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Virtual training on the hybrid close loop system in people with type 1 diabetes (T1D) during the COVID-19 pandemic

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ABSTRACT

Background and aims: In Colombia, the government established mandatory isolation after the first case of COVID-19 was reported. As a diabetes care center specialized in technology, we developed a virtual training program for patients with type 1 diabetes (T1D) who were upgrading to hybrid closed loop (HCL) system. The aim of this study is to describe the efficacy and safety outcomes of the virtual training program.

Method: ology: A prospective observational cohort study was performed, including patients with diagnosis of T1D previously treated with multiple doses of insulin (MDI) or sensor augmented pump therapy (SAP) who were updating to HCL system, from March to July 2020. Virtual training and follow-up were done through the Zoom video conferencing application and Medtronic Carelink System version 3.1 software. CGM data were analyzed to compare the time in range (TIR), time below range (TBR) and glycemic variability, during the first two weeks corresponding to manual mode with the final two weeks of follow-up in automatic mode.

Results: 91 patients were included. Mean TIR achieved with manual mode was 77.3 ± 11.3, increasing to 81.6% ± 7.6 ($p < 0.001$) after two weeks of auto mode use. A significant reduction in TBR <70 mg/dL (2,7% ± 2,28 vs 1,83% ± 1,67, $p < 0,001$) and in glycemic variability (% coefficient of variation 32.4 vs 29.7, $p < 0.001$) was evident, independently of baseline therapy.

Conclusion: HCL systems allows T1D patients to improve TIR, TBR and glycemic variability independently of previous treatment. Virtual training can be used during situations that limit the access of patients to follow-up centers.

1. Introduction

Hybrid closed-loop (HCL) systems use various combinations of control algorithms, glucose sensors, and insulin pumps. HCL system is the first system that automatically increases, decreases, and suspends insulin delivery in response to continuous glucose monitoring. HCL has demonstrated increased time in range and reductions in A1c, hyperglycemia and hypoglycemia [1].

Training, education, and support are the most important factors in achieving success with continuous subcutaneous insulin delivery in people with type 1 diabetes (T1D), this training in our center has been traditionally delivered in person by either individual or group sessions, where the training program has been the basis of therapy

Abbreviations: A1c, glycosylated hemoglobin; CV%, coefficient of variation; CGM, continuous glucose monitoring; GMI, Glucose management indicator; PLGM, Predictive low-glucose management; IQR, Interquartile range; SAP, Sensor-augmented pump therapy; T1D, Type 1 Diabetes; TAR, Time above the range; TBR, Time below the range; TIR, Time in range; HCL, Hybrid Closed Loop; AID, Automated insulin delivery system; MDI, Multiple Doses of Insulin; SH, severe hypoglycemia; HU, hypoglycemia unawareness.

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success [2].

The first case of COVID19 in Colombia was reported in March 2020, immediately after MiniMed TM 670G system was launched. At that time, the government established the response plan, including mandatory isolation at national level [3], restricting the displacement to health care centers of patients with diabetes. So, we had to modify our face-to-face education programs to a virtual modality using new tools for medical and educational purposes with all our patients, including the development of a virtual course for patients who were updating to HCL system.

Although there is experience with telemedicine in diabetes programs, few data are available about the effect of shifting to virtual training on the HCL system in people with T1D, as it was necessary during the COVID-19 pandemic. The aim of this study was to describe the outcomes of a virtual training program, such as time in range (TIR) between 70 and 180 mg/dL, time above range (TAR), time below range (TBR) and glycemic variability using coefficient of variation (CV%) comparing manual and automatic mode.

2. Methods

A prospective observational cohort study was conducted, including T1D patients who were upgrading to HCL system (Minimed 670G insulin pump, Medtronic, Northridge, CA, USA) at Hospital Universitario San Ignacio in Bogotá, Colombia. Recruitment was performed between March and July 2020. T1D patients older than 14 years old who were being treated with multiples doses of insulin (MDI), Sensor Augmented Pump (SAP) Therapy with Low Glucose Suspend (LGS) (Paradigm VEO®, Medtronic MiniMed, Inc, Northridge, CA, USA) or Sensor Augmented Pump Therapy with Predictive low-glucose management (SAP-PLGM) (MiniMed 640G®, Medtronic MiniMed, Inc, Northridge, CA, USA) were selected for the study. The exclusion criteria were pregnancy, alcohol consumption or refusal to sign the informed consent. This study was approved by the Ethics Committee of Hospital Universitario San Ignacio and Pontificia Universidad Javeriana.

In all patients, the training program was directed by the diabetes physician, with the support of education and nutrition teams. The number of virtual sessions depended on baseline therapy as it is shown in Fig. 1. Patients with MDI and Paradigm VEO® as baseline therapy had two additional sessions, including carbohydrate counting, device overview and basic concepts about continuous glucose monitoring. All virtual sessions were performed through Zoom Enterprise Version of the Zoom video conferencing application (Zoom Video Communications, San Jose, California). In all cases, prior to the initiation of therapy, the device was programed according Medtronic clinical recommendations [4]. Subjects treated with SAP-LGS or SAP-PGLM therapy and TIR above 70% continued with their baseline settings. The PLGM function was indicated to be turned on with a threshold of 60 mg/dl. For patients with history of severe hypoglycemia (SH) and hypoglycemia unawareness (HU), a threshold of 70 mg/dl was set. Active insulin function was set to 3 h, except if the GFR was below 30 ml/min.

The first two weeks the device remained in manual mode. Follow-up was performed within the first 24 and 72 h and weekly thereafter. In every 30-min session patients were prompted to download continuous glucose monitoring (CGM) data to evaluate adherence, carbohydrate counting, proper timing of bolus delivery and sensor calibration. After that, adjustments were made to the insulin pump settings for at least seven sessions to improve the TIR. A maximum of 10 sessions were carried out in those patients who remained with TIR below 60% using manual mode. During this phase, a diabetes healthcare professional was available by phone 24 h a day. The first infusion set change was supervised using zoom conferencing app, on the 3rd day and the first sensor replacement on the 6th day. After the first 2 weeks, patients were turned to auto mode if the TIR was over 60%. In every session the proper use and advantages of the auto mode feature was reinforced.

SH was defined by the need for assistance from a third person for recovery and HU was detected using the Clarke questionnaire with a score ≥4. For continuous variables, mean and standard deviation (SD) or median and interquartile ranges (IQR) were reported, according with variables characteristics. For categorical variables, frequencies and percentages were reported. CGM data were analyzed to evaluate TIR, TBR, TAR, CV%, mean glucose and Glucose management indicator (GMI) during the first two weeks corresponding to manual mode and the final two weeks of follow-up in automatic mode. Comparison of both periods were done using a paired *t*-test. STATA version 15.0 was used for the analysis.

3. Results

Ninety-one patients were included in the analysis. Baseline demographic and clinical characteristics are shown in Table 1. 51% were women and the median age was 33 years (IQR 17–71 years). The whole population reported hypoglycemia as an indication for

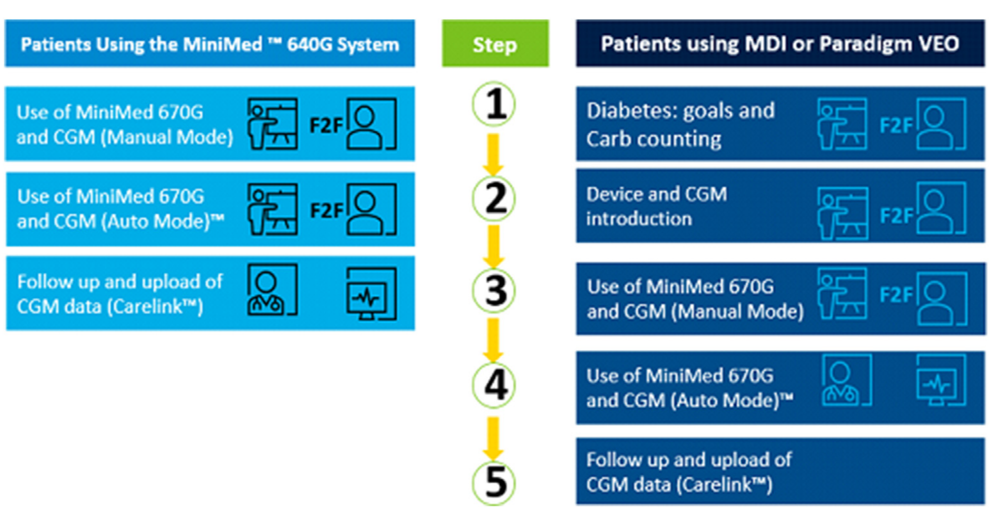

Fig. 1. Virtual training program for the 670G system during the COVID 19 pandemic.

Table 1
Baseline characteristics.

	n = 91
Age in years, median (IQR)	33 (17–71)
Female	51 (56,6)
Duration of diabetes in years, mean (SD)	18,2 (11,6)
Creatinine, median (IQR)	0,79 (0,5–11,5)
Body mass index, mean (SD)	24,35 (3,7)
Insulin pump time, years Median (IQR)	5 (0–10)
Indication for use insulin pump, n(%)	
Severe hypoglycemia	15 (24,6)
Poor metabolic control	11 (18)
Variability	22 (36)
Insulin pump technology n (%)	
MiniMed® 640G with SmartGuard	10 (10,9)
Paradim VEO	37 (40,7)
MDI	44 (48,4)
Macrovascular complications n (%)	
Myocardial infarction	4 (3,7)
Peripheral arterial disease	1 (0,9)
Microvascular complication n (%)	
Diabetic retinopathy	20 (18,5)
Diabetic nephropathy	16 (14,8)
Diabetic neuropathy	12 (11,1)
Diabetic gastroparesis	3 (2,77)
Severe hypoglycemia in the last year n (%)	37 (40)
Initial Clarke score n (%)	
Clarke questionnaire score ≤3	48 (52)
Clarke questionnaire score ≥4	31 (35)
Diabetic Ketoacidosis in the last year, n (%)	4 (4,17)

SD: standard deviation; IQR: interquartile range.

insulin pump therapy, with SH in 24.6% and HU detected in 35%. Poor metabolic control was observed in 18% of the patients and 36% also presented high glycemic variability (CV%>34).

At the beginning of our virtual training program, the mean A1c was 7.1% ± 1.95 and about half of the patients had been previously managed with multiple doses of insulin. The most common microvascular complication was diabetic retinopathy (18.5%), followed by diabetic nephropathy (14.8%) (Table 1).

3.1. Efficacy

Mean TIR (70–180 mg/dl) changed from 77.3% ± 11.3. in manual mode to 81,6% ± 7.6 at the end of follow up using auto mode (Mean difference $p < 0.001$) (Fig. 2). Similar results were found for MDI and SAP-LGS groups (Table 2). Change in glycemic control of subjects previously treated with SAP- PLGM did not reach statistical significance (80.1% vs 82,5%, p: 0.317) (Table 2).

3.2. Safety

The prevalence of SH and HU before the use of HCL system are shown in Table 1. The TBR <70 mg/dl and <54 mg/dl decreased rapidly with the use of auto mode feature ($p = 0.01$) (Fig. 2). In subjects previously treated with SAP-PLGM the TBR <54 mg/dl decreased from 1,22% ± 0,35 to 0,11% ± 0,33, ($p = 0{,}013$) (Table 2). A significant reduction of CV% was found, (32.4% ± 5.48 vs 29.72% ± 5.9; $p < 0{,}001$). This reduction was significant in all groups (Table 2). No ketoacidosis or SH events were reported.

3.3. Adherence

All patients showed sensor use compliance greater than 90% during training and follow up. The auto mode feature was used 98.5% of time and it remained above 95% at the end of the training. The mean number of self-monitoring of blood glucose (SBMG) was 6.09 ± 1.99. The mean time for changing the infusion set was every 3.58 ± 0.91 days.

4. Discussion

The spread of COVID 19 has challenged health care systems from all the world [5]. Given the current contingency, studies consider that the use of teleconsultation has increased by 80% during 2020 [6]. Therefore, it was necessary to design and evaluate an educational program through virtual platforms for patients planning to start HCL therapy that complies with government regulations [7] and allows frequent follow-up. Our data suggest that a program with these characteristics significantly increases TIR and reduces TBR and glycemic variability, outcomes that are similar to those reported with face-to-face training.

Previous clinical studies showed a significant reduction of A1c, % CV and TBR with an increase of TIR from 66.7% to 72.2% after the implementation of HCL system. This improvement was associated with the use of auto mode feature ≥80% of the time [8]. Akturk described similar results with the transition from SAP therapy to HCL with face-to-face follow up, demonstrating the increase of 18% in TIR from a baseline of 59.1% ± 15.2% at third month, change that was maintained at 6 months [9]. However, there is little data about the effectiveness of HCL system after the implementation of an educational program using virtual platforms, as was necessary in the context of the COVID-19 pandemic. Vikersky reported Glycemic outcomes data from CareLink™ Personal database from patients who were new to using the MiniMed™ 670 G system during the pre-COVID-19 and the intra-COVID-19 eras. He did not reported the number of patients evaluated, nor the basal TIR in previous therapy, however he found that the TIR was similar in both periods (70.4 vs 68.4%), suggesting than virtual training of individuals results comparable with in-person training [6]. Our data are consistent with this conclusion, suggesting than the outcomes are at least similar to those reported for face-to-face training. Further studies are needed to assess whether the results can be even better with virtual training related to patients not having to come to an office for training that may entail time away from their work or home obligations. In fact, Vikersky found a higher level of satisfaction for patients trained by virtual platforms.

An interesting finding was our high baseline TIR in manual mode. Previously, we presented a multicenter prospective cohort study in Latin America (Chile and Colombia) with subjects with T1D treated with SAP-PLGM. We found TIR greater than 70%, similar to the TIR achieved using manual mode in this study [10]. We consider that these good values are associated to an intensive training program. In 2013 our group published the predictors of good metabolic control in SAP-LGS and SAP-PLGM users (2), showing that face-to-face training focused on adherence to the use of the sensor and bolus wizard allowed the achievement of adequate metabolic control with reduction of hypoglycemia and glycemic variability during long-term follow-up.

Despite the fact that the TIR achieved in manual mode was higher than 70% in our study, it was notable that significant increase in TIR was observed after two weeks of using the device in automatic mode [9]. This increase was independent of previous treatment, but greater in patients treated with MDI, which was the group with lower TIR at baseline. Similar findings have been described in clinical studies, real-life trials and meta-analyzes evaluating the outpatient use of HCL in face-to-face follow-up with an increase in TIR (70–180 mg/dl) by approximately 10% compared to control therapy. The increased TIR is caused by less time in hyperglycemia (TAR) especially at night time with no significant changes in TBR [8,11].

As a relevant finding, despite the fact that the population had a relatively low basal glycemic variability, a significant decrease in % CV was achieved, associated with the significant reduction in TBR in this study. Similar to previous reported cases using this modality, in

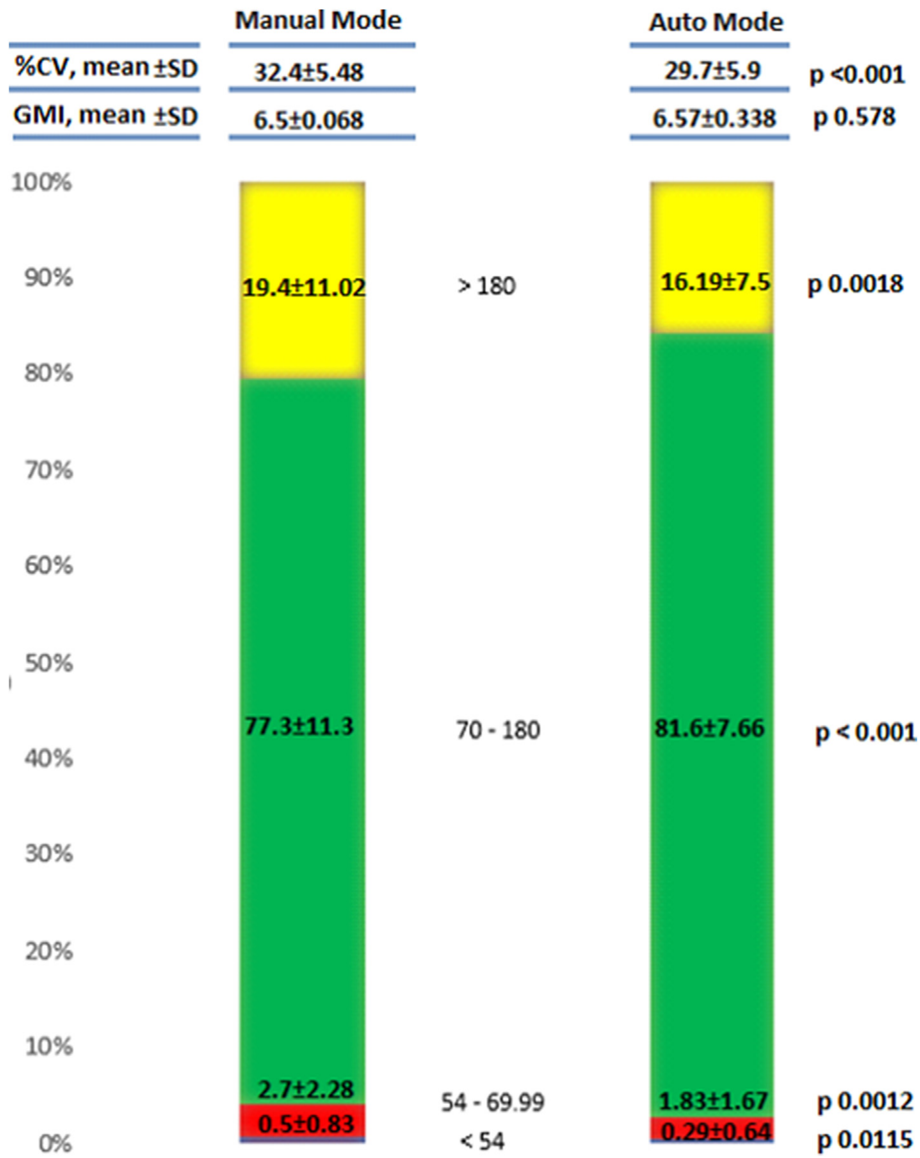

Fig. 2. Times-in-ranges for patients with T1D using MiniMed TM 670G system manual mode (left) and auto mode (right). SD: standard deviation; TIR: time in range; TAR: time above range; TBR: time below range; CV%: coefficient of variation; GMI: glucose management index.

Table 2
Glycemic control under manual versus automatic mode of HCL system.

	Total			MDI			SAP-PLGM			SAP-LGS		
	Manual	Automatic	p	Manual	Automatic	p	Manual	Automatic	p	Manual	Automatic	p
%TIR 70–180 mg/dL, mean (SD)	77,3 (11,32)	81,6 (7,66)	0,0001	75,2 (13,2)	81,51 (8)	0,0063	80,1 (6,88)	82,5 (4,1)	**0,317**	78,36 (10,12)	81,57 (8,1)	0,005
%TAR >180 mg/dl, mean (SD)	19,4 (11,02)	16,19 (7,5)	0,0018	20,3 (13,2)	15,68 (7,61)	0,028	17 (6,1)	15,9 (3,5)	**0,57**	19,1 (10,4)	16,6 (8,09)	0,029
%TBR 54–70 mg/dL (mean, SD)	2,7 (2,28)	1,83 (1,67)	0,0012	3,4 (2,57)	2,17 (1,85)	0,016	2,7 (2,43)	1,44 (0,88)	**0,155**	2,06 (1,78)	1,61 (1,64)	**0,123**
%TBR% <54 mg/dL (mean, SD)	0,5 (0,83)	0,29 (0,64)	0,0115	0,6 (0,93)	0,44 (0,86)	**0,226**	1,22 (0,35)	0,11 (0,33)	0,013	0,25 (0,51)	0,19 (0,40)	**0,511**
CV%, mean (SD)	32,4 (5,48)	29,72 (5,9)	0,0002	33,2 (5,2)	30,3 (7,14)	0,034	32,88 (4,9)	29,8 (4,28)	0,039	31,8 (5,9)	29,2 (0,91)	0,006

SD: standard deviation; TIR: time in range; TAR: time above range; TBR: time below range; CV%: coefficient of variation; GMI: glucose management index; MDI: multiple doses of insulin; SAP-PLGM: sensor augmented pump with predictive low glucose management; SAP-LGS: sensor augmented pump with low glucose suspend.

this study there were no SH or hyperglycemia [12].

Regarding adherence in our study the use of the automatic mode was greater than 95%, compared to real-life data with face-to-face follow-up, in which the use of this function was 87% [13]. In order to highlight the advantages of the use of telemedicine, we can say it allows frequent follow-up by a multidisciplinary group, technical support 24 h a day, the availability of assistance to upload data and access to health personnel through technology, which can improve adherence to the use of the sensor and spending more time in auto mode.

To our knowledge, this is the largest prospective non-sponsored study including adults trained through a virtual platform. One strength is the application of a personalized education plan for patients with different baseline therapy, allowing the generalization of results. Additionally, this is the first prospective study to show the experience in a developing country, demonstrating that the program can be easily adopted in different centers.

Among the limitations, this is an observational study without a control group under face-to-face training, for this reason we cannot compare directly virtual vs. face-to-face modalities. However, our data represent the usual care under COVID-19 pandemic and open the doors for virtual training as a permanent standard of care. Furthermore, a short follow-up period was assessed which may not represent long-term results. Future studies are needed to overcome these limitations.

5. Conclusion

The use of HCL systems allows T1D patients to increase TIR and reduce glycemic variability and TBR <70 and < 54 mg/dL. Implementing a virtual education program is a challenge. However, virtual training and follow-up with the use of the Carelink platform allows physicians to provide education and is an appropriate option during situations that limit the access of patients to follow-up centers.

Declaration of competing interest

AMG reports speaker fees from Novo Nordisk, Elli Lilly, Boehringer Ingelheim, Abbott and Medtronic. DCH reports speaker fees from Novo Nordisk, Medtronic and Abbott. No other potential conflicts are reported.

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