0.001            |
| CGM glucose measures | 81      | 151 ±25            | 148 ±21           | 148 ±23           | 49                  | 162 ±24            | 157 ±22           | 158 ±23           | 136 ±18            | 134 ±12           | 133 ±13           | 0.22              |
| Mean glucose (mg/dl) |         |                    | 186 ±92           | 96 ±92            | 966 ±1151           | 1,151 ±1,139       | 1,135 ±1,135      | 0.02              |
| Glucose level (min/day) |      | 71–180 mg/dl        | 1,026 ±31         | 1,066 ±31         | 866 ±92            | 962 ±96            | 966 ±96           | 1.151 ±1,139      | 1,135 ±1,135      | 0.02              |
| ≤70 mg/dl            | 62      | 53 ±4              | 33 ±4             | 43 ±5             | 82 ±6              | 65 ±6             | 72 ±6             | 0.06              |
| ≤60 mg/dl            | 30      | 23 ±5              | 16 ±5             | 14 ±2             | 38 ±6              | 13 ±6             | 25 ±6             | 0.003             |
| ≤50 mg/dl            | 7       | 7 ±3               | 3 ±3              | 4 ±2              | 6 ±6               | 6 ±6              | 5 ±6              | 0.002             |
| >180 mg/dl           | 385     | 483 ±29            | 378 ±25           | 422 ±25           | 219 ±21            | 231 ±21           | 211 ±21           | 0.12              |
| >200 mg/dl           | 246     | 335 ±18            | 252 ±15           | 289 ±15           | 133 ±13            | 137 ±13           | 116 ±13           | 0.05              |
| >250 mg/dl           | 77      | 121 ±49            | 61 ±49            | 78 ±49            | 28 ±33             | 33 ±33            | 19 ±33            | 0.02              |
| Summary values       |         |                    |                   |                   |                     |                   |                   |                   |
| Hypoglycemia area    | 0.5     | 0.3 ±0.3           | 0.3 ±0.3          | 0.4 ±0.3          | 0.6 ±0.3           | 0.3 ±0.3          | 0.4 ±0.3          | 0.002             |
| Low blood glucose    | 1.2     | 1.0 ±1.0           | 1.0 ±1.0          | 0.9 ±0.9          | 1.6 ±1.3           | 1.3 ±1.3          | 1.3 ±1.3          | 0.01              |
| Hyperglycemia area   | 11.6    | 8.6 ±8.1           | 8.1 ±8.1          | 16.0 ±11.0        | 5.4 ±5.5           | 4.8 ±5.5          | 4.8 ±5.5          | 0.05              |
| High blood glucose   | 5.6     | 4.8 ±4.6           | 4.6 ±4.6          | 6.6 ±5.5          | 3.3 ±3.7           | 3.7 ±3.7          | 3.4 ±3.7          | 0.08              |
| Variability          |         |                    |                   |                   |                     |                   |                   |                   |
| Standard deviation   | 56      | 52 ±52             | 52 ±52            | 61 ±57            | 46 ±47             | 45 ±45            | 45 ±45            | 0.02 (0.03)       |
| Mean amplitude of    | 107     | 101 ±97            | 114 ±106          | 107 ±107          | 91 ±89             | 93 ±89            | 93 ±89            | 0.03 (0.04)       |
| glycemic excursion   | Mean absolute rate of change (mg · dl⁻¹ · min⁻¹) | 0.63 ±0.65 | 0.63 ±0.65 | 0.69 ±0.67 | 0.69 ±0.69 | 0.57 ±0.58 | 0.63 ±0.63 | 0.11 (0.03) |
| Coefficient of variation** | 0.36 ±0.35 | 0.34 ±0.37 | 0.37 ±0.37 | 0.35 ±0.34 | 0.33 ±0.33 | 0.33 ±0.33 | 0.07 (0.10) |       |

Data are means ± SD or median. *P values for the comparison of baseline vs. month 12 for all subjects pooled. For variability, the unadjusted and adjusted P values for mean glucose are both given: unadjusted (adjusted). †Baseline data are from blinded CGM use for approximately 4–7 days prior to randomization. ‡Self-reported blood glucose meter monitoring. §Subjects required to have at least 24 h of glucose data at all three time points to be included in analysis. One subject with zero use in month 12 and one subject whose CGM use in month 12 was imputed with the self-reported data at the month 12 visit as a result of a missing download data were excluded. | Total area under the curve <70 mg/dl reflects both percentage and severity of glucose values in the hypoglycemic range. ¶Blood glucose index (ref. 8). #Total area under the curve above 180 mg/dl. **SD divided by mean glucose.

A1C%
0–16.7) during the second 6 months (P = 0.18). The rate was not associated with baseline A1C (Spearman r = −0.004; P = 0.97). In subjects with baseline A1C ≥7%, the incidence fell from 20.5 events per 100 person-years in the first 6 months to 12.1 events per 100 person-years in the second 6 months, whereas in the A1C <7% cohort, the incidence fell from 23.6 events per 100 person-years to no events during the second 6 months (supplemental Fig. S2).

The median amount of time per day with glucose in the range of 71–180 mg/dL increased significantly (P = 0.02) from baseline to 12 months, reflecting a decrease in both hypoglycemia and hyperglycemia. Similar trends were seen both in subjects with baseline A1C ≥7.0% and in those with baseline A1C <7.0% (Table 1). The increase in time in range was seen during both daytime and nighttime (supplemental Table S2). Variability assessed with the SD of glucose values (P = 0.02) and mean amplitude of glycemic excursions (P = 0.03) was reduced with CGM use from baseline to 12 months. Body weight, daily insulin dose, and frequency of daily blood glucose meter tests did not change meaningfully during the study.

CONCLUSIONS — In this 6-month extension to a randomized clinical trial, we found that most adults ≥25 years of age continued to use CGM on a daily or near-daily basis and had sustained benefits of improved glucose control noted by A1C levels and the amount of time sensor glucose values were in the target range. These benefits persisted despite less-intensive follow-up, designed to approximate usual clinical practice, than that during the 6-month randomized phase of the study.

An additional important observation was the remarkably low rate of severe hypoglycemic events during the extension phase of the study. The rate of severe hypoglycemia in our CGM subjects with a mean A1C of 6.8% during the 6-month extension phase was markedly lower than the rate of severe hypoglycemia in the Diabetes Control and Complications Trial (DCCT) intensive treatment group, which had mean A1C of 7.1% (7 vs. 62 events per 100 person-years) (6). The total absence of severe hypoglycemia during the second 6 months of the study in the subjects who had a baseline A1C <7.0% is particularly striking, especially because these subjects were able to maintain a mean A1C of 6.4%.

It is possible that the decline in severe hypoglycemic events during the second 6 months of the study resulted from learning from prior experience, including appropriate setting of the low alarms, glucose targets, and titration of basal and bolus insulin doses. It is also intriguing to speculate that the reduction in exposure to biochemical hypoglycemia over the 12 months of the study may have protected subjects from severe hypoglycemic events by enhancing their counteregulatory hormone defense mechanisms against hypoglycemia (7).

Our findings demonstrate that the benefits of CGM can be sustained for at least 12 months in motivated adults with type 1 diabetes practicing intensive diabetes management. In such individuals, CGM provides the ability to achieve target A1C levels much more safely than previously reported.

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