DIABETES TECHNOLOGY & THERAPEUTICS
Volume 22, Number 6, 2020

DOI: 10.1089/dia.2019.0400

ORIGINAL ARTICLE

Prospective Analysis of the Impact of Commercialized Hybrid Closed-Loop System on Glycemic Control, Glycemic Variability, and Patient-Related Outcomes in Children and Adults: A Focus on Superiority Over Predictive Low-Glucose Suspend Technology

Pilar Isabel Beato-Víbora, PhD,[1] Fabiola Gallego-Gamero, MD,[1] Lucía Lázaro-Martín, MD,[1] Maria del Mar Romero-Pérez, MD,[2] and Francisco Javier Arroyo-Díez, PhD[3]

Abstract

Background: Automatization of insulin delivery by closed-loop systems represents a major step in type 1 diabetes management. The aim of this study was to analyze the effect of the commercialized hybrid closed-loop system, the MiniMed 670G system, on glycemic control, glycemic variability, and patient satisfaction.
Methods: A prospective study, including type 1 diabetes patients consecutively starting on the 670G system in one adult and two pediatric hospitals, was performed. Baseline and 3-month visits were documented. Two weeks of data from the system were downloaded. Glycemic variability measures were calculated. Adults and adolescents completed a set of questionnaires (Gold and Clarke scores, Hypoglycemia Fear Survey, Diabetes Quality of Life [DQoL], Diabetes Treatment Satisfaction [DTS], Diabetes Distress Scale, Pittsburgh Sleep Quality Index).
Results: Fifty-eight patients were included (age: 28 ± 15 years [7–63], <18 years old: 38% [$n = 22$], 59% [$n = 34$] females, previous use of SAP-PLGS [predictive low-glucose suspend]: 60% [$n = 35$]). HbA1c was reduced from 57 ± 10 to 53 ± 7 mmol/L ($7.4\% \pm 0.9\%$ to $7.0\% \pm 0.6\%$) ($P < 0.001$) and time in range 70–180 mg/dL was increased from $63.0\% \pm 11.4\%$ to $72.7\% \pm 8.7\%$ ($P < 0.001$). In patients with high baseline hypoglycemia risk, time <54 and <70 mg/dL were reduced from $0.9\% \pm 1.1\%$ to $0.45\% \pm 0.7\%$ ($P = 0.021$) and from $3.3\% \pm 2.8\%$ to $2.1\% \pm 2.1\%$ ($P = 0.019$), respectively. Glycemic variability measures improved. Time in auto mode was $85\% \pm 17\%$, the number of auto mode exits was 0.6 ± 0.3 per day, and the number of alarms was 8.5 ± 3.7 per day. Fear of hypoglycemia, DQoL, DTS, and diabetes distress improved, while the percentage of patients with poor sleep quality was reduced. The discontinuation rate was 3%.
Conclusion: The commercialized hybrid closed-loop system improves glycemic control and glycemic variability in children and adults, reducing the burden of living with type 1 diabetes.

Keywords: Type 1 diabetes, Hybrid closed-loop system, Sensor-augmented pump therapy, Continuous glucose monitoring, Hypoglycemia.

[1]Endocrinology and Nutrition Department, Badajoz University Hospital, Badajoz, Spain.
[2]Paediatrics Department, Virgen de Macarena Hospital, Sevilla, Spain.
[3]Paediatrics Department, Materno-Infantil Hospital, Badajoz, Spain.

Introduction

Type 1 diabetes is a chronic disease that requires exogenous insulin for its treatment. Insulin requirements are constantly changing in type 1 diabetes patients, depending on multiple factors. Continuous subcutaneous insulin infusion, continuous glucose monitoring (CGM), and sensor-augmented pumps (SAP), with different levels of automatization (low-glucose suspend [LGS] function and predictive low-glucose suspend [PLGS] function), have been shown to improve glycemic control in randomized control trials and real-world studies.[1–5]

Closed-loop systems represent an evolutionary step toward the goal of achieving normoglycemia.[6,7] In these systems, an insulin pump automatically delivers insulin depending on sensor data gathered by a CGM device. An algorithm connects both devices, adjusting the amount of insulin delivered every few minutes. The first closed-loop system, the Medtronic MiniMed 670G system, was approved in the United States in August 2016 and Europe in June 2018. This system operates in auto mode (closed-loop) but exits to manual mode (open-loop) in certain circumstances. The pivotal trial before the commercial launch in the United States had shown a reduction in HbA1c of 5 mmol/L (0.5%) and an increase in time in range (TIR) 70–180 mg/dL of 5.5%.[8,9] Subsequent prospective and retrospective analyses of the use of the 670G system in the United States have shown similar or better results, with improvements in HbA1c between 5 and 8 mmol/L (0.5%–0.7%) and improvements in TIR 70–180 mg/dL ranging from 4% to 14%.[10–14]

The aim of the study was to evaluate the outcomes of the commercialized hybrid closed-loop system in children and adults with type 1 diabetes following its commercialization in Europe.

Materials and Methods

Patients who were consecutively starting the use of the hybrid closed-loop system, Medtronic MiniMed 670G, were evaluated in a prospective longitudinal design study. A standardized education program was administered to all the patients in the three centers, including two to three sessions (4 h each session) for previous pump users and four to five sessions (4 h each session) for patients previously on multiple daily injections (MDIs). Baseline and 3-month follow-up visits were programmed. The baseline visit was the day of auto mode start, after 2 weeks of use of the system in manual mode with PLGS activated. This period was the time used for the initialization of the system. The 3-month visit took place 3 months after the auto mode start. In both cases, 2 weeks of data were downloaded from the system

At each visit, point-of-care HbA1c, measured by Afinion™ AS100, was collected. Two weeks of data from the system were downloaded. TIR 70–180 mg/dL and time >180, >250, <70. and <54 mg/dL were documented. Glycemic variability measures were calculated from sensor data using the EasyGV® software.[15] Adolescents older than 13 years old and adults completed a set of questionnaires: Gold and Clarke scores to evaluate hypoglycemia awareness, Hypoglycemia Fear Survey (HFS) with behavior and worry subscales, Diabetes Quality of Life (DQoL), Diabetes Treatment Satisfaction (DTS), Diabetes Distress Scale (DDS), and Pittsburgh Sleep Quality Index. The pumps were uploaded, and data reviewed with the participants, during a clinical visit scheduled 3–4 weeks after auto mode start.

Data analysis was conducted using SPSS statistics software v22. Results are presented as mean ± standard deviation values or median (interquartile range [IQR]). A paired Student's *t*-test was used for the analysis of differences. For unpaired samples, the independent samples *t*-test was used. Comparisons between proportions were analyzed by a chi-squared test. A *P*-value <0.05 was considered statistically significant. The study was approved by the local research ethics committees.

Results

Fifty-eight patients participated in the study. Demographic characteristics are shown in Table 1. The age range was from 7 to 63 years old. For previous SAP-PLGS users ($n = 35$), the median time on SAP-PLGS was 3.2 years [1.7–3.7]. For previous pump+SMBG (self-monitoring of blood glucose) users ($n = 11$), the median time on pump was 2.5 years [3.3–4.1]. Patients on CGM+MDI before starting 670G ($n = 5$) had been using CGM for a median time of 1 year.

Glycemic control and glycemic variability

The changes in HbA1c and time in different glycemic ranges are shown in Table 2. The percentage of patients with HbA1c ≤63 mmol/L (7%) increased from 31% to 53% ($P < 0.001$) at the 3-month follow-up visit. The change in HbA1c was significantly different in patients with baseline HbA1c ≤53 mmol/L (7%) ($n = 18$), mean difference: −1 mmol/L, 95 CI: −1 to 4 (0.1%, 95 CI: −0.1 to 0.4) than in patients with baseline HbA1c between 53 mmol/L (7%) and 64 mmol/L (8%) ($n = 26$): mean difference: −4 mmol/L, 95 CI: −7 to −2 (−0.4%, 95 CI: −0.6 to −0.2), and patients with baseline HbA1c >64 mmol/L (8%) ($n = 14$): mean difference: −12 mmol/L, 95 CI: −16 to −8 (−1.1% [95 CI: −1.5 to −0.8]), $P < 0.001$. The percentage of patients with TIR 70–180 mg/dL >70% increased from 21% at baseline to 60% at the 3-month visit ($P = 0.013$). No episodes of severe hypoglycemia or diabetic ketoacidosis were observed during follow-up.

In patients considered with high baseline risk for hypoglycemia (baseline time <70 mg/dL >4% or baseline time

Table 1. Demographic Characteristics

Age, years	28 ± 15
Children and adolescents (<18 years old), % (*n*)	38 (22)
Gender (female), % (*n*)	59 (34)
Diabetes duration, years	15 ± 9
Previous treatment	
SAP-PLGS, % (*n*)	60 (35)
Pump+SMBG, % (*n*)	19 (11)
MDI+SMBG, % (*n*)	12 (7)
MDI+CGM, % (*n*)	9 (5)

$N = 58$. Data are expressed as mean ± standard deviation unless otherwise indicated.

CGM, continuous glucose monitoring; MDI, multiple daily insulin injections; SAP-PLGS, sensor-augmented pump with predictive low-glucose suspend feature; SMBG, self-monitoring of blood glucose.

Table 2. Glycemic Control, Use of the System, and Glycemic Variability

	Baseline, mean ± SD	*3 Months, mean ± SD*	*Mean diff (SE)*	*95% CI*	t	P
Glycemic control						
HbA1c, mmol/L, %	57 ± 10 7.4 ± 0.9	53 ± 7 7.0 ± 0.6	−4 (1) −0.4 (0.1)	−4 to −7 −0.2 to −0.6	4.558	**<0.001**
Estimated HbA1c, mmol/L, %	56 ± 8 7.3 ± 0.7	52 ± 4 6.9 ± 0.4	−4 (1) −0.4 (0.1)	−2 to −5 −0.2 to −0.5	5.207	**<0.001**
Sensor glucose, mg/dL	163 ± 19	153 ± 12	−10 (2.1)	−6 to −14	4.999	**<0.001**
TIR 70–180 mg/dL, %	63.0 ± 11.4	72.7 ± 8.7	9.7 (1.1)	12.1 to 7.3	−8.127	**<0.001**
Time >180 mg/dL, %	34.7 ± 12.1	25.4 ± 9.0	−9.3 (1.3)	−6.8 to −11.8	7.473	**<0.001**
Time >250 mg/dL, %	8.8 ± 6.4	5.1 ± 3.7	−3.8 (0.7)	−2.3 to −5.2	5.319	**<0.001**
Time <70 mg/dL, %	2.5 ± 2.4	2.0 ± 1.8	−0.5 (0.3)	−0.2 to 1.1	1.440	0.155
Time <54 mg/dL, %	0.59 ± 0.86	0.41 ± 0.70	−0.17 (0.1)	−0.1 to 0.4	1.427	0.159
Glycemic variability						
SD of glucose, mg/dL	57 ± 11	50 ± 9	−7 (1.2)	−5 to −10	5.823	**<0.001**
CV, %	35 ± 4	33 ± 4	−2 (0.6)	−1 to −3	3.544	**0.001**
MAGE, mg/dL	117 ± 25	102 ± 21	−15 (3.1)	−9 to −21	4.906	**<0.001**
CONGA1	141 ± 17	129 ± 12	−11 (2.0)	−7 to −15	5.797	**<0.001**
MODD	60 ± 12	50 ± 10	−9 (1.5)	−6 to −12	6.318	**<0.001**
ADRR	527 ± 34	508 ± 28	−19 (3.5)	−12 to −26	5.386	**<0.001**

Bold values mean significant difference.
$n = 58$. Data are expressed as mean ± standard deviation or mean difference (standard error).
CI, confidence interval; TIR, time in range.

<54 mg/dL >1%, or impaired awareness of hypoglycemia [Gold Score or Clarke Score >3]) ($n = 29$), time in hypoglycemia range was significantly reduced at 3 months compared with baseline (time <54 mg/dL: 0.45% ± 0.7% vs. 0.9% ± 1.1%, $P = 0.021$, time <70 mg/dL: 2.1% ± 2.1% vs. 3.3% ± 2.8%), $P = 0.019$, and HbA1c improved from 60 ± 11 to 54 ± 8 mmol/L (7.6% ± 1.0% to 7.1% ± 0.7%), $P = 0.001$.

In the group of patients using 640G system with PLGS before 670G ($n = 35$), HbA1c improved from 56 ± 9 to 53 ± 5 mmol/L (7.3% ± 0.8% to 7.0% ± 0.5%), $P = 0.004$, and TIR 70–180 mg/dL was increased from 63% ± 13% to 73% ± 10%, $P < 0.001$. In this group of patients, time in hypoglycemia was not significantly different after 3 months of 670G system use compared with baseline: time <54 mg/dL: 0.49% ± 0.8% versus 0.63% ± 0.9% ($P = 0.406$), time <70 mg/dL: 2.2% ± 1.9% versus 2.5% ± 2.5% ($P = 0.563$). Improvement in TIR 70–180 mg/dL was not different in previous SAP-PLGS users compared with nonusers (10% ± 9% vs. 9% ± 10%, $P = 0.574$). The reduction in HbA1c was also not significantly different in previous SAP-PLGS users compared with nonusers ($P = 0.174$).

Also, previous pump users ($n = 46$) had similar improvement in TIR 70–180 mg/dL to patients previously on MDIs ($n = 12$): 10 ± 8 versus 9 ± 13, $P = 0.686$. Likewise, previous CGM users ($n = 40$) had similar improvement in TIR 70–180 mg/dL compared with nonusers ($n = 18$): 11% ± 9% versus 7% ± 9%, $P = 0.155$.

End of follow-up HbA1c was significantly higher in children compared with adults: 56 ± 8 mmol/L versus 52 ± 5 mmol/L (7.3% ± 0.7% vs. 6.9% ± 0.5%), $P = 0.028$. However, the improvement in TIR 70–180 mg/dL was not different in children compared with adults (12% ± 8% vs. 8% ± 9%, $P = 0.099$). Similarly, the use of faster aspart insulin in the system ($n = 21$) did not affect the change in TIR 70–180 mg/dL compared with lispro insulin or aspart insulin (8% ± 10% vs. 11% ± 10%, $P = 0.405$). No differences in time in hypoglycemia <54 or <70 mg/dL were found in patients using faster aspart in the system compared with patients using lispro or aspart insulin, either. Total daily dose and programmed carbohydrate:insulin ratios in any of the meals were not different between those two groups. Bolus insulin was lower in patients using faster aspart insulin compared with patients using lispro or aspart insulin (46.0% ± 6.5% vs. 52.5% ± 10.5%, $P = 0.018$). The frequency of use of faster aspart was similar in adults compared with children ($P = 0.143$). The frequency of infusion set issues or frequency of infusion set changes was not specifically recorded.

The coefficient of variation of the total insulin delivered by the system at the 3-month visit was 15% ± 4%, and it was similar in adults compared with children. A significant negative correlation was found between the coefficient of variation of basal insulin delivery at 3 months and the improvement achieved in TIR 70–180 mg/dL ($r = -0.351$, $P = 0.008$).

In a multivariate regression analysis, including age and diabetes duration as independent variables, baseline HbA1c, and baseline TIR 70–180 mg/dL were the only significant predictors of improvement in TIR 70–180 mg/dL ($\beta = 5.9$, 95% CI: 2.9–9.0; $P < 0.001$, and $\beta = 0.5$, 95% CI: 0.2–0.8; $P = 0.001$, respectively).

Use of the system

At the 3-month follow-up visit, auto mode was enabled for 85% ± 17% (median [IQR]: 90% [79%–97%]) of the time. A correlation between time in auto mode and TIR 70–180 mg/dL was found ($r = 0.272$, $P = 0.039$). This correlation was significant for the whole group, but not when adults and children were analyzed separately.''

The number of exits from auto mode to manual mode was 4 ± 2 per patient per week (0.6 ± 0.3 per patient per day). Seventeen percent of the exits had an unidentified reason. Sensor issues caused the majority of explained exits (39%),

followed by prolonged hyperglycemia (23%), auto mode disabled by user (16%), and maximum or minimum insulin delivery (13%). The frequency of exit reasons is shown in Figure 1. The number of times the auto mode exit was initiated by the user was not different in previous SAP-PLGS users or previous pump users compared with nonusers.

Sensor use was not significantly different at 3 months compared with baseline (86% ± 13% vs. 85% ± 13%, $P = 0.741$). CGM use before closed-loop initiation did not affect sensor use at 3 months.

The number of alarms per day received by the patient was 8.5 ± 3.7 (3–17), and the number of SMBG performed was 7 ± 2 per day (3–15). The frequency of alarms was not different in adults compared with children (7.9 ± 3.3 vs. 9.6 ± 4.3, $P = 0.108$), and there was no significant correlation between the frequency of alarms and the age of the participants.

Regarding insulin requirements, basal insulin increased from 48% ± 11% to 51% ± 9% ($P = 0.042$). Total daily insulin dose remained unchanged [0.7 ± 0.2 U/(kg·day), 44 ± 14 U/day]. The amount of carbohydrate entered in the system did not change significantly during follow-up (162 ± 52 g/day at baseline to 154 ± 65 g/day at the 3-month visit; $P = 0.277$). The carbohydrate to insulin ratios programmed decreased from baseline to end of follow-up for all meals: from 8.5 ± 3.5 to 8.1 ± 3.0 g per unit ($P = 0.016$) for breakfast, from 9.0 ± 3.0 to 8.6 ± 2.8 g per unit ($P = 0.005$) for lunch, and from 9.8 ± 4.2 to 9.1 ± 3.5 g per unit ($P = 0.002$) for dinner.

Patient-related outcomes

The changes in impaired awareness of hypoglycemia frequency and the scores in the different questionnaires are shown in Table 3. HFS score was reduced, both in worry and behavior scales. DQoL, DTS, and DDS scores improved. Sleep quality was improved from 49% of ''poor sleepers'' to 40% at the 3-month follow-up visit ($P = 0.004$).

Discontinuation rate was 3% ($n = 2$). One of the patients (male, 49 years old, previous treatment: MDI+SMBG) stopped using the system after 2 months because he felt uncomfortable wearing a pump. The second patient (female, 40 years old, previous SAP-PLGS user) stopped using the system after 4 months and went back to SAP-PLGS because of a persistent hyperglycemia pattern in the evenings. The rest of the patients ($n = 56$) expressed their desire to keep using the system.

The main outcomes regarding glycemic control, glycemic variability, and patient-related outcomes in the four subgroups of treatment prior 670G start are summarized in Figure 2.

Discussion

The improvement in glycemic control achieved in our patients was similar to the improvement found in the pivotal study and subsequent analyses of the MiniMed 670G system use, with a reduction in HbA1c between 4 and 5 mmol/L (0.4%–0.5%).[8,9,12,13] Also, this benefit was highly related to baseline glycemic control, being the patients with the highest baseline HbA1c who obtained a greater benefit.[12,14] Also, the benefit was similar in previous CGM users than in non-CGM users, as previously reported.[16] The improvement in TIR 70–180 mg/dL in our data was 9.7%, greater than that reported in the pivotal study and in subsequent prospective and retrospective analysis in adults and children.[8,9,11,12,14]

The experience with the 670G system in the United States comes from patients previously using MDIs with or without

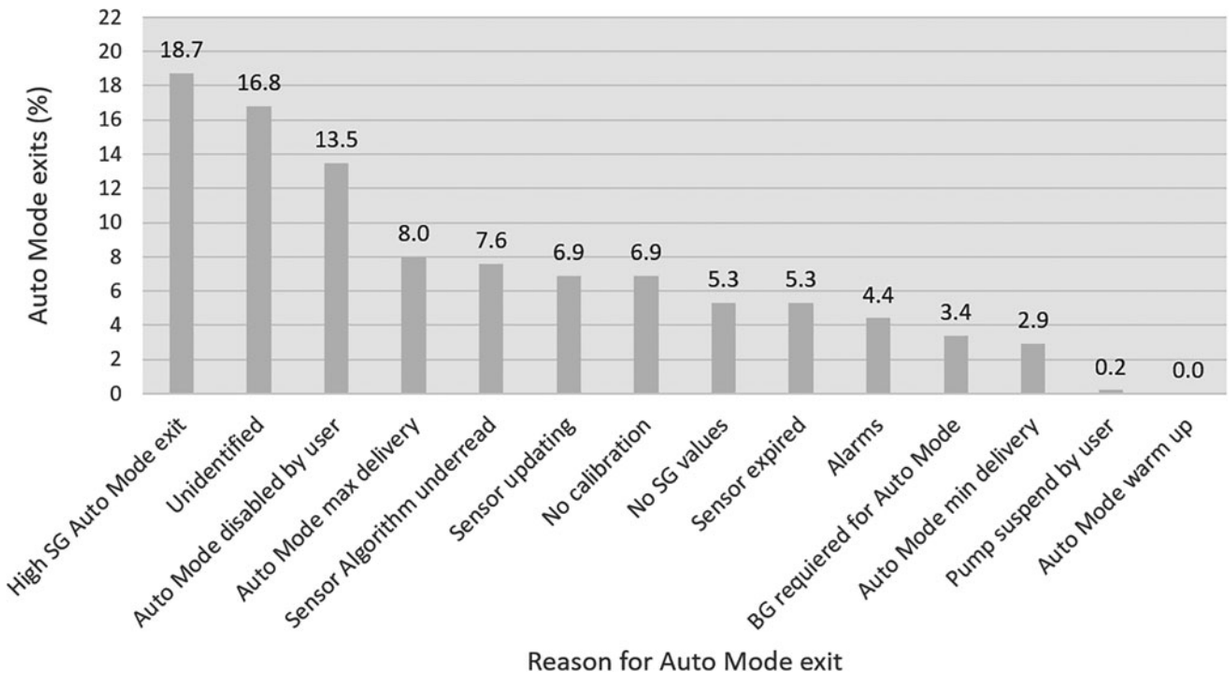

FIG. 1. Frequency of reasons for auto mode exit.

Table 3. Patient-Related Outcomes

	Baseline, mean ± SD	*3 Months, mean ± SD*	*Mean diff (SE)*	t	P
Hypoglycemia unawareness (Gold Score or Clarke Score >3), %	37	27	10	—	0.001
Clarke score	2.4 ± 1.8	1.9 ± 1.5	0.5 (0.2)	2.354	0.023
HFS	41 ± 23	31 ± 18	9.5 (3.2)	2.971	0.005
HFS behavior	16 ± 9	13 ± 8	3 (1.3)	2.343	0.024
HFS worry	24 ± 17	18 ± 12	5.8 (2.3)	2.526	0.016
DQoL	87 ± 22	78 ± 18	9.0 (2.1)	4.306	<0.001
DTS	29 ± 7	31 ± 4	–2. (0.9)	–2.154	0.037
DDS	40 ± 19	34 ± 16	5.1 (1.6)	3.258	0.002
PSQI >5 (poor sleep quality) (%)	49	40	9	—	0.004

$n = 51$ (only patients ≥13 years old). Data are expressed as mean ± standard deviation or mean difference (standard error), unless otherwise indicated. Lower scores indicating less fear of hypoglycemia (HFS), a better quality of life (DQoL), less satisfaction (DTS), and less diabetes distress (DDS).

DDS, Diabetes Distress Scale; DQoL, Diabetes Quality of Life; DTS, Diabetes Treatment Satisfaction; HFS, Hypoglycemia Fear Survey; PSQI, Pittsburgh Sleep Quality Index.

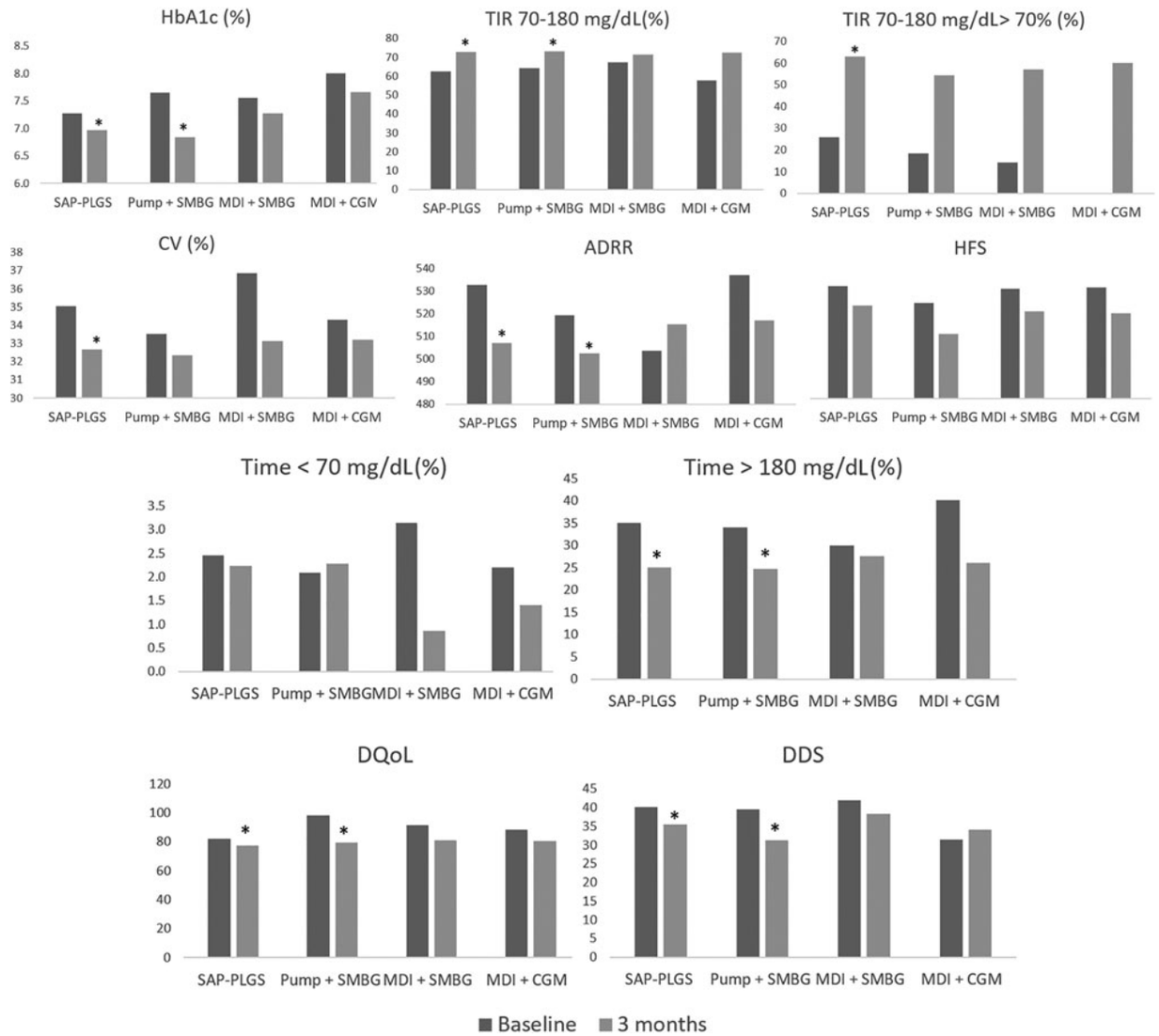

FIG. 2. Glycemic control, glycemic variability, and patient-related outcomes in the four subgroups of treatment prior 670G start: SAP-PLGS ($n = 35$), Pump+SMBG % ($n = 11$), MDI+SMBG ($n = 7$), MDI+CGM ($n = 5$).*$P < 0.005$ to baseline. CGM, continuous glucose monitoring; PLGS, predictive low-glucose suspend; SAP, sensor-augmented pumps; SMBG, self-monitoring of blood glucose.

CGM, or pumps with or without CGM. When SAP was used, the only automatic feature was the threshold suspend, equivalent to the LGS feature, as the PLGS feature had only been commercialized outside the United States. Indeed, in the pivotal study, during the warm-up period, the 670 system was used in manual mode with the automatic features off.[8] In contrast, in our study, 60% of the patients were experienced users of SAP-PLGS, and during the initialization period (which was used as the baseline period), the PLGS feature was activated in all the patients. It is likely that only a short period of time, such as 2 weeks, is not enough time for the patients to optimize the use of the SAP system, so some of the benefits of the hybrid closed-loop system in the pivotal trial could be attributed to the sensor and pump integration.[17] Our data answer that question, as in the group of patients with previous use of SAP-PLGS, the outcomes were similar in TIR 70–180 mg/dL and in HbA1c improvement to the non-SAP-PLGS users. Recently, a retrospective analysis in a smaller group of patients in Italy has shown similar results.[18]

It has been reported that patients with high variability in insulin requirements could benefit more from closed-loop systems.[19] We found a negative correlation between the coefficient of variation of basal insulin delivery (%) and the improvement in TIR 70–180 mg/dL. This could be interpreted as these highly variable insulin requirements representing a greater challenge to the algorithm.

A reduction in glycemic excursions is one of the main goals of diabetes management. A reduction in the coefficient of variation of glucose with 670G has been previously reported.[8,12] We showed that in patients with diabetes already considered to be stable (CV <36%),[20] a further reduction in glycemic variability could be achieved.

The time in auto mode in our patients (median: 90%) was higher than previously reported[8,11,12] (median from 81% to 87%), which explains the favorable glycemic outcomes in our patients. The total insulin dose has been reported to increase[8,9,11] or to remain unchanged.[10,12,14] In our patients, the total insulin dose remained unchanged, but the percentage of basal insulin increased significantly. The number of alarms is not quantified in the Carelink™ report, so we manually counted the alarm icons in the Carelink daily reports to obtain a quantitative impression on how often the system was requiring patient intervention. A better glycemic control should reduce the number of high and low blood glucose alarms, but on the contrary, the patients must respond to the alarms prompted by the system to stay in auto mode. Regarding the reasons for auto mode exit, prolonged hyperglycemia was the reason for auto mode exit in 18.7% of the exits and maximum insulin delivery in 8% of the exits. Any of them could be explained by missed or delayed meal boluses.

Hypoglycemia reduction is not consistent in all the previous studies, being reduced in some reports[8,11] but not in others.[13,14] In our patients, hypoglycemia was not reduced in the whole cohort, in which baseline hypoglycemia frequency was already low, according to international consensus.[21] Nevertheless, similarly to previous reports with other hybrid closed-loop systems,[22] in the subgroup of patients with high hypoglycemia frequency and risk, from our cohort, the frequency of hypoglycemia was reduced and HbA1c also was reduced. Interestingly, hypoglycemia fear, both in worry and behavior subscales, was reduced in the whole cohort, reflecting the feeling of safety generated by the automated insulin infusion.

The effect of closed-loop systems on psychosocial outcomes, and specifically on sleep quality, has been evaluated with different results.[23–30] In our analysis, the percentage of patients with poor sleep quality was reduced from 49% to 40%, meaning that better glycemic control and less glycemic variability have a positive impact on sleep quality and counteract the negative effect of the system alarms and the finger stick requirements generated by the system. Similarly, quality of life, DTS, and diabetes distress improved after 3 months of hybrid closed-loop system use, reflecting an overall positive balance between technology overload, on one hand, and better glycemic outcomes with less diabetes burden, on the other hand. We had previously analyzed the changes in glycemic control, glycemic variability, and patient satisfaction, including sleep quality, in a cohort of patients upgrading from SAP-LGS to SAP-PLGS.[31] From the present data, we can state that the use of the MiniMed 670G system appears to be a further step on the path to optimal diabetes management.

Grando et al.[23] have reported a high level of satisfaction in 670G users. On the contrary, a high discontinuation rate, 33%, has been reported in a 1-year prospective observational study in the United States.[32] In our group of patients, the discontinuation rate was low and most of the patients considered that the system lessened the burden of diabetes management and wanted to continue using it. It could be hypothesized that a more recent generation of the system has been an advantage to the European users.

Regarding the training for the use of the system, the substantial education time provided to the participants could have had an impact on the results and explain, in part, the difference in maintaining auto mode and the improvement in TIR 70–180 mg/dL, compared with previous reports. Nevertheless, in the three participant centers, 16–20 h of training are delivered as part of the routine training program for SAP (16 h for pump training and 4 h for sensor training), and so, there was no additional training time for this study compared with standard of care in our centers.

The main strengths of the study are the broad age range of patients included, between 7 and 63 years, as well as the prospective and multicenter study design. Particularly, the use of the same educational program in the three hospitals is a major strength. Also, the analysis of patient-related outcomes, including impaired awareness of hypoglycemia, fear of hypoglycemia, patient satisfaction, diabetes distress, and, especially, quality of life and quality of sleep, adds information to the role of the hybrid closed-loop systems in diabetes management. In addition, we specifically prospectively addressed the outcomes in the group of experienced SAP-PLGS users, which has not previously been reported to the best of our knowledge.

Our study also has several limitations. First, no blind CGM was used neither at baseline nor at the 3-month follow-up visit. Second, we did not include a control group not using 670G, so each patient acts as his or her own control. Also, daytime and nighttime were not analyzed separately and a cost evaluation was not performed.

In conclusion, the use of hybrid closed-loop systems improves glycemic control, reduces glycemic variability, and ameliorates diabetes burden in children and adults with type 1 diabetes.

Author Disclosure Statement

No competing financial interests exist.

Funding Information

No funding was received

References

1. Pickup JC, Sutton AJ: Severe hypoglycaemia and glycaemic control in type 1 diabetes: meta-analysis of multiple daily insulin injections compared with continuous subcutaneous insulin infusion. Diabet Med 2008;25:765–774.
2. Beato-Víbora P, Yeoh E, Rogers H, et al.: Sustained benefit of continuous subcutaneous insulin infusion on glycaemic control and hypoglycaemia in adults with type 1 diabetes. Diabet Med 2015;32:1453–1459.
3. Abraham MB, Nicholas JA, Smith GJ, et al.: Reduction in hypoglycemia with the Predictive Low-Glucose Management System: a long-term randomized controlled trial in adolescents with type 1 diabetes. Diabetes Care 2018;41:303–310.
4. Beato-Víbora PI, Quirós-López C, Lázaro-Martín L, et al.: Impact of sensor-augmented pump therapy with predictive low-glucose suspend function on glycemic control and patient satisfaction in adults and children with type 1 diabetes. Diabetes Technol Ther 2018;20:738–743.
5. Beato-Víbora P, Chico-Ballesteros A, Giménez M, et al.: A national survey on the efficacy and safety of continuous subcutaneous insulin infusion in patients with type 1 diabetes in Spain. Diabetes Res Clin Pract 2018;137:56–63.
6. Weisman A, Bai JW, Cardinez M, et al.: Effect of artificial pancreas systems on glycaemic control in patients with type 1 diabetes: a systematic review and meta-analysis of outpatient randomised controlled trials. Lancet Diabetes Endocrinol 2017;5:501–512.
7. Bekiari E, Kitsios K, Thabit H, et al.: Artificial pancreas treatment for outpatients with type 1 diabetes: systematic review and meta-analysis. BMJ 2018;361:k1310.
8. Garg SK, Weinzimer SA, Tamborlane WV, et al.: Glucose outcomes with the in-home use of a hybrid closed-loop insulin delivery system in adolescents and adults with type 1 diabetes. Diabetes Technol Ther 2017;19:155–163.
9. Bergenstal RM, Garg S, Weinzimer SA, et al.: Safety of a hybrid closed-loop insulin delivery system in patients with type 1 diabetes. JAMA 2016;316:1407–1408.
10. Messer LH, Forlenza GP, Sherr JL, et al.: Optimizing hybrid closed-loop therapy in adolescents and emerging adults using the MiniMed 670G system. Diabetes Care 2018;41:789–796.
11. Stone MP, Agrawal P, Chen X, et al.: Retrospective analysis of 3-month real-world glucose data after the MiniMed 670G system commercial launch. Diabetes Technol Ther 2018;20:689–692.
12. Forlenza GP, Pinhas-Hamiel O, Liljenquist DR, et al.: Safety evaluation of the MiniMed 670G system in children 7–13 Years of age with type 1 diabetes. Diabetes Technol Ther 2019;21:11–19.
13. Salehi P, Roberts AJ, Kim GJ: Efficacy and safety of real-life usage of MiniMed 670G automode in children with type 1 diabetes less than 7 years old. Diabetes Technol Ther 2019;21:448–451.
14. Faulds ER, Zappe J, Dungan KM: Real-world implications of hybrid close loop (HCL) insulin delivery. Endocr Pract 2019;25:477–484.
15. Hill NR, Oliver NS, Choudhary P, et al.: Normal reference range for mean tissue glucose and glycemic variability derived from continuous glucose monitoring for subjects without diabetes in different ethnic groups. Diabetes Technol Ther 2011;13:921–928.
16. Cordero TL, Garg SK, Brazg R, et al.: The effect of prior continuous glucose monitoring use on glycemic outcomes in the pivotal trial of the MiniMed(™) 670G hybrid closed-loop system. Diabetes Technol Ther 2017;19:749–775.
17. Castle JR: Will the first approved automated insulin delivery system be a game-changer in type 1 diabetes management? Diabetes Technol Ther 2017;19:137–139.
18. Lepore G, Scaranna C, Corsi A, et al.: Switching from suspend-before-low insulin pump technology to a hybrid closed loop system improves glucose control and reduces glucose variability: a retrospective observational case-control study. Diabetes Technol Ther 2019. [Epub ahead of print]; DOI: 10.1089/dia.2019.0302.
19. Dovc K, Boughton C, Tauschmann M, et al.: Young children have higher variability of insulin requirements: observations during hybrid closed-loop insulin delivery. Diabetes Care 2019;42:1344–1347.
20. Danne T, Nimri R, Battelino T, et al.: International consensus on use of continuous glucose monitoring. Diabetes Care 2017;40:1631–1640.
21. Battelino T, Danne T, Bergenstal RM, et al.: Clinical targets for continuous glucose monitoring data interpretation: recommendations from the International Consensus on Time in Range. Diabetes Care 2019;42:1593–1603.
22. Anderson SM, Buckingham BA, Breton MD, et al.: Hybrid closed-loop control is safe and effective for people with type 1 diabetes who are at moderate to high risk for hypoglycemia. Diabetes Technol Ther 2019;21:356–363.
23. Grando MA, Bayuk M, Karway G, et al.: Patient perception and satisfaction with insulin pump system: pilot user experience survey. J Diabetes Sci Technol 2019;13:1142–1148.
24. Barnard KD, Wysocki T, Thabit H, et al.: Psychosocial aspects of closed- and open-loop insulin delivery: closing the loop in adults with type 1 diabetes in the home setting. Diabet Med 2015;32:601–608.
25. Musolino G, Dovc K, Boughton CK, et al.: Reduced burden of diabetes and improved quality of life: experiences from unrestricted day-and-night hybrid closed-loop use in very young children with type 1 diabetes. Pediatr Diabetes 2019;20:794–799.
26. Muñoz Muñoz-Velandia O, Guyatt G, Devji T, et al.: Patient values and preferences regarding continuous subcutaneous insulin infusion and artificial pancreas in adults with type 1 diabetes: a systematic review of quantitative and qualitative data. Diabetes Technol Ther 2019;21:183–200.
27. Lawton J, Blackburn M, Rankin D, et al.: Participants' experiences of, and views about, daytime use of a day-and-night hybrid closed-loop system in real life settings: longitudinal qualitative study. Diabetes Technol Ther 2019;21:119–127.
28. Adams RN, Tanenbaum ML, Hanes SJ, et al.: Psychosocial and human factors during a trial of a hybrid closed loop system for type 1 diabetes management. Diabetes Technol Ther 2018;20:648–653.
29. Weissberg-Benchell J, Hessler D, Fisher L, et al.: Impact of an automated bihormonal delivery system on psychosocial

outcomes in adults with type 1 diabetes. Diabetes Technol Ther 2017;19:723–729.
30. Barnard KD, Wysocki T, Ully V, et al.: Closing the loop in adults, children and adolescents with suboptimally controlled type 1 diabetes under free living conditions: a psychosocial substudy. J Diabetes Sci Technol 2017;11: 1080–1088.
31. Beato-Víbora PI, Gil-Poch E, Galán-Bueno L, et al.: The incremental benefits of the predictive low-glucose suspend function compared to the low-glucose suspend function as automation against hypoglycemia in sensor-augmented pump therapy. J Diabetes Sci Technol 2018;12:1241–1243.
32. Lal RA, Basina M, Maahs DM, et al.: One year clinical experience of the first commercial hybrid closed-loop. Diabetes Care 2019;42:2190–2196.

Address correspondence to:
Pilar Isabel Beato-Víbora, PhD
Endocrinology and Nutrition Department
Badajoz University Hospital
Avda. Elvas s/n
Badajoz 06006
Spain

E-mail: pilar.beato@salud-juntaex.es