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Effectiveness of Sensor-Augmented Insulin-Pump Therapy in Type 1 Diabetes

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ABSTRACT

BACKGROUND

Recently developed technologies for the treatment of type 1 diabetes mellitus include a variety of pumps and pumps with glucose sensors.

METHODS

In this 1-year, multicenter, randomized, controlled trial, we compared the efficacy of sensor-augmented pump therapy (pump therapy) with that of a regimen of multiple daily insulin injections (injection therapy) in 485 patients (329 adults and 156 children) with inadequately controlled type 1 diabetes. Patients received recombinant insulin analogues and were supervised by expert clinical teams. The primary end point was the change from the baseline glycated hemoglobin level.

RESULTS

At 1 year, the baseline mean glycated hemoglobin level (8.3% in the two study groups) had decreased to 7.5% in the pump-therapy group, as compared with 8.1% in the injection-therapy group ($P<0.001$). The proportion of patients who reached the glycated hemoglobin target (<7%) was greater in the pump-therapy group than in the injection-therapy group. The rate of severe hypoglycemia in the pump-therapy group (13.31 cases per 100 person-years) did not differ significantly from that in the injection-therapy group (13.48 per 100 person-years, $P=0.58$). There was no significant weight gain in either group.

CONCLUSIONS

In both adults and children with inadequately controlled type 1 diabetes, sensor-augmented pump therapy resulted in significant improvement in glycated hemoglobin levels, as compared with injection therapy. A significantly greater proportion of both adults and children in the pump-therapy group than in the injection-therapy group reached the target glycated hemoglobin level. (Funded by Medtronic and others; ClinicalTrials.gov number, NCT00417989.)

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Improved glycemic control can reduce the microvascular and macrovascular complications associated with type 1 diabetes mellitus,[1-3] and diabetes practitioners are continuously challenged to optimize glucose control while minimizing severe hypoglycemia and weight gain. Insulin pumps and systems for continuous glucose monitoring represent technologies designed to assist patients with type 1 diabetes in safely reaching glycemic goals. Among adults, the use of an insulin pump has been shown to reduce glycated hemoglobin levels without an increased risk of hypoglycemia, as compared with a regimen of multiple daily insulin injections, but results in children have been inconsistent.[4] Recent studies have suggested that patients who used sensor-augmented pump therapy with adherence to continuous glucose monitoring had improved glycated hemoglobin levels without an increased rate of hypoglycemia.[5-7] Similarly, in a multicenter trial of continuous glucose monitoring in patients with type 1 diabetes, sponsored by the Juvenile Diabetes Research Foundation (JDRF) (ClinicalTrials.gov number, NCT00406133), the use of a continuous glucose-monitoring device was effective in reducing glycated hemoglobin levels among patients who were 25 years of age or older but not among patients under the age of 25 years.[8]

Sensor-augmented pump therapy integrates these two technologies into one system and allows patients and clinicians to monitor treatment and response through Internet-based software. Whether, and to what extent, switching directly to sensor-augmented pump therapy might improve metabolic control in patients with type 1 diabetes who were previously unable to reach glycemic targets with a regimen of multiple daily injections and conventional blood-glucose monitoring is unknown. In this unmasked, randomized, controlled trial, called Sensor-Augmented Pump Therapy for A1C Reduction (STAR) 3, we evaluated the use of sensor-augmented pump therapy and injection therapy at 30 diabetes centers in the United States and Canada for 1 year.[9]

Methods

Patients

Patients with type 1 diabetes were eligible if they were between the ages of 7 and 70 years, had received multiple daily injections that included a long-acting analogue insulin during the previous 3 months, had a glycated hemoglobin level between 7.4% and 9.5%, and had been under the care of the principal investigator or a referring physician for at least 6 months. Patients were required to have access to a computer and to have a history of testing blood glucose an average of four or more times per day for the previous 30 days. Exclusion criteria were the use of insulin-pump therapy within the previous 3 years, a history of at least two severe hypoglycemic events in the year before enrollment, the use of a pharmacologic noninsulin treatment for diabetes during the previous 3 months, and pregnancy or the intention to become pregnant. All patients provided written informed consent.

Treatments

Patients were randomly assigned to receive either sensor-augmented pump therapy (pump therapy) or a regimen of multiple daily injections (injection therapy) with the use of a block design, stratified according to age group: adults (19 to 70 years of age) or children (7 to 18 years of age). Levels of glycated hemoglobin and blood glucose in the two study groups and sensor glucose values in the pump-therapy group were disclosed to investigators, caregivers, and patients in order to optimize glycated hemoglobin levels and to minimize the risk of severe hypoglycemia.

The pump-therapy group used a device that integrates an insulin pump with continuous glucose monitoring (MiniMed Paradigm REAL-Time System, Medtronic) (see Fig. 1 in the Supplementary Appendix, available with the full text of this article at NEJM.org). Before randomization, all patients received training in intensive diabetes management, including carbohydrate counting and the administration of correction doses of insulin. Patients were first placed on insulin-pump therapy for 2 weeks, and then glucose sensors were introduced. During the 5 weeks after randomization, patients in the pump-therapy group completed online insulin-pump training and attended additional visits for insulin-pump and sensor training. This group used insulin aspart (NovoLog or NovoRapid, Novo Nordisk). The injection-therapy group used both insulin glargine (Lantus, Sanofi-Aventis) and insulin aspart under the guidance of the treating clinician. Sensor glucose values were collected for 1-week periods at baseline, 6 months, and 1 year in the two study groups. In the injection-therapy group, a device for continu-

ous glucose monitoring that collected but did not display data (Guardian REAL-Time Clinical, Medtronic) was used.

All patients were seen at 3, 6, 9, and 12 months after randomization and used diabetes-management software (CareLink Therapy Management System for Diabetes–Clinical, Medtronic). Between visits, communication with clinicians was initiated at the discretion of the patient.

At follow-up clinic visits, glucose data were reviewed, therapy was adjusted, glycated hemoglobin was measured, and data on adverse events were collected. Severe hypoglycemia was defined as an episode requiring assistance and was confirmed by documentation of a blood glucose value of less than 50 mg per deciliter (2.8 mmol per liter) or recovery with restoration of plasma glucose. Quest Clinical Trials Laboratory measured glycated hemoglobin by means of immunoturbidimetry.

STUDY OVERSIGHT

The institutional review board at each study site approved the protocol, and the conduct of the study was consistent with the Good Clinical Practice provisions of the Declaration of Helsinki and local regulatory requirements. Data management and statistical analyses were conducted by Parexel International, an independent clinical research organization, which transferred all data to the sponsor, Medtronic. Novo Nordisk supplied all insulin aspart used in the study, and LifeScan, Bayer Healthcare, and Becton Dickinson supplied blood glucose meters.

All authors had access to the data, wrote the first draft of the manuscript with editorial assistance from representatives of the sponsor, subsequently revised the manuscript, and made the decision to submit the manuscript for publication. All authors vouch for the accuracy and completeness of the data and analyses. The STAR 3 steering committee was responsible for the study design and methods.[9]

The study was conducted in accordance with the original trial protocol, with the following exceptions: the eligibility cutoff level for glycated hemoglobin was lowered from 7.5% to 7.4%, the exclusion criteria were changed from no previous use of insulin-pump therapy to no such use within the previous 3 years, the sample size was increased from 336 patients at 25 centers to 552 patients at 30 centers, results on the Hypoglycemia Fear Survey were moved from a secondary end point to a tertiary end point, the Telemetered Glucose-Monitoring System (Medtronic) was replaced with the MiniLink transmitter (Medtronic), and three visits during the 5 weeks after randomization were removed from the schedule for the injection-therapy group. (The trial protocol is available at NEJM.org.)

STATISTICAL ANALYSIS

The primary outcome was the change from baseline in the glycated hemoglobin level at 1 year. Severe rates of hypoglycemia were analyzed as a secondary outcome. We calculated that the enrollment of 495 patients would provide a power of 90% to detect an absolute difference of 0.35 percentage points in the primary outcome. Analyses were performed in the intention-to-treat population, defined as patients who underwent at least one measurement of glycated hemoglobin after randomization, with the last observation carried forward for the imputation of missing data.

Differences in the change in glycated hemoglobin levels were analyzed with the use of analysis of covariance (ANCOVA) with three categorical variables (study group, pooled investigative site, and sex) and four continuous variables (age, duration of diabetes, body-mass index, and baseline glycated hemoglobin level) as fixed effects. The proportion of patients reaching glycated hemoglobin targets was analyzed with the use of a logistic-regression model with two categorical variables (study group and sex) and the above-mentioned continuous variables as fixed effects. The effect of sensor use on glycated hemoglobin levels was analyzed with the use of an ANCOVA model with three categorical variables (sensor-use categories, pooled investigative site, and sex) and the above-mentioned continuous variables as fixed effects. Changes in weight were analyzed with the use of a general linear model with adjustment for baseline weight. Incidences of adverse events were compared with the use of a logistic-regression model, and rates of adverse events per 100 person-years were compared with the use of an ANCOVA model; both models had two categorical variables (study group and sex) and the above-mentioned continuous variables as fixed effects. The area under the curve is the product of the magnitude and duration of the sensor-measured glucose level above or below a specified cutoff level. Higher values for this calculation indicate more numerous, severe, or protracted gly-

Table 1. Baseline Characteristics of the Patients.*

Characteristic	Sensor-Augmented Pump Therapy			Injection Therapy		
	All Patients (N=244)	Adults (N=166)	Children (N=78)	All Patients (N=241)	Adults (N=163)	Children (N=78)
Mean age — yr	32.2±17.5	41.9±12.3	11.7±3.0	31.5±16.5	40.6±12.0	12.7±3.1
Male sex — no. (%)	140 (57)	94 (57)	46 (59)	134 (56)	93 (57)	41 (53)
Race or ethnic group — no. (%)†						
Hispanic	7 (3)	5 (3)	2 (3)	7 (3)	3 (2)	4 (5)
White	221 (91)	151 (91)	70 (90)	222 (92)	153 (94)	69 (88)
Other	16 (7)	10 (6)	6 (8)	12 (5)	7 (4)	5 (6)
Nonsmoking — no. (%)	220 (90)	142 (86)	78 (100)	217 (90)	139 (85)	78 (100)
No alcohol use — no. (%)	133 (55)	56 (34)	77 (99)	127 (53)	50 (31)	77 (99)
Employment status — no. (%)‡						
Disabled	3 (1)	3 (2)	0	4 (2)	4 (2)	0
Employed or volunteer	140 (57)	139 (84)	1 (1)	128 (53)	127 (78)	1 (1)
Homemaker	8 (3)	8 (5)	0	7 (3)	7 (4)	0
Retired	8 (3)	8 (5)	0	8 (3)	8 (5)	0
Student	87 (36)	9 (5)§	78 (100)	99 (41)	21 (13)§	78 (100)
Unemployed	6 (2)	6 (4)	0	7 (3)	7 (4)	0
Country of residence — no. (%)						
United States	216 (89)	138 (83)	78 (100)	211 (88)	133 (82)	78 (100)
Canada	28 (11)	28 (17)	0	30 (12)	30 (18)	0
Interval since diagnosis of diabetes — yr	15.2±12.5	20.2±12.2	4.7±3.1	15.4±12.0	20.2±11.7	5.4±3.7
Glycated hemoglobin — %	8.3±0.5	8.3±0.5	8.3±0.6	8.3±0.5	8.3±0.5	8.3±0.5
Weight — kg	71.9±25.3	80.8±15.9§	49.0±17.9	73.0±21.8	85.1±18.5§	51.6±19.3
Body-mass index¶	25.3±6.0	27.4±4.4	20.2±3.8	25.6±5.6	28.4±5.7	20.6±4.5

* Plus–minus values are means ±SD. Percentages may not total 100 because of rounding.
† Race or ethnic group was self-reported.
‡ Patients could select more than one answer in this category.
§ P<0.05 for the comparison between the pump-therapy group and the injection-therapy group.
¶ The body-mass index is the weight in kilograms divided by the square of the height in meters.

cemic events. The areas under the curve that were calculated from continuous glucose monitoring at 1 year were compared with the use of an ANCOVA model with three categorical variables (study group, pooled investigative site, and sex) and four continuous variables (age, duration of diabetes, body-mass index, and baseline area under the curve) as fixed effects. Baseline characteristics were compared with the use of a two-sample t-test for continuous variables and either the chi-square test or Fisher's exact test for categorical variables.

Analyses were conducted with SAS software, version 9.2 (SAS Institute). All reported P values are two-sided; a P value of less than 0.05 was considered to indicate statistical significance for comparisons of the primary outcome, baseline characteristics, and safety.

RESULTS

STUDY RECRUITMENT AND BASELINE CHARACTERISTICS

From January 2007 through December 2008, a total of 495 patients underwent randomization; follow-up data on glycated hemoglobin levels were missing for 10 patients, who were not included in the primary analysis. Of the remaining 485 patients, 4 (1%) were lost to follow-up, 32 (7%) discontinued the study or were withdrawn, and 6 (1%) did not provide 1-year results for glycated hemoglobin, leaving 443 patients in the primary analysis (Fig. 2 in the Supplementary Appendix). Baseline characteristics were similar in the two study groups, except for weight (P=0.02) and student status (P=0.02) among adult patients (Table 1).

PRIMARY AND SECONDARY OUTCOMES

At 1 year, the baseline mean glycated hemoglobin level (8.3% in the two study groups) had decreased to 7.5% in the pump-therapy group (absolute reduction, 0.8±0.8 percentage points), as compared with 8.1% in the injection-therapy group (absolute reduction, 0.2±0.9 percentage points), for a between-group difference in the pump-therapy group of −0.6 percentage points (95% confidence interval [CI], −0.7 to −0.4; P<0.001) (Fig. 1). Among adults, the absolute reduction in the mean glycated hemoglobin level was 1.0±0.7 percentage points in the pump-therapy group and 0.4±0.8 percentage points in the injection-therapy group, for a between-group difference in the pump-therapy group of −0.6 percentage points (95% CI, −0.8 to −0.4; P<0.001). Among children, there was an absolute reduction in glycated hemoglobin of 0.4±0.9 percentage points in the pump-therapy group and an increase of 0.2±1.0 percentage points in the injection-therapy group, for a between-group difference favoring the pump-therapy group of −0.5 percentage points (95% CI, −0.8 to −0.2; P<0.001), with adjustment for the statistical model.

Post hoc analyses that included only data from observed patients and used multiple imputation of missing values yielded similar results (Table 1 in the Supplementary Appendix). In both adults and children in the pump-therapy group, glycated hemoglobin levels fell rapidly from baseline to 3 months and remained lower than levels in the injection-therapy group for the remainder of the study (Fig. 1). An increased frequency of sensor use was associated with a greater reduction in glycated hemoglobin levels at 1 year (P=0.003 with adjustment for the baseline glycated hemoglobin level) (Fig. 2).

The numbers of patients who reached a glycated hemoglobin value of 7% or less were 67 of 244 patients (27%) in the pump-therapy group and 23 of 241 patients (10%) in the injection-therapy group (P<0.001); these numbers included 57 of 166 adults (34%) in the pump-therapy group and 19 of 163 adults (12%) in the injection-therapy group (P<0.001) and 10 of 78 children (13%) in the pump-therapy group and 4 of 78 children (5%) in the injection-therapy group (P=0.15) (Fig. 3). In a post hoc analysis that used glycated hemoglobin targets recommended by the American Diabetes Association for children between the ages of 6 and 12 years (<8%) and adolescents between the ages of 13 and 19 years (<7.5%),[10] a total of 35 of the 80 children and adolescents (44%) in the pump-therapy group and 16 of the 80 (20%) in the injection-therapy group reached these targets at 1 year (P=0.005). Among adults, weight increased by 2.4 kg in the pump-therapy group and by 1.8 kg in the injection-therapy group (P=0.19).

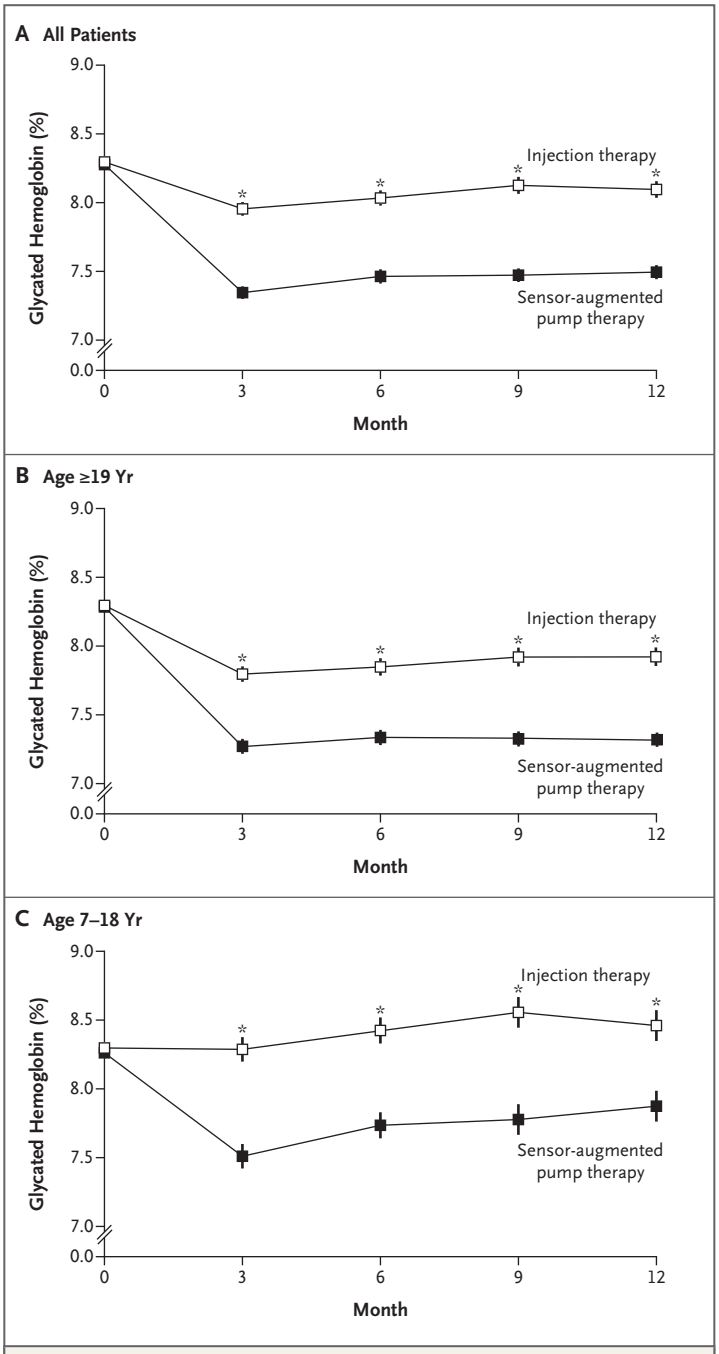

Figure 1. Glycated Hemoglobin Levels at 3, 6, 9, and 12 Months in All Patients and in Subgroups According to Age.

Values are means ±SE. Asterisks denote P<0.001 for all comparisons between pump therapy and injection therapy at each time point.

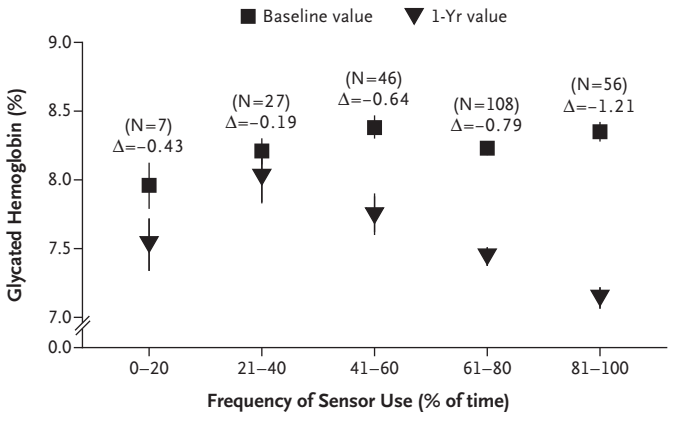

Figure 2. Sensor Use and Change in Glycated Hemoglobin Levels in 244 Patients Using a Sensor-Augmented Insulin Pump with Continuous Glucose Monitoring.

Values are means, with vertical lines indicating standard errors. The numbers in the graph are the changes from baseline to 1 year. An increased frequency of sensor use was associated with a greater reduction in the glycated hemoglobin level at 1 year (P=0.003, with adjustment for the baseline glycated hemoglobin level).

ADVERSE EVENTS

Rates of severe hypoglycemia and diabetic ketoacidosis were similar in the two study groups and in the two age groups. The area under the curve that was calculated from continuous glucose monitoring was similar in the two groups at 1 year for patients with hypoglycemia (defined either as <70 mg per deciliter [<3.9 mmol per liter] or as <50 mg per deciliter [<2.8 mmol per liter]) and was significantly lower in the pump-therapy group for patients with hyperglycemia (defined either as >180 mg per deciliter [>10.0 mmol per liter] or as >250 mg per deciliter [>13.9 mmol per liter]) (Table 2). At 1 year, 5 of 100 patients (5%) with a glycated hemoglobin level of 7% or less had severe hypoglycemia, as compared with 33 of 395 patients (8%) with a glycated hemoglobin level of more than 7% (P=0.12). There were no severe hypoglycemic events in either study group among children who had a glycated hemoglobin level of 7% or less at 1 year.

There were two hospital admissions in the pump-therapy group for cellulitis related to insertion-site infections and one death from sudden cardiac arrest in a patient in the injection-therapy group who had a history of cardiovascular disease.

DISCUSSION

In this study comparing sensor-augmented pump therapy with multiple-injection therapy, the between-group difference in glycated hemoglobin levels favored pump therapy and was statistically and clinically significant among both adults and children. More patients in the pump-therapy group reached the prespecified target glycated hemoglobin value of 7% or less, and lower glycated hemoglobin levels were achieved in this group by reducing biochemical hyperglycemia without increasing biochemical hypoglycemia or the rate of severe hypoglycemic events. The incidence of diabetic ketoacidosis was negligible, and there was no significant between-group difference in weight gain among adults.

Among adults, who had a mean baseline glycated hemoglobin level of 8.3±0.5%, the reduction of 1.0 percentage point in the pump-therapy group was significantly greater than the reduction of 0.4 percentage points in the injection-therapy group. In comparison, in the JDRF study of continuous blood glucose monitoring, adults in both the pump-therapy group and the injection-therapy group had a reduction of 0.5 percentage points (mean baseline value, 7.6±0.5%), whereas glycated hemoglobin levels increased slightly in the group undergoing standard blood glucose monitoring.[8] Although we cannot directly compare our findings with those of the JDRF study, in our study, the reduction of 0.5 percentage points in glycated hemoglobin levels among children in the pump-therapy group, as compared with the injection-therapy group, differed from the results of the JDRF study, which showed no between-group difference at 6 months among patients who were 8 to 14 years of age or among those who were 15 to 24 years of age. In the JDRF study, the only variables that predicted successful use of continuous glucose monitoring were an older age and an increased frequency of daily blood glucose measurement.[11] Also of interest is our finding that nearly half the children in the pump-therapy group reached the American Diabetes Association's age-specific targets for glycated hemoglobin by the end of the study.[10]

Other studies have compared pump therapy with injection therapy, as well as continuous glucose monitoring with conventional blood glucose monitoring with a meter. In one randomized, con-

trolled trial,[5] investigators examined the efficacy of introducing these technologies together in patients who had not used either pumps or sensors. In our study, the decision to introduce these technologies one at a time during the first 5 weeks proved to be an effective strategy. Clinicians may wish to consider this approach when implementing sensor-augmented pump systems in patients who have not undergone such therapy.

Since previous studies have examined the effect of individual components of the sensor-augmented pump system, our study was designed to examine how the combined system compares with optimal injection therapy. In contrast to the findings in previous studies, our results suggest that the effects of the combined system were greater than what would be expected from the individual components alone. In our study, a frequency of sensor use of 41 to 60% was associated with a reduction of 0.64 percentage points in glycated hemoglobin levels, and increasing sensor use to more than 80% doubled the effect. In contrast, in both the JDRF study (in which patients maintained their prestudy insulin-pump or injection regimen) and the STAR 1 study (in which patients maintained their prestudy insulin-pump regimen or switched to sensor-augmented pump therapy), lower glycated hemoglobin levels were observed only in patients who used the sensor 60% or more of the time.[6,8] The improvements in metabolic control that we observed were also much greater than expected with insulin-pump therapy alone, since two recent meta-analyses of pump therapy versus injection therapy[4,12] have shown reductions of 0.3 and 0.2 percentage points, respectively, in glycated hemoglobin levels with insulin-pump therapy. Additional studies designed to identify the independent benefits of sensors and insulin pumps are warranted. It is also likely that in our study, the use of therapy-management software benefited patients using sensor-augmented pump therapy. However, we limited the effect of this factor by making the data-management program available to all patients.

Patients in our two study groups had much lower rates of severe hypoglycemia than did patients with corresponding glycated hemoglobin levels who underwent intensive insulin treatment in the Diabetes Control and Complications Trial (DCCT) (NCT00360815).[1,2] This difference may be due to the multiple advances in diabetes therapy — such as the use of insulin analogues[13] — that have occurred since the initiation of the DCCT or to our exclusion of patients who had had two or more episodes of severe hypoglycemia dur-

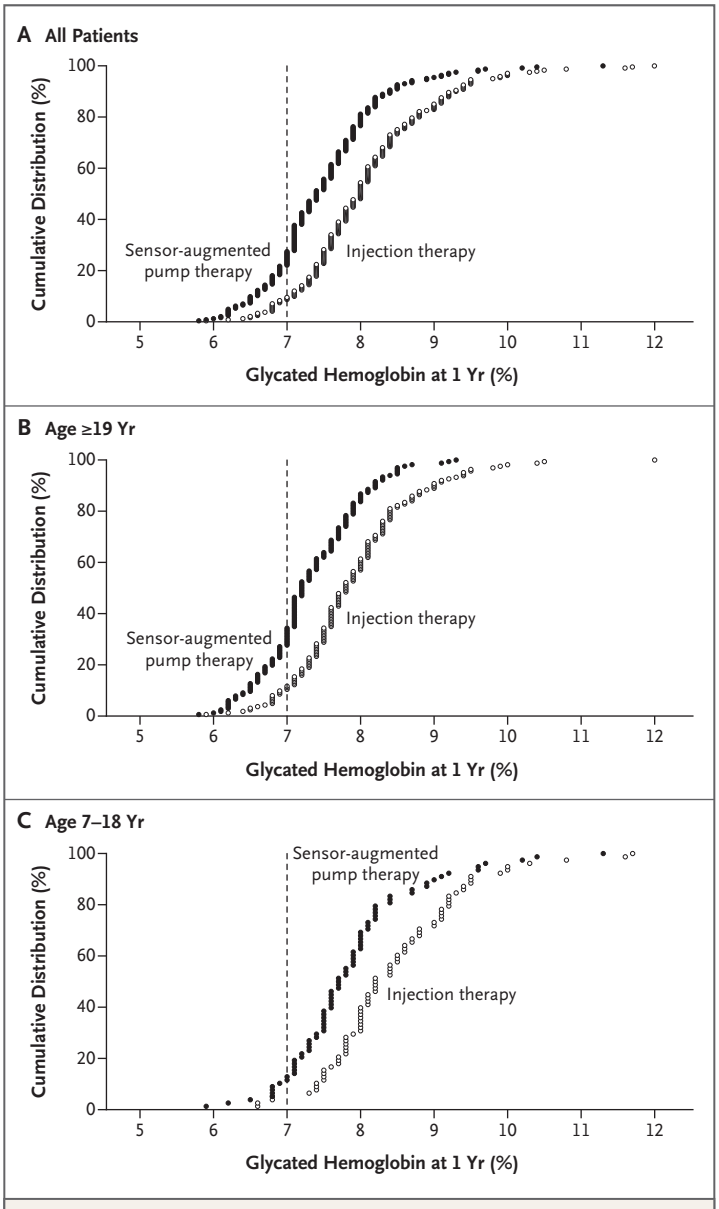

Figure 3. Cumulative Distribution of Glycated Hemoglobin Levels at 1 Year among All Patients and in Subgroups According to Age.

The proportion of patients in the pump-therapy group who reached the glycated hemoglobin target of less than 7% (as indicated by the vertical dashed line) was 28%, as compared with 10% of those in the injection-therapy group (P<0.001). These proportions were 34% and 12%, respectively, among adults 19 years of age or older (P<0.001) and 13% and 5%, respectively, among children between the ages of 7 and 18 years (P=0.15).

Table 2. Severe Hypoglycemia, Diabetic Ketoacidosis, and Area under the Curve Calculated from Continuous Glucose Monitoring.*

Variable	All Patients			Adults			Children		
	Sensor-Augmented Pump Therapy (N=247)	Injection Therapy (N=248)	P Value	Sensor-Augmented Pump Therapy (N=169)	Injection Therapy (N=167)	P Value	Sensor-Augmented Pump Therapy (N=78)	Injection Therapy (N=81)	P Value
Severe hypoglycemia									
No. of events	32	27	0.58	25	23	0.53	7	4	0.53
No. of patients	21	17		17	13		4	4	
Rate per 100 person-yr	13.31	13.48	0.84	15.31	17.62	0.66	8.98	4.95	0.35
Diabetic ketoacidosis									
No. of events	3	2	0.38	2	0	NA	1	2	0.49
No. of patients	3	1		2	0		1	1	
Rate per 100 person-yr	0.01	<0.01	0.60	0.01	0	NA	0.02	0.02	0.20
Area under the curve calculated from continuous glucose monitoring — $mg \cdot dl^{-1} \cdot min$									
>250 mg/dl									
At baseline	9.99±9.63	10.62±9.64		8.16±8.31	7.98±7.98		13.89±11.04	16.23±10.46	
At 1 yr	5.41±6.60	10.70±11.90	<0.001	3.74±5.01	7.38±8.62	<0.001	9.20±8.08	17.64±14.62	<0.001
>180 mg/dl									
At baseline	32.26±19.70	33.38±19.72		28.92±17.80	28.04±17.03		39.36±21.70	44.68±20.34	
At 1 yr	20.36±15.73	32.23±23.41	<0.001	16.06±12.84	26.01±19.52	<0.001	30.11±17.34	45.29±25.57	<0.001
<70 mg/dl									
At baseline	0.27±0.50	0.29±0.48		0.28±0.54	0.31±0.49		0.26±0.40	0.23±0.44	
At 1 yr	0.24±0.43	0.28±0.51	0.54	0.25±0.44	0.29±0.55	0.63	0.23±0.41	0.25±0.41	0.79
<50 mg/dl									
At baseline	0.02±0.09	0.02±0.06		0.02±0.10	0.02±0.07		0.01±0.04	0.02±0.05	
At 1 yr	0.02±0.05	0.02±0.08	0.25	0.02±0.04	0.03±0.09	0.16	0.02±0.07	0.01±0.05	0.64

* Higher values for the area under the curve indicate more numerous, severe, or protracted glycemic events. The areas under the curve that were calculated from continuous glucose monitoring at 1 year were compared by means of analysis of variance, with three categorical variables (study group, pooled investigative site, and sex) and four continuous variables (age, duration of diabetes, body-mass index, and baseline area under the curve) as fixed effects. The area under the curve was evaluated for patients in two subgroups of hypoglycemia (<70 and <50 mg of glucose per deciliter) and those in two subgroups of hyperglycemia (>180 and >250 mg of glucose per deciliter). P values for the comparisons of numbers of events are based on the number of patients with at least one episode of severe hypoglycemia or diabetic ketoacidosis. P values for the area under the curve at 1 year have been adjusted for baseline values. To convert the values for glucose to millimoles per liter, multiply by 0.05551. NA denotes not applicable.

ing the previous year. The most striking difference between the two studies was in the number of severe hypoglycemic events among children. In our study, children in the pump-therapy group (mean glycated hemoglobin level, 7.9%) had 9.0 severe hypoglycemic events per 100 patient-years, as compared with adolescents in the DCCT (mean glycated hemoglobin level, 8.1%) undergoing intensive insulin treatment, who had 85.7 such events per 100 person-years.[1]

Our study has several limitations. First, because of the nature of the medical devices that were used, the interventions were known to patients, investigators, and caregivers. Second, we did not study the effect of insulin-pump therapy alone versus sensor-augmented pump therapy to determine the contribution of each component of the system. Third, the generalizability of the study's results may in part be limited by the use of a mandated range for glycated hemoglobin (7.4 to 9.5%) as an inclusion criterion. Fourth, our patients may have been particularly motivated because they were participating in a study. However, they were generally representative of patients with type 1 diabetes who are considered to be candidates for further intensification of insulin therapy and diabetes care (i.e., those who are not able to reach desired glycemic targets with a regimen of multiple daily insulin injections and appropriate medical support), and the results indicate that sensor-augmented pump therapy is a consideration for patients. Finally, for reasons of technical device training, patients in the pump-therapy group received more contact with clinical staff members than did patients in the injection-therapy group during the first 5 weeks of the study; thereafter, clinical contacts were designed to be identical in the two study groups.

In conclusion, in patients with type 1 diabetes with suboptimal glycemic control, the use of a sensor-augmented insulin pump was associated with significant improvement in glycated hemoglobin levels, as compared with a regimen of multiple daily injections of recombinant insulin analogues.

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APPENDIX

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