ENDOCRINOLOGY RESEARCH AND PRACTICE

SOCIETY OF ENDOCRINOLOGY AND METABOLISM OF TURKEY

ORIGINAL ARTICLE
Endocrinol Res Pract. 2023;27(2):48-53

Assessment of a Program Based on Digital Tools in Monitoring Type 1 Diabetes Patients Using Closed-Loop Systems

ABSTRACT

Objective: The aim of this study is to evaluate the efficacy of glycemic control of Care Connect, a program based on digital tools designed for remote monitoring of type 1 diabetes patients.

Methods: This is a retrospective cohort study that assesses glycemic control, at baseline and after 3 months, in patients included in the first 45 days whose data were downloaded at least twice during the observation period.

Results: Fifty-three subjects were included in the portal in the first 45 days after implantation, 27 men and 26 women, mean age 44.5 ± 11.69 years, all of them were closed-loop system users. Three months after starting remote monitoring, the glucose management indicator decreased from 7.04% ± 0.53% to 6.89% ± 0.45%, the percentage of time in hyperglycemia> 250 mg/dL reduced from 7.83% ± 8.13% to 5.04% ± 5.9% and the percentage of time in hyperglycemia> 180 mg/dL reduced from 23.06% ± 12.92% to 19.17% ± 9.71% while the percentage of time in range increased from 65.52% ± 17.80% to 73.60% ± 13.98%, all these differences being statistically significant.

Conclusions: A care program based on digital tools can improve glycemic control in type 1 diabetic patients using a closed-loop system. This type of digital health technology could be useful to optimize control in this patient profile.

Keywords: Closed-loop system, diabetes, digital health technology, distal technologies, type 1 diabetes

Introduction

The aim of type 1 diabetes (T1DM) treatment is to prevent macrovascular and microvascular complications by maintaining blood glucose levels within the normal range.[1] A value of glycated hemoglobin (HbA1c) < 7%[2] has now generally been established as a glycemic control target. Strategies that increasingly imitate physiological insulin secretion are employed to achieve this target. New technologies are among the therapeutic resources available, and they are becoming increasingly popular.

Type 1 diabetes affects 0.02%-0.08% of the Spanish population,[3] and according to recent data, 20.7% of patients use a continuous subcutaneous insulin infuser (CSII) and 24.8% use some form of continuous glucose monitoring.[4] Although CSII and closed-loop systems are the best-known and most-studied proximal technologies in diabetes, other valuable elements should be considered in order to achieve a comprehensive approach to the disease, such as diabetes self-management education, telemedicine, or multidisciplinary teams. Combining these well-known positive elements and technology, diabetes patients can be benefited.[5] In recent years, diabetes technology has grown dramatically to include other devices used for communication, education, and intervention, known as distal technologies or digital tools in diabetes.[6] Online counseling includes telemedicine, mobile phone applications, social media platforms, and patient portals.[5-7]

Patient portals are interactive online treatment environments to exchange personal health data between the patient and the healthcare professionals responsible for their care. They also provide multiple methods for self-management of health-related information such as managing appointments, diabetes education, professional support options, and the ability to share, view, and manage health information.[5] Data have been published on the usefulness of patient portals in pediatric/adolescent and adult populations, with varying results on glycemic control.[8-12]

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Received: July 19, 2022
Revision Requested: September 1, 2022
Last Revision Received: December 4, 2022
Accepted: January 9, 2023
Publication Date: April 20, 2023

Cite this article as: Garcia MJA, Izquierdo FJE, Vaquero AAC, *et al.* Assessment of a program based on digital tools in monitoring type 1 diabetes patients using closed-loop systems. *Endocrinol Res Pract.* 2023;27(2):48-53.

DOI: 10.5152/erp.2023.2281118

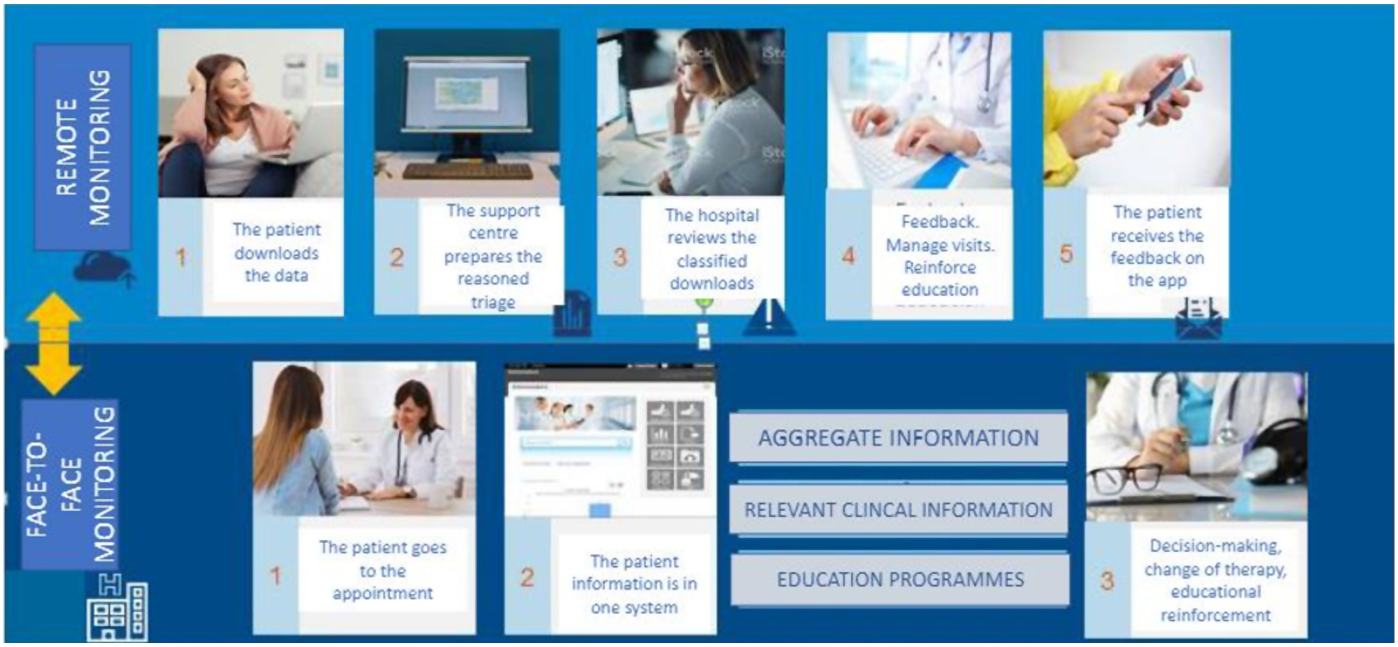

Figure 1. Operating of the Care Connect integrated remote patient monitoring system.

Care Connect is an integrated solution for remotely monitoring patients with diabetes using Medtronic devices created to optimize their care. It combines a digital platform and exclusive services provided by the Medtronic Remote Monitoring Support Center to patients and healthcare professionals. Through a service and analysis center, triage is offered based on glucose and adherence data provided by the specialized software (CareLink Pro v4.0C®; Medtronic Inc., Dublin, Ireland) to healthcare professionals, who assess remotely the patient's information and issue a medical report with the therapeutic recommendations. Care Connect allows physicians to focus on the patients who need it the most by combining face-to-face appointments and scheduling visits when needed, all in a patient-friendly digital interface. Following its implementation in our center, a pilot study was conducted to assess the efficacy of glycemic control using an integrated remote monitoring solution for adult T1DM patients treated in our healthcare area, users of CSII, and continuous glucose sensors.

Materials and Methods

A retrospective cohort study that analyzes the efficacy of glycemic control of remote monitoring through the Care Connect solution of adult T1DM patients in the Cáceres Health Area included between April 30 and June 15, 2021.

MAIN POINTS

- A care program based on digital tools can improve glycemic control in diabetic patients using a closed-loop system.
- A remote follow-up system integrated into the care activity of the professionals, operated by a team responsible for the usual care of patients and a support center, increases the efficiency of type 1 diabetes care.
- Remote monitoring of diabetic patients using the closed-loop system is safe and effective and can be included in the routine care

All adult T1DM patients who use an integrated system or sensor-augmented pump in our healthcare area (MiniMed™ 640G, MiniMed™ 670G or MiniMed™ 780G, GuardianTM 2 Link Transmitter and Enlite TM sensor; Medtronic, Northridge, Calif, USA) and have signed an informed consent have been registered in the system. Once the patients registered on the portal, they receive an e-mail invitation with a link to download an application called Caaring on their mobile phones for one-way hospital-patient information, through which regular reminders are automatically sent for monthly uploading from their devices. The data of patients using the MiniMed Mobile App are uploaded automatically every month. The information received in both cases is obtained through the CareLink™ platform, a specialized Medtronic device download software used in routine clinical practice for face-to-face or remote monitoring of patients with T1DM. This information includes CSII usage parameters (treatment adherence) and the full report on the standard outpatient glucose profile[13] (Figure 1). According to the values obtained in the blood glucose data, following the criteria specified in Table 1, the patient's download is classified by the system as high, intermediate, or low priority.

Every 10 days, a doctor from the Endocrinology and Nutrition Unit analyzes all the downloads and issues a clinical report with therapeutic recommendations, which is then sent to the patient electronically or by telephone contact with the nurse educator, depending on the complexity of the information to be transmitted.

A retrospective cohort study was conducted within 45 days of its commencement, assessing all patients in the portal who had uploaded their data at least twice in the 3 months following their inclusion.

Fifty-seven patients using CSII, sensor-augmented pump, or the integrated system had been included in the Care Connect solution between April 30 and June 15, 2021. Of these, 53 patients uploaded their data at least twice in a 3-month follow-up period, 31 uploaded data regularly based on notifications received through the App,

Table 1. Classification of Downloads into 3 Priority Levels in Sensor-Using Patients

Glucometric Parameter	Assigned Priority Level
• Time in hyperglycemia > 180 mg/dL ≥ 32% • Time in hypoglycemia < 54 mg/dL ≥ 1%	High
• Time in range 70-180 ≤ 65% • Time in hypoglycemia < 70 mg/dL ≥ 3% • Glycemic variability ≥ 36% • Glucose management indicator ≥ 7%	Intermediate
• Glucose management indicator < 7% • Time in range 70-180 mg/dL > 65% • Time in hyperglycemia > 180 mg/dL < 32% • Time in hypoglycemia < 54 mg/dL < 1% • Glycemic variability < 36%	Low

and 22 patients had the automatic upload set up on the MiniMed Mobile App.

The inclusion criteria were having been T1DM diagnosed, being over 18 years old, being a user of CSII, sensor-augmented CSII, or the integrated system, being monitored by the Endocrinology and Nutrition Unit of the San Pedro de Alcántara Hospital, having signed the consent to participate in the platform, and having downloaded data at least twice during the monitoring period. No exclusion criteria have been applied.

The protocol was approved by the Ethics and Research Committee of San Pedro de Alcántara Hospital (Date: January 28, 2022, Decision No: 117-2021). All participants gave their informed consent.

Demographic data (age and sex) and the following clinical variables were collected: type of device used by the patient, use of sensor, and number of downloads during the study period. The following continuous glucose sensor parameters were included for a 14-day period, at baseline and at 3 months: glucose management indicator (%); coefficient of variation (CV) (%), defined as the standard deviation of interstitial glucose concentration between the mean interstitial glucose concentration; percentage of time in range (TIR) (70-180 mg/dL); percentage of time in hypoglycemia < 70 mg/dL; percentage of time in hypoglycemia < 54 mg/dL, percentage of time in hyperglycemia > 180 mg/dL; and percentage of time in hyperglycemia > 250 mg/dL.

Statistical Package for the Social Sciences 12.0 (SPSS Inc., Chicago, Ill, USA) was used for data analysis. Quantitative variables were expressed as mean and standard deviation if normally distributed and as median and interquartile range if otherwise. Student's *t*-test for paired samples was used to compare quantitative variables because parametric test assumptions were met. A *P*-value of less than .05 was considered significant for all calculations.

Results

In the first 45 days of the usage of the portal, 57 patients were included, 53 of whom uploaded their data at least twice during the period analyzed (from patient inclusion to September 15, 2021). We evaluated 27 men and 26 women, with a mean age of 44.5 ± 11.69 years (range 19-72). All were users of a closed-loop system, 90.4% of the MiniMed 780G advanced hybrid closed-loop system and 9.6% of the 670G closed-loop system.

Uploads during the study period ranged from 2 to 5 per patient (mean 3.32, standard deviation 0.956). Of the total uploads, 41.50% were classified as low priority, 20.80% as intermediate priority, and 37.70% as high priority, according to the criteria in Table 1 defining priority levels (Figure 2).

Before starting remote monitoring, the glucose monitoring indicator was 7.04% ± 0.53%, the coefficient of variation was 34.16% ± 6.55%, the percentage time in hyperglycemia > 250 mg/dL was 7.83% ± 8.13%, the percentage time in hyperglycemia > 180 mg/dL was 23.06% ± 12.92%, the percentage TIR was 65.52% ± 17.80%, and the time in hypoglycemia < 70 mg/dL was 2.96% ± 2.71%.

Three months after starting the remote monitoring, a statistically significant decrease in the glucose monitoring indicator was noted, which became 6.89% ± 0.45% ($P = .013$), and in the times in hyperglycemia > 250 mg/dL and hyperglycemia > 180 mg/dL, the

Figure 2. Classification of downloads according to the priority levels as described in Table 1.

Table 2. Glycemic Control Variables

	Basal[a]	3 Months[a]	Difference with Basal	P
GMI (%)	7.04 ± 0.53	6.89 ± 0.45	−0.15	.013*
Coefficient of variation (%)	34.16 ± 6.55	33.30 ± 4.88	−0.90	.274
Hyperglycemia > 250 mg/dL (%)	7.83 ± 8.13	5.04 ± 5.9	−2.75	.006*
Hyperglycemia > 180 mg/dL (%)	23.06 ± 12.92	19.17 ± 9.71	−3.98	.031*
Time in range (%)	65.52 ± 17.80	73.60 ± 13.98	−8.08	.001*
Hypoglycemia < 70 mg/dL (%)	2.96 ± 2.71	2.23 ± 2.27	−0.73	.087
Hypoglycemia < 54 mg/dL (%)	0.60 ± 0.89	0.53 ± 0.93	−0.11	.428

GMI, glucose management indicator.
[a]Mean ± standard deviation.
*$p < .05$

percentages of which became 5.04% ± 5.9% ($P = .006$) and 19.17% ± 9.71% ($P = .031$), respectively. The TIR increased to 73.60% ± 13.98% ($P = .001$) and this difference was statistically significant. The coefficient of variation also improved to 33.30 ± 4.88%, but the difference did not reach statistical significance ($P = .274$) (Table 2).

At the end of the monitoring, the rating of the downloads was 49.1% low priority, 18.9% intermediate priority, and 32.1% high priority (Figure 2).

Discussion

Distal technologies are electronic systems designed to provide remote services and include heterogeneous systems such as telemedicine, social media platforms, web platforms, and mobile phone applications. Studies that have assessed its impact on glycemic control are heterogeneous in terms of the population studied, the type of distal technology assessed, and the study objective. The results obtained in glycemic control have been variable, although an improvement in HbA1c between 0.2% and 0.4% is suggested. Patient portals improved by 0.2%.[5-7]

The Medtronic MiniMed 780 advanced closed-loop hybrid system was commercialized in Europe in October 2020 and the 670 closed-loop system in December 2018, so neither of the referenced studies analyzed the potential benefit of patient portals in using these devices. In addition, introducing continuous glucose monitoring has changed the paradigm of glycemic control assessment, moving beyond HbA1c to include glucose monitoring parameters, which allow a more accurate approximation of each patient's blood glucose levels.[14]

Our results reveal that the glucose management indicator and the time in hyperglycemia > 180 mg/dL fall within the desirable targets according to outpatient glucose profile standards. However, the coefficient of variation and time to hypoglycemia were within the target at baseline discharge and were not significantly modified.

Prior experiences in applying distal technologies to the follow-up of CSII users have differed greatly from the one carried out in our center (Table 3). A study published in 2012[14] analyzed results from 15 patients using CSII with a sensor or a glucometer, who e-mailed monthly blood glucose and infuser data and received an e-mail response from healthcare professionals. Over the 6-month study period, they observed improvements in HbA1c and capillary blood glucose levels, concluding that a remote monitoring system, complementary to standard care, may benefit patients with acceptable previous metabolic control. Petrovski et al[15] addressed the use of social media (Facebook and Skype) along with CareLink as tools to improve glycemic control in adolescents and young adults using CSII and continuous glucose monitoring systems. Patients downloaded data at home and received recommendations from healthcare professionals through social media. This remote follow-up was compared with standard face-to-face care, and both groups improved in HbA1c levels, with no differences between them.

Studies on T1DM patient portals have yielded varied results (Table 3), but perhaps the key feature has been the heterogeneity in many aspects, such as the population studied, the communication channel used and the objectives assessed. Only one study published in 2012 specifically included young users of CSII patients and used, as in our study, the CareLink software, with or without telephone booster, and found no differences in A1c.[9]

In the evidence, there is no remote follow-up system operated by a team responsible for the usual care of patients, including adult patients, exclusively users of integrated systems, with a system for stratifying patient priority, carried out systematically in most patients targeted and integrated into the care activity of the professionals. The support center constitutes a differentiating element compared to the rest of the telemedicine experiences. It assumes administrative tasks inherent to remote monitoring and those related to patients' adherence to the program. Overall, this scalable and replicable solution allows for increasing the efficiency in T1DM care, improves health outcomes, and empowers patients.

The clinical utility of this monitoring is based on blood glucose monitoring as a fundamental tool in the management of patients using new technologies, complementing standard HbA1c monitoring. Limitations include the unavailability of HbA1c, which, as mentioned, is not temporally linked to monthly patient downloads but to face-to-face appointments as part of routine care.

Another drawback of this remote monitoring system is the need for patient downloads, partly overcome by the MiniMed Mobile App, which automatically downloads the data every month. Despite this, 7.02% of the patients registered on the portal did not download data at least twice during the evaluation period.

The patients were all users of closed-loop systems, as, since their commercialization, they have been the predominant treatment in patients using CSII. As in other studies of closed-loop system users in our setting,[16] baseline metabolic control was good, with a previous glucose management indicator of 7.04% ± 0.53%, as these are usually patients highly involved in managing their disease. This patient profile facilitates remote assessments yet hinders the possibility of improvement.

Overall, the Care Connect solution is a digital remote clinical monitoring tool that combines a digital platform and services, to improve the glycemic control of T1DM patients using closed-loop systems by facilitating communication with the team of healthcare professionals responsible for their routine care. From the professionals' viewpoint,

Table 3. Studies assessing patient portals and other distal technologies in CSII users (modified from Duke et al).[6]

Author	Type of Study	Population	n	Type of Treatment	Results
Studies assessing patient portals in type 1 diabetes					
Esmatjes et al[8] (2014) Spain	RCT	Adults 18-55	154	Internet-based telemedicine system (2 face-to-face appointments and 5 telemedicine appointments)	HbA1c, improvement in both groups Health status (EuroQol), no change in either of the 2 groups Improved adherence in both groups Improvement in diabetes knowledge (DKQ2) in both groups
Landau et al[9] (2012), Israel	RCT	Adolescents and young adults (11-20 years)	70	Medtronic Carelink plus other telephone feedback by diabetes care team vs. no feedback at all	HbA1c, no difference between the 2 groups Hypoglycemia or diabetic ketoacidosis, no differences between groups No. of visits: no differences between groups
Boogerd et al[10] (2014), Netherlands	RCT	Adolescents and young adults (11-21 years)	62	Usual care by multidisciplinary team plus other online vs. offline approach	HbA1c, no improvement, no difference between both groups Assessment of care (PEQ-D) and QoL improved over time in the online approach group, but no differences between the 2 groups.
Berndt et al[11] (2014), Germany	RCT	Youth 8-18 years	68	Mobile phone-based diabetes management system vs. conventional treatment	HbA1c, improvement in both groups, no difference between the groups. Diabetes-specific QoL (DQOLY): no improvement during the study, no difference between the groups
Schiaffini et al[12] (2015), Italy	RCT	Adolescents (age range not specified)	29	Telemedicine portal (monthly remote assistance with the medical team) vs. face-to-face hospital visits every 3 months	HbA1c improved in the telemedicine group at 12, 42, 48, and 60 months, but there were no differences at 6, 18, or 36 months. In the telemedicine group, using the sensor, the average number of boluses per day and the number of capillary blood glucose self-monitoring increased.
Studies assessing distal technologies other than patient portals with CSII users					
González Molero et al[14] (2012), Spain	Prospective cohort study (telemedicine)	Adults (mean 40.5, SD 8.4 years)	15	Medical responses via e-mail with CSII and real-time continuous glucose sensor	HbA1c improved during the study. Time in hypoglycemia, time in hyperglycemia, time of sensor use and days with less than three boluses, no change during the study. Number of capillary blood glucose levels per day improved during the study
Petrovski et al[15] (2015), Macedonia	RCT (social media platform)	Adolescents and young adults (14-23)	56	Use of Carelink software with web-based interventions v. standard medical protocol with regular face-to-face visits	HbA1c improved in both groups at 12 months follow-up.

CSII, continuous subcutaneous insulin infuser; HbA1c, glycated hemoglobin; RCT, randomized controlled trial; SD, standard deviation.

it is also a resource for the care activity organization, complementing standard care and allowing patients to be classified according to their glycemic control parameters to focus on the patients who need it the most. This must occur in an environment subject to appropriate security and privacy regulations.

Type 1 diabetes mellitus patients using closed-loop systems and remote monitoring systems via an integrated solution improved glycemic control parameters obtained from ambulatory glucose profiling. This difference was statistically significant for the glucose management indicator, the percentage of time in hyperglycemia > 250 mg/dL, the percentage of time in hyperglycemia > 180 mg/dL, and the percentage of TIR. This monitoring could be a tool to optimize glycemic control in this patient profile.

Ethics Committee Approval: Ethical committee approval was received from the Ethics Committee of San Pedro de Alcántara Hospital (Date: January 28, 2022, Decision No: 117-2021).

Informed Consent: All participants gave their informed consent.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – F.J.E.I.; Design – F.J.E.I.; Data Collection and/or Processing – All authors; Analysis and/or Interpretation – All authors; Literature Review – All authors; Writing – M.J.A.G; Critical Review – All authors.

Declaration of Interests: The authors have no conflicts of interest to declare.

Funding: The authors declared that this study has received no financial support.

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