Transitioning of People With Type 1 Diabetes From Multiple Daily Injections and Self-Monitoring of Blood Glucose Directly to MiniMed 780G Advanced Hybrid Closed-Loop System: A Two-Center, Randomized, Controlled Study

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Diabetes Care 2022;45:2628–2635 | https://doi.org/10.2337/dc22-0470

OBJECTIVE

The aim of this study was to evaluate the outcomes of transitioning to the MiniMed 780G advanced hybrid closed-loop (AHCL) system in adult individuals with type 1 diabetes mellitus (T1DM) naive to continuous subcutaneous insulin infusion (CSII) and continuous glucose monitoring (CGM) technologies.

RESEARCH DESIGN AND METHODS

This was a two-center, randomized, controlled, parallel-group trial with evaluation of individuals with T1DM aged 26–60 years managed with multiple daily injections (MDI) and self-monitoring of blood glucose (BGM) with HbA_{1c} <10%.

RESULTS

A total of 41 participants were recruited and randomized to either the AHCL (*n* = 20) or the MDI+BGM (*n* = 21) group, and 37 participants (mean ± SD age 40.3 ± 8.0 years, duration of diabetes 17.3 ± 12.1 years, BMI 25.1 ± 3.1 kg/m^2, HbA_{1c} 7.2 ± 1.0%) completed the study. Time spent with glucose levels in target range increased from 69.3 ± 12.3% at baseline to 85.0 ± 6.3% at 3 months in the AHCL group, while remaining unchanged in the control group (treatment effect 21.5% [95% CI 15.7, 27.3]; *P* < 0.001). The time with levels below range (<70 mg/dL) decreased from 8.7 ± 7.3% to 2.1 ± 1.7% in the AHCL group and remained unchanged in the MDI+BGM group (treatment effect −4.4% [95% CI −7.4, −2.1]; *P* < 0.001). Participants from the AHCL group also had significant improvements in HbA_{1c} levels (treatment effect −0.6% [95% CI −0.9, −0.2]; *P* = 0.005) and in quality of life (QoL) in specific subscales compared with the MDI+BGM group.

CONCLUSIONS

People with T1DM naive to CSII and CGM technologies initiating AHCL significantly and safely improved their glycemic control, as well as their QoL and psychological well-being.

Despite many advances in type 1 diabetes therapies, most people with diabetes are unable to maintain near-normal blood glucose levels and to reduce the risk of

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Received 7 March 2022 and accepted 25 July 2022

Clinical trial reg. no. NCT04616391, clinicaltrials.gov

This article contains supplementary material online at https://doi.org/10.2337/figshare.20409342.

both acute and chronic complications of the disease (1–4). Hybrid closed-loop (HCL) insulin delivery technology automatically increases, decreases, and suspends insulin delivery based on real-time continuous glucose monitoring (CGM) data (5,6). The MiniMed 780G system (Medtronic) contains an advanced HCL algorithm (AHCL) and in addition delivers autocorrection boluses for high glucose levels (6,7).

To date, published studies have provided evidence that AHCL technology is effective in safely improving glycemic control in individuals with type 1 diabetes mellitus (T1DM) (8–12). In these randomized controlled trials as well as clinical experiences the effectiveness of the MiniMed 780G system was evaluated predominantly in individuals who had previously used diabetes technologies, either insulin pumps (continuous subcutaneous insulin infusion [CSII]) or CGM systems, with or without various levels of insulin delivery automation (9,10,12). It remained an open question, however, to what extent the effectiveness of the MiniMed 780G system depended on prior experience of CSII or CGM technologies. The capability of people with T1DM to undergo transition directly from a relatively simple multiple daily injections (MDI) and self-monitoring of blood glucose (BGM)–based treatment to the most advanced AHCL technology was questioned, leading to a stepwise approach of implementing diabetes-related technologies. What is more, previous observations with technologies with no or less automation of glucose control suggested that transitioning to a more advanced system might require more trust in the equipment, creating possible challenges (13).

The impacts of advanced technology use in T1DM on quality of life (QoL) and patient-related outcomes are other important topics to address. Studies have indicated that better QoL of T1DM patients is associated with improvement of glycosylated hemoglobin and reduced hypoglycemic episodes (14,15). Studies have also suggested that proper implementation of new technologies in T1DM treatment may significantly improve not only metabolic control but also psychological well-being and QoL (16–19). Whether these positive outcomes hold true in transitioning from technology naive to use of advanced hybrid systems remains unclear.

We therefore performed a randomized controlled study to address these questions. The primary objective was to evaluate whether the MiniMed 780G AHCL system improves glycemic control and QoL perception in adult individuals with T1DM and naive to CSII and CGM technologies.

RESEARCH DESIGN AND METHODS

Study Design

This was a two-center, randomized, controlled, parallel-group trial that consisted of a 2 week run-in period and a 3 month study period (ClinicalTrials.gov reg. no. NCT04616391, protocol identifier 1072.61201.8.2020) (Supplementary Fig. 1).

We included individuals who actively responded to announcements in outpatient clinics/social media. Participants with T1DM diagnosed at least 2 years prior the study, aged 26–60 years, with HbA_{1c} $<$10% (86 mmol/mol), treated with MDI and BGM, and without any previous experience of CSII or CGM entered the 2 week run-in period during which they were required to demonstrate tolerance to wearing the sensor and compliance with blinded CGM (a full list of inclusion and exclusion criteria can be found in Supplementary Table 1). Following the run-in period, participants were randomly allocated to either the AHCL group or the MDI+BGM group and were followed up for 3 months. The primary end point was the between-group difference in the percentage of time sensor glucose (SG) was within the range of 70–180 mg/dL (TIR) at the end of study. Secondary end points included time spent in the hyperglycemic, euglycemic, and hypoglycemic ranges; glycemic variability; HbA_{1c}; and QoL. Between-group comparison of CGM-derived measures was based on the period of the last 2 weeks of the study. These were calculated for the overall (00:00–23:59 h), daytime (06:01–23:59 h), and nighttime (00:00–06:00 h) periods. Safety end points included the number of severe hypoglycemic events and the number of diabetic ketoacidosis events. A continued observation phase with AHCL therapy for an additional 9 months was offered to participants from the AHCL arm.

Procedures

All participants were met by a diabetes educator at screening for verification of knowledge related to intensive, functional insulin therapy. Educational sessions for the MiniMed 780G group lasted on average for 4–6 h, depending on patients' responsiveness. The dietitian provided a single online educational session for each patient in both groups lasting for ~30 min. People with diabetes not meeting the basic knowledge requirements, as assessed by the diabetologist, were not eligible to pursue the study. All participants were trained on the CGM usage and wore the Guardian Link 3 Transmitter and Guardian Sensor 3 in a blinded manner for 2 weeks for baseline measurement and assessment of compatibility with the device. CGM data were downloaded in the clinic, and the blinded data were not used for therapy adjustment. Randomization was performed with Random Allocation Software to allow fair distribution among sites and eliminate place for bias (https://random-allocation-software.software.informer.com/2.0/). Participants were randomized to the AHCL or the MDI+BGM group in a 1:1 ratio. The randomization code was generated by a statistician using block randomization with the random variable block size method. Participants allocated to the AHCL group initiated the MiniMed 780G system in open loop with the "Suspend before low" feature for 3 days and then initiated AHCL therapy with a glucose target of 100 mg/dL and an active insulin time (AIT) of 2.0–2.5 h. Since the study participants had well-controlled diabetes at baseline, their respective insulin carbohydrate ratio settings were used with some minor modifications. The participants were instructed not to adjust system settings without consulting with the physician. Insulin carbohydrate ratio and AIT were adjusted by the physician during the study as per investigator judgement; glucose target was adjusted only in case of safety concerns. Participants' interaction with the system and glycemic control was reviewed and the system settings were reassessed and adjusted as needed at each visit in the clinic or remotely (Supplementary Fig. 2). Participants randomized to the MDI+BGM group continued with their previous treatment and repeated a 2 week blinded CGM period at the end of the 3 months. HbA_{1c} measurements were performed at screening and at the end of the 3 months with an NGSP-certified laboratory test.

QoL was assessed with use of the Polish-validated version of the QoL-Q Diabetes questionnaire, which is a standardized questionnaire allowing for exploratory analysis (Speight et al. [20]).

The questionnaire is a self-assessment scale composed of two parts: the first a measure of QoL with diabetes in a given (1 of 23) life area (range score for each item: 1, strongly disagree, 5, strongly agree [answer of N/A was not included in further analyses]) and the second a measure of the importance of each of the 23 aspects of life, assessed on a three-dimension scale (1, not at all important, 3, extremely important [answer of N/A was also assessed as 1]). We calculated the score value for a given area (1 of 23) by multiplying the result of the first part of the test by the second part of the test result (for a given area). The mean value for a given area is 6, minimum is 1, and maximum is 15. We calculated the overall QoL score by summing up points from all 23 areas. The maximum test result is 345 points; the higher the result, the better the QoL assessed by the patient.

Statistical Analysis

Using data from the Medtronic MiniMed 670G Hybrid Closed-Loop Pivotal Trial in T1D (>21 years old) (21) and Multiple Daily Injections and Continuous Glucose Monitoring in Diabetes (DIAMOND) study (22), we assume a mean ± SD TIR 70 ± 15% for the AHCL group and 55 ± 15% for the MDI group. For a two-sided two-sample *t* test, a total sample size of 40 subjects is required to test the hypothesized difference in population means of 15% with a 95% confidence level, 80% power, and attrition rate of 15%.

The primary population consisted of subjects who fulfilled eligibility criteria, demonstrated tolerance to wearing the sensor and compliance with blinded CGM, received allocated intervention, and completed the study. All the analyses we performed were based on this primary population.

All available data were used in computing means and SDs. No imputation method was applied for missing data.

For comparison of two independent variables, Student or Welch *t* test was used for normally distributed (Shapiro-Wilk test) continuous variables; otherwise, the Mann-Whitney *U* test was conducted. For comparison of two dependent groups, paired *t* test or Wilcoxon signed rank test, when appropriate, was used. For examination of the differences between categorical variables χ^2 test was used.

To test for the effect of treatment allocation on outcomes, we conducted ANCOVA, with adjustment for treatment arm and baseline values. Once the significant interactions were confirmed we included them into the model, and then we estimate the adjusted mean difference between the treatment arms. When ANCOVA assumption was not met the Wilcoxon rank sum test was used.

Analyses of correlation between TIR change and QoL score change in subscales was performed with use of Pearson correlation.

All *P* values are two tailed. Analyses were performed with *R*, version 4.1.0, and RStudio, version 1.3.959.

RESULTS

Trial participants (*n* = 41) were recruited between 25 March 2021 and 20 April 2021 and were randomized to the AHCL (*n* = 20) or the MDI+BGM (*n* = 21) group (Supplementary Fig. 1). Four participants randomized to the MDI+BGM group withdrew their consent: three due to not being allocated to the AHCL arm (at randomization day) and one because of unplanned pregnancy (1.5 months after randomization). These four participants were included in neither the data analysis nor the baseline characteristics. All the other participants randomized in either the AHCL (*n* = 20) or the MDI+BGM (*n* = 17) group completed the 3-month study. Mean ± SD age was 40.3 ± 8.0 years, mean duration of diabetes 17.3 ± 12.1 years, mean BMI 25.1 ± 3.1 kg/m^2, and a mean HbA_{1c} 7.2 ± 1.0% (55 ± 11 mmol/mol). The AHCL and the MDI+BGM groups did not differ at baseline in sex, BMI, body weight, duration of diabetes, age, thyroid stimulating hormone, estimated glomerular filtration rate, or AST (Table 1).

Mean ± SD TIR increased from 69.3 ± 12.3% at baseline to 85.0 ± 6.3% at 3 months in the AHCL group, while remaining unchanged in the control group (*P* = 0.684): 62.8 ± 10.7% to 61.5 ± 11.2% (treatment effect 21.5% [95% CI 15.7, 27.3]; *P* < 0.001) (Table 2). All participants in the AHCL group (20 of 20) achieved a TIR >70%, compared with 29.4% (5 of 17) in the MDI+BGM group (*P* < 0.001).

All other CGM-derived outcomes turned out to be significantly in favor of the AHCL group (Table 2). Mean ± SD time with glucose levels below target range (TBR), <70 mg/dL, decreased from 8.7 ± 7.3% to 2.1 ± 1.7% in the AHCL group, while remaining unchanged in the MDI+BGM group (7.5 ± 7.9% to 8.1 ± 7.1%; *P* = 0.575) (treatment effect −4.4% [95% CI −7.4, −2.1]; *P* < 0.001). TBR <54 mg/dL was changed by treatment effect −0.9% [95% CI −1.6, −0.3]; *P* = 0.010), and TAR was changed by treatment effect −14.7% [95% CI −21.4, −8.0]; *P* < 0.001. The average glucose level was significantly reduced in the AHCL group (treatment effect 15.4 mg/dL [95% CI −26.5, −4.2]; *P* = 0.008), as well as the glucose variability, as indicated by the coefficient of variation (CV) of the average glucose (treatment effect 9.4% [95% CI −12.9, −5.6]; *P* < 0.001). The magnitude of the benefits was more pronounced during the nighttime with a treatment effect of 26.2% TIR and −7.0% TBR in favor of AHCL (20.5% and −5.0% during the daytime, respectively), reaching 89.8% TIR (Table 3).

Table 1—Baseline characteristics of randomized participants

	Treatment arm (*n* = 20), MiniMed 780G system	Control arm (*n* = 17), MDI+BGM	*P*
Sex, F (%)	8 (40.0)	8 (47.1)	0.920
Age (years)	39.8 ± 8.3	40.9 ± 7.8	0.671
Diabetes duration (years)	17.1 ± 12.2	17.6 ± 12.2	0.749
HbA_{1c} (%; mmol/mol)	7.05 ± 0.8; 54 ± 9	7.4 ± 1.2; 57 ± 13	0.349
BMI (kg/m^2)	24.5 ± 3.3	25.6 ± 2.64	0.280
Body weight (kg)	76.3 ± 14.7	77.7 ± 14.4	0.774
eGFR (mL/min)	112 ± 23	119 ± 24	0.341
Thyroid stimulating hormone (μU/mL)	1.51 ± 0.75	1.81 ± 0.73	0.241
AST (units/L)	26.4 ± 7.7	24.9 ± 4.7	0.720

Data are means ± SD or *n* (%). eGFR, estimated glomerular filtration rate; F, female.

Table 2—Primary and secondary glucose and clinical outcomes

	Treatment arm (n = 20)		Control arm (n = 17)		Estimated difference		
	Baseline	MiniMed 780G system	Baseline	MDI+BGM	(780G − MDI)†	95% CI	P
HbA_{1c} (%; mmol/mol)	7.05 ± 0.8; 54 ± 9	6.7 ± 0.4; 50 ± 5	7.4 ± 1.2; 57 ± 13	7.4 ± 0.8; 57 ± 9	−0.6	−0.9, −0.2	0.005
SG (mg/dL)	139.9 ± 21.2	133.2 ± 8.9	151.0 ± 23.6	153.1 ± 25.3	−15.4	−26.5, −4.2	0.008
GMI (%)	6.66 ± 0.51	6.50 ± 0.21	6.92 ± 0.56	6.97 ± 0.61	−0.4	−0.6, −0.1	0.008
CV of SG (%)	39.0 ± 7.1	30.6 ± 4.7	39.5 ± 4.7	40.7 ± 6.3	−9.4‡	−12.9, −5.6	<0.001
%SG <54 mg/dL	2.9 ± 3.8	0.3 ± 0.4	2.7 ± 4.9	2.6 ± 3.9	−0.9‡	−1.6, −0.3	0.010
%SG <70 mg/dL	8.7 ± 7.3	2.1 ± 1.7	7.5 ± 7.9	8.1 ± 7.1	−4.4‡	−7.4, −2.1	<0.001
%SG 70–180 mg/dL	69.3 ± 12.3	85.0 ± 6.3	62.8 ± 10.7	61.5 ± 11.2	21.5	15.7, 27.3	<0.001
%SG >180 mg/dL	22.0 ± 12.3	12.9 ± 5.8	29.8 ± 13.4	30.5 ± 14.2	−14.7	−21.4, −8.0	<0.001
%SG >250 mg/dL	5.2 ± 6.4	1.6 ± 1.6	7.6 ± 5.8	9.3 ± 8.3	−4.5‡	−11.0, −2.0	<0.001
Body weight (kg)	76.3 ± 14.7	75.6 ± 16.5	77.7 ± 14.4	77.8 ± 15.3	−2.9‡	−12.5, 8.1	0.637
BMI (kg/m^2)	24.5 ± 3.3	24.3 ± 3.9	25.6 ± 2.6	25.6 ± 2.9	−1.7‡	−3.9, 1.2	0.244

Data are means ± SD unless otherwise indicated. %SG indicates percentage of time with SG in range. 780G − MDI, MiniMed 780G system − MDI+BGM; GMI, glucose management indicator. †ANCOVA with adjustment for baseline value. Once the significant interaction was confirmed we included it into the model. Mean difference is presented. ‡Wilcoxon rank sum test was applied when ANCOVA assumption was not meet, and median difference is provided.

Laboratory-measured HbA_{1c} levels also demonstrated a significant reduction in the AHCL group compared with the MDI+BGM group (treatment effect −0.6% [95% CI −0.9, −0.2]; P = 0.005). Additionally, significant improvement in glucose management indicator was observed (treatment effect −0.4% [95% CI −0.6, −0.1]) (Table 2).

Body weight and BMI did not change between screening and study end for either group (AHCL group P = 0.513 and P = 0.408, respectively, and MDI group P = 0.946 and P = 0.972). There was no between-group difference in body weight or BMI at the study end (P = 0.774 and P = 0.280) (Table 1).

Over the 3 months of the study following AHCL initiation, participants in the AHCL group used the sensor for a mean of 95.6% of the time, spent a mean of 97.8% of the time in AHCL, and experienced a mean of 0.5 AHCL exits per week. While in AHCL, the glucose target of 100 mg/dL and the AIT of 2 h were used for 80.6% and 92.9% of the time, respectively.

There was no events of severe hypoglycemia or diabetic ketoacidosis during the study in any of the groups.

Mean ± SD overall QoL-Q Diabetes score in the MDI+BGM group did not change from baseline (173 ± 46) to 3 months (173 ± 53) but improved in the AHCL group, from 187 ± 32 to 202 ± 54. With adjustment for baseline values, there was no between-group difference (P = 0.287) (Table 4). However, in analyses of the 23 areas describing QoL, the AHCL group reported a significant increase in 4 essential of them, in comparison with the MDI+BGM group: feeling well (2.3 [95% CI 0.1–4.6]; P = 0.042), working (2.8 [95% CI 0.7–4.9]; P = 0.012), eating as I would like (3.1 [95% CI 0.8–5.4], P = 0.011) and doing

Table 3—Time spent in glycemic ranges during daytime and nighttime

	Treatment arm (n = 20)		Control arm (n = 17)		Estimated difference		
Category	Baseline	MiniMed 780G system	Baseline	MDI+BGM	(780G − MDI)†	95% CI	P
Daytime (06:01–23:59 h)							
%SG <54 mg/dL	2.2 ± 3.0	0.3 ± 0.4	2.7 ± 4.8	2.3 ± 3.3	−1.8	−2.5, −1.0	<0.001
%SG <70 mg/dL [%]	7.2 ± 5.7	2.3 ± 1.9	7.4 ± 7.9	7.4 ± 6.3	−5.0	−7.0, −3.0	<0.001
%SG 70–180 mg/dL	69.0 ± 12.1	83.3 ± 6.9	62.7 ± 10.3	60.5 ± 11.1	20.5	14.8, 26.3	<0.001
%SG >180 mg/dL	23.8 ± 12.3	14.5 ± 6.5	29.8 ± 12.7	32.1 ± 14.1	−15.3	−22.0, −8.6	<0.001
%SG >250 mg/dL	5.3 ± 5.8	1.8 ± 1.6	7.9 ± 5.6	9.9 ± 8.3	−5.6‡	−10.5, −2.4	<0.001
Nighttime (00:00–06:00 h)							
%SG <54 mg/dL	5.0 ± 7.7	0.2 ± 0.4	2.9 ± 6.3	3.7 ± 5.6	−1.6‡	−2.7, −0.0	0.007
%SG <70 mg/dL	13.0 ± 14.7	1.7 ± 1.8	7.6 ± 8.8	10.5 ± 11.0	−7.0‡	−13.6, −0.3	0.025
%SG 70–180 mg/dL	70.1 ± 19.6	89.8 ± 7.1	63.3 ± 14.5	65.3 ± 16.4	26.2‡	33.5, 16.1	<0.001
%SG >180 mg/dL	17.0 ± 17.4	8.5 ± 7.1	29.1 ± 17.3	24.2 ± 19.2	−14.1‡	−23.9, −3.9	0.009
%SG >250 mg/dL	5.1 ± 10.9	0.8 ± 2.1	6.9 ± 8.1	7.1 ± 9.8	−1.8‡	−4.5, −0.0	0.013

% SG, percentage of time with SG in range. Data are means ± SD unless otherwise indicated. †ANCOVA with adjustment for baseline value. Once the significant interaction was confirmed we included it into the model. Mean difference is presented. ‡Wilcoxon rank sum test was applied when ANCOVA assumption was not met, and median difference was provided.

Table 4—Outcomes of the QoL-Q Diabetes questionnaire

	Treatment arm (n = 20)		Control arm (n = 17)		Estimated difference		
	Baseline	MiniMed 780G System	Baseline	MDI+BGM	(780G − MDI)†	95% CI	P
Overall QoL Score	187.2 ± 32	202.5 ± 54.2	173.87 ± 46.24	173.6 ± 53.34	19.9	−17.7, 57.6	0.287
Feeling well	7.9 ± 3.2	9.8 ± 3.1	6.73 ± 3.31	7.87 ± 3.38	2.3	0.1, 4.6	0.042
Working	7.4 ± 2	10.4 ± 2.9	7.93 ± 4.15	7.33 ± 3.02	2.7	0.7, 4.6	0.010
Eating as I would like	4.9 ± 2.7	7.1 ± 3.3	3.87 ± 1.88	4.07 ± 2.62	3.1	0.8, 5.4	0.0110
Doing “normal” things	7.6 ± 2.9	9.9 ± 3.7	8.33 ± 3.66	8.21 ± 3.85	2.8	0.2, 5.4	0.0343
Family relationships/friendships	9.9 ± 3.4	10 ± 3.5	8.27 ± 3.13	10.2 ± 3.49	<−0.001‡	−2.99, 2.0	0.604
Going out or socializing	8.2 ± 2.7	8 ± 2.8	8.07 ± 3.43	9.33 ± 2.97	−1.02	−3.1,1.0	0.311
Partner/spouse relationship	9.8 ± 3	9.7 ± 4	9.53 ± 3.34	9.73 ± 4.1	−0.1	−3.0, 2.8	0.943
Enjoying sexual activity	8.4 ± 2.3	8.8 ± 3.1	8.71 ± 2.43	9.21 ± 3.91	−0.32	−2.9, 2.3	0.797
Being physically active	8 ± 2.1	8.8 ± 2.8	7.47 ± 3.14	8.36 ± 3.08	0.71	−1.7, 3.1	0.544
Feeling in control of my body	7.9 ± 2.5	8.7 ± 3.4	7.5 ± 2.44	8.93 ± 3.59	<−0.001‡	−2.0, 2.0	0.801
Looking good	7.2 ± 2.2	7.7 ± 2.5	7.79 ± 2.78	8.2 ± 3.38	0.3	−1.6, 2.3	0.718
Having holidays	8.9 ± 3.5	9.3 ± 3.4	6.93 ± 3.01	7.53 ± 2.59	1.3	−0.9, 3.5	0.234
Affording the things I would like	8.7 ± 2.7	8.9 ± 3.6	8.2 ± 3.47	8.07 ± 3.2	1.4	−0.9, 3.7	0.214
Driving	8.6 ± 3.4	9.1 ± 3.2	7.8 ± 4.18	7.93 ± 3.79	0.9	−1.2, 3.1	0.393
Practicing my religion	8.4 ± 3.9	8.4 ± 3.8	7.18 ± 4.33	6.3 ± 3.92	0.9	−0.7, 2.6	0.249
Sleeping	8.6 ± 2.5	9.8 ± 3.3	7.27 ± 2.09	7.5 ± 4.31	2.1	−0.3, 4.5	0.087
Looking after or being useful to others	8.9 ± 2.2	8.7 ± 1.9	7.33 ± 2.47	7.31 ± 3.3	2.0‡	−4.5, 4.0	0.081
Pets/animals	7.7 ± 1.9	8.8 ± 3.7	7.09 ± 2.88	6.44 ± 2.35	2.1	−0.1, 4.4	0.065
Being independent	9.7 ± 3.2	11.1 ± 3.1	9.8 ± 2.93	9.62 ± 3.73	1.5	−0.7, 3.8	0.178
Being in control of my life	9.2 ± 3.2	10.6 ± 3.5	9.2 ± 3.21	8.57 ± 4.26	1.7	−1.0, 4.5	0.208
Being spontaneous	6.5 ± 2.7	6.5 ± 2.7	6.67 ± 3.62	6.67 ± 3.62	1‡	−2.0, 4.0	0.430
Being treated as “normal”	9 ± 2.9	9.3 ± 4.1	9.4 ± 3.14	9.36 ± 4.29	0.5	−2.7, 3.7	0.750
Having confidence	9 ± 2.2	9.3 ± 3.3	8.2 ± 3.21	8.29 ± 4.1	−0.9	−2.8, 0.9	0.310

Data are means ± SD unless otherwise indicated. 780G − MDI, MiniMed 780G system − MDI+BGM. †ANCOVA with adjustment for baseline value. Once the significant interaction was confirmed we included it into the model. Mean difference is presented. ‡Wilcoxon rank sum test was applied when ANCOVA assumption was not met, and median difference is provided.

normal things (2.8 [95% CI 0.2; 5.4]; P = 0.0343).

Of interest, we found a significant correlation between TIR change and QoL score change in one area: eating as I would like (AHCL group: r = 0.56, P = 0.029).

CONCLUSIONS

To our knowledge this is the first randomized study with evaluation of the outcomes of automated insulin delivery system use in individuals with T1DM and no previous experience with CSII or CGM technologies. At the end of this two-center, randomized trial, TIR, as measured with CGM, was 21.5 percentage points higher among participants using the AHCL system compared with those in the MDI+BGM group. This TIR increase in the AHCL group was accompanied by an impressive 4.4% reduction in TBR (below 70 mg/dL) and a 9.4% reduction in CV, which is remarkable given the average glucose reduction was 15.4 mg/dL. These beneficial glycemic effects associated with the AHCL system were observed during both daytime and nighttime and were even more prominent during the night, when individuals are most vulnerable. Glycated hemoglobin level improved after 3 months in participants using the AHCL system and remained unchanged in people with diabetes on MDI therapy with BGM. Of note, our studied group was not just a random sample of people with T1DM; they represent a group of motivated individuals with well-controlled and relatively long-standing diabetes but free from advanced complications of the disease. This can also be considered as one of the limitations of the study, limiting its generalizability.

The TIR achieved by participants using the MiniMed 780G system in our study was higher than that reported in previous studies with use of the same AHCL technology. Collyns et al. (12) compared AHCL to predictive low glucose suspend (PLGS) technology and reported increased mean ± SD TIR with AHCL of 12.5 ± 8.5% (70.4 ± 8.1% vs. 57.9 ± 11.7%, $P < 0.001$). The population they evaluated was, however, more heterogenous and included children, adolescents, and adults. Carlson et al. (10) performed a single-arm study in 157 adolescents and

adults with T1DM in which they reported a TIR of 74.5 ± 6.9%. That was an increase from TIR of 68.8 ± 10.5% during the 14 day run-in phase in which the study participants used the MiniMed HCL system with either PLGS or HCL technology ($P < 0.001$). In an observational study, Beato-Víbora et al. (8) assessed 52 individuals with T1D who transitioned from the PLGS system to the MiniMed 780G system and reported a TIR increase from 67.3 ± 13.6% at baseline to 80.1 ± 7.5% at 3 months ($P = 0.001$). Of note, baseline TIR in this and other studies were slightly worse than the baseline TIR in our analysis (8,10,11,23). Schoelwer et al. (23) showed that higher baseline TIR is the strongest predictor of TIR on a closed-loop system. The TIR achieved by 4,120 MiniMed 780G users in real-world conditions was 76.2 ± 9.1%, as reported by Da Silva et al. (11). One has to underline, however, that in all comparisons of the outcomes of our study with those of trials published before, the fundamental difference in the baseline characteristics of the studied groups should be taken into consideration. Our study was the only one to include exclusively individuals who were naive to advanced technologies like CSII or CGM, with no lower restriction on HbA_{1c} levels at baseline.

There are several distinctions of the population studied. The group of adult subjects with T1DM (mean ± SD age 40.3 ± 8.0 years) had long experience of diabetes management (duration of diabetes 17.3 ± 12.1 years) with diabetes fairly well controlled at baseline, 7.2 ± 0.8% (55 ± 11 mmol/mol) HbA_{1c} (69.3 ± 12.3% TIR for the AHCL group), which is better than usually achieved with MDI therapy (23–25). These achievements at baseline also reflect the challenge in reaching glycemic goals with MDI, which is the large amount of time spent below range. It should be highlighted that the usage of AHCL was not only associated with additional reduction of HbA1c from a relatively good baseline toward the goal of <7% (53 mmol/mol) but also with the critical reduction of the TBR (from 8.7% ± 7.3 to 2.1% ± 1.7), while no effect on TBR was demonstrated in the control group. These results therefore can be generalized to whole populations of people with T1DM.

An important contributing factor to the achievement of 85% TIR in our study could have been the strict adherence to the predefined AHCL settings of AIT set to 2.0–2.5 h and glucose target set to 100 mg/dL. At initiation of the study, target blood glucose was set to 100 mg/dL for all patients; however, in the course of 3 months of the study, due to hypoglycemia concerns, it was increased for four patients (for three to 110 mg/dL and for one to 120 mg/dL). AIT was set, for most patients, to 2.5 h; however, it was later shortened (90% of the participants had AIT set to 2 h at the end of 3-month period). On the basis of our experience, it can be recommended to choose optimal settings of the MiniMed 780G system (target glucose 100 mg/dL, AIT 2 h) from the very beginning. The inbuilt algorithms provide safety mechanisms for the use of these settings. In a recent study of Da Silva et al. (11) only 50.3% of participants set glucose target to 100 mg/dL and 35.3% set AIT to 2 h (mean TIR 76.2%). In a study by Petrovski et al. (26), >90% of participants finished the study with the algorithm of glucose targets set to 100 mg/dL or 110 mg/dL with AIT from 2–3 h (TIR 80.2%, weeks 9–12). Finally, using only optimal algorithm settings, glucose target 100 mg/dL and AIT 2 h, was associated with TIR at 3 months 80.1% (8). The observed time on AHCL mode, exits from auto-mode per week, and time of sensor use were close to those observed in other AHCL studies (8,11,26). Another important factor could be the adjustment of the system carbohydrate ratio to provide more insulin per meals. These factors have been demonstrated to be associated with safe and higher achievement of glycemic control in previous clinical studies, which was also confirmed by the data from the real-world users of the system (10).

Finally, the fact that the participants were technology naive could have made them less prone to unnecessary intervention with the operation of the system, which, unlike conventional wisdom, might be associated with better outcomes in comparison with outcomes in those with prior experience with less advanced technologies. Patient-related outcomes should be part of the therapy goals, beyond optimization of metabolic parameters. Sense of psychological well-being and QoL (24,25,27) including physical and mental health, social relations, education, recreation and leisure, safety and freedom, sexual satisfaction, employment and financial status, and religious beliefs were assessed through validated questioner (28). Three months after AHCL initiation, the participants' overall adjusted QoL-Q Diabetes did not differ between the groups ($P = 0.287$) (Table 4). However, of the 23 areas describing QoL, the AHCL group reported an increase in 4 of the very essential ones in comparison with MDI+BGM group: feeling well, working, eating as I would like, and doing normal things. This indicates significantly higher scores for QoL in terms of professional functioning, freedom of eating, general well-being, and subjective feeling of no restrictions in daily activities in comparison with the MDI group. For none of the 23 areas analyzed was there a lower score in the AHCL group compared with the MDI+BGM group, which may indicate that the transition of people with T1DM from MDI+BGM directly to this MiniMed 780G AHCL system did not deteriorate the QoL of people with diabetes in any aspects.

The applied QoL-Q Diabetes questionnaire allowed for an exploratory analysis of various psychological areas and indicated an increase in several of them: feeling well, working, doing normal things, and eating as I would like. This can be linked to other positive aspects of the MiniMed 780G usage, like lower level of anxiety connected with possible hypo- and hyperglycemia, greater comfort in terms of insulin dosage and glucose control, much less painful punctures of the pads, less preoccupation with possible late complications, and greater subjective feeling that the diabetes is well managed and under control (29–31). The direct correlation between TIR and QoL in terms of eating indicates that while using the MiniMed 780G AHCL people with diabetes experienced major comfort improvement, gaining the subjective feeling of more freedom in their eating choices alongside more stable glycemic levels. A statistically significant correlation was not found between TIR and other aspects of QoL that significantly improved in the AHCL group.

These results indicate that transitioning from MDI+BGM treatment to AHCL may significantly improve the QoL and psychological well-being of the people with diabetes within only 3 months. The rapidity of these changes suggests that they may be related to the significant

improvement in glycemic outcomes obtained with AHCL treatment.

The major strength of our study is the unique, technology-naive, population who participated in the trial. We were able to show that not only that such a population may benefit from the direct switch to AHCL but also that the improvements in glucose-related diabetes management parameters may exceed those seen in other populations.

Our study has some limitations, one being that we did not include a random sample of people with diabetes. We can speculate that those who actively seek new opportunities for use of new technologies are more motivated to control their diabetes. Second, an imbalance in TIR between groups at baseline was observed. This was, however, addressed by the adjustments for the baseline values in all the between-groups comparisons.

Another limitation of our study was a relatively short, 3 months, follow-up period and intensive visit schedule. The sustainability of the glycemic outcomes observed in this initial 3 months will be evaluated in the extension phase of the study, which is currently being conducted, consisting of additional observation of 9 months.

Conclusion

The transition of adults with T1DM naive to technology, previously treated for a long time with MDI+BGM with relatively good glycemic control, directly to AHCL therapy was successful, allowing for significant TIR increase and TBR reduction. These individuals with a relatively long-diabetes duration, and probably no earlier exposure to advanced technologies, also have significantly improvement in the subjective feeling of life satisfaction and psychological well-being in terms of the impact of diabetes on essential life areas.

Funding. Medtronic supplied MiniMed 780G insulin pumps, Guardian 3 Link transmitters, Guardian Sensors 3, Transmitter Docks, and Accu-Check Guide Link glucometers.

Duality of Interest. The study was supported by Medtronic (ERP-2019-12000). B.M has received speakers honorarium from Ascensia, Roche, and Medtronic. K.C. has received speakers honorarium from Abbott and Ascensia. B.K.-W. has received speakers honorarium from Ascensia. A.J. has received speakers honorarium from Ascensia, Roche, Medtronic, Novo Nordisk, Eli Lily, Merck, and Boehringer Ingelheim. T.K. has received speakers honorarium from Eli Lilly, Sanofi, Novo Nordisk, Ascensia, Abbott, Roche, Medtronic, Boehringer Ingelheim, Bioton, and Servier; served on an advisory panel for Eli Lilly, Sanofi, Boehringer Ingelheim, Ascensia, and Abbott; and provided research support for Medtronic. M.T.M. has received speakers honorarium from Eli Lilly, Sanofi, Novo Nordisk, Ascensia, Abbott, Roche, Medtronic, Boehringer Ingelheim, Bioton, and Servier and served on an advisory panel for Eli Lilly, Sanofi, Boehringer Ingelheim, Ascensia, and Abbott. J.D.S. and O.C. are employees of Medtronic. No other potential conflicts of interest relevant to this article were reported.

Author Contributions. B.M., A.J., B.K.-W., K.C., S.K., and T.K. researched data. B.M., K.C., and T.K. wrote the manuscript and researched data. B.M., O.C., J.D.S., M.T.M., and T.K. contributed to the discussion and reviewed and edited the manuscript. T.K. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Prior Presentation. Parts of this study were presented in poster form and in a lecture at the 15th International Conference on Advanced Technologies & Treatments for Diabetes (ATTD 2022), 27–30 April 2022, Barcelona, Spain.

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