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Impact of COVID-19 lockdown on glycemic control in patients with type 1 diabetes

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ABSTRACT

Introduction: The COVID-19 pandemic has forced governments to take exceptional measures to minimize its spread, imposing lockdown policies. The aim of this study was to evaluate the impact of lockdown on type 1 diabetes (T1D) glycemic control.

Material and methods: People with T1D using flash glucose monitoring were included. Data from the 14 days before lockdown were compared with data from the last 14 days after 8 weeks of lockdown.

Results: A total of 307 patients were included (age 45.8 ± 12.6 years, 50.2% male, diabetes duration 21.1 ± 12.3 years). Only one patient had COVID-19 infection.

Mean glucose decreased from 166.89 ± 29.4 to 158.0 ± 29.0 mg/dL and estimated HbA1c declined from 7.4 ± 1.0 to 7.1 ± 1.0% (54 ± 10.9 vs 57 ± 10.9 mmol/mol; $p < 0.001$). Time in range increased from 57.8 ± 15.8 to 62.46 ± 16.1%. Time in hyperglycemia > 180 mg/dL and >250 mg/dL decreased from 37.3 ± 1.9% to 32.0 ± 17.1% and from 13.0 ± 11.3 to 10.3 ± 10.6%, respectively; ($p < 0.001$). Time in hypoglycaemia <70 mg/dL increased from 4.9 ± 4.0% to 5.5 ± 4.4% ($p < 0.001$). No differences in time <54 mg/dl, coefficient of variation (CV%) or number of scans per day were found.

Conclusion: Despite the limitations of lockdown, glycemic control improved in patients with T1D. These results suggest that having more time for self-management may help improve glycemic control in the short term.

1. Introduction

In late 2019, a new coronavirus that causes severe acute respiratory syndrome (SARS-CoV-2) emerged in Wuhan (China) [1]. Coronavirus disease 2019 (COVID-19) spread rapidly in many countries and by March 11, 2020 it was declared a pandemic disease [2]. Since then, exceptional measures have

Abbreviations: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; COVID-19, coronavirus disease 2019; T1D, type 1 diabetes; CGM, continuous glucose monitoring; FGM, flash glucose monitoring; eHbA1c, estimated HbA1c; TIR, time in range; CV, coefficient of variation; MDI, multiple daily insulin injections; T2D, type 2 diabetes

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been taken by governments and public health authorities all over the world to minimize the virus spread.

In Spain a national state of emergency was declared on 14 March 2020 and an almost complete lockdown was imposed [3]. During lockdown, only essential activities were allowed, and mobility of most people was limited to the acquisition of food and medicines, while teleworking was encouraged. All citizens were requested to stay at home and no outdoor exercise was allowed. While hospitals and health care professionals were dealing with hundreds of patients with COVID-19, outpatient clinics were closed and only remote visits were made, except for emergencies.

It is well known that changes in daily routines of people with type 1 diabetes (T1D) can have an impact on glucose levels [4]. Achieving and maintaining good glycemic control is a challenge. It is essential for people with T1D to consider well-known sources of variation, such as diet, exercise or insulin adjustments, and less measurable conditions, such as emotions, stress, social relations or working activities [5,6]. It has been suggested that people with chronic diseases, such as diabetes, could suffer the most from lockdown due to changes in lifestyle and the restrictions in access to outpatients clinics [7]. Nevertheless, data about the impact of lockdown on glycemic control in T1D is scarce. A recent study conducted in the southwest of Spain has reported no deleterious effect on glycemic control after 5 weeks of lockdown in 147 people with T1D on multiple daily insulin injections using continuous glucose monitoring (CGM) or flash glucose monitoring (FGM) [8]. In the same way, Bonora et al. have reported beneficial effects on glycemic control during the first week of lockdown in Italy in 20 patients with T1D using FGM who had stopped working, suggesting that slowing down routine daily activities could have beneficial effects on T1D management, at least in the short term [9].

The use of CGM and FGM systems has allowed healthcare professionals to remotely monitor changes in glycemic control during the COVID-19 pandemic lockdown. In our region, FGM is currently reimbursed to all people with T1D, which enabled the expansion of its use. FGM has been shown to improve glycemic control among patients with T1D, and to reduce hypoglycemia and glycemic variability [10–12].

The aim of this study was to assess the impact that lockdown policies during the COVID-19 pandemic have had on glycemic control in people with T1D using FGM in our clinic.

2. Material and methods

People with T1D using the FreeStyle Libre FGM system (Abbott Diabetes Care) for at least 3 months were included. All patients were routinely being followed at the Endocrinology and Nutrition Department in a general hospital in the Basque Country (northern Spain). Only people who had their sensor data uploaded in real-time and were sharing data with our clinic on a web-based cloud system (LibreView®) were included. People with <70% coverage of sensor data were excluded.

Data from the 14 days before the start of the lockdown, between 1 March 2020 and 14 March 2020, were compared with data from the last 14 days after 8 weeks of consecutive lockdown, between 25 April 2020 and 9 May 2020.

The following metrics were recorded, according to previous international consensus [13]: mean glucose, estimated HbA1c (eHbA1c %), time in glucose range [TIR (70–180 mg/dl)], time in hypoglycemia < 70 mg/dl and <54 mg/dl, time in hyperglycemia > 180 mg/dl and >250 mg/dl, coefficient of variation (CV%) and number of scans per day. A change in eHbA1c $\geq$ 0.4% (4.4 mmol/mol) and an increase in TIR $\geq$ 5% were considered as clinically relevant.

Medical records were reviewed to see if patients had been hospitalized or had had COVID-19 infection confirmed by PCR during this period.

Data were analyzed using SPSS statistics software version 25. Results are presented as mean ± SD values. A paired Student's *T*-test was performed to analyze differences. A p value of <0.05 was considered statistically significant.

All individuals agreed to share their data with the hospital when registering in the Libreview® platform and gave permission for their data to be accessed remotely and used for research purposes when they started using the FGM device.

3. Results

A total of 307 patients with T1D were included in the analysis. Median age was 45.8 ± 12.6 years, 50.2% were male (n = 154), and median diabetes duration was 21.1 ± 12.3 years. Ninety three percent of them (n = 286) were on multiple daily insulin injections (MDI), while 7% (n = 21) were on insulin pump therapy. According to medical records, 51.5% of patients were remotely attended during lockdown period as part of their routine follow-up. Only one patient (0.3%) had COVID-19 infection confirmed by PCR (polimerase chain reaction).

Table 1 shows the comparison of glycemic metrics between baseline (14 days before the lockdown) and data from the last 14 days after 8 weeks of consecutive lockdown. Comparing lockdown period with baseline, we found a reduction in mean glucose (−8.8 ± 19.8 mg/dl; p < 0.001), eHbA1c [−0.3 ± 0.7% (3.3 ± 7.7 mmol/mol); p < 0.001], and time in hyperglycemia >180 mg/dL (−5.2 ± 11.2%; p < 0.01) and >250 mg/dL (−2.7 ± 7.0%; p < 0.01). Time in hypoglycemia < 70 mg/dL increased during lockdown (0.6 ± 4.1%; p < 0.01), whereas there were no differences in time in hypoglycemia < 54 mg/dL, coefficient of variation (CV%) or number of scans per day.

Considering relevant a change in HbA1c $\geq$ 0.4% (4,4 mmol/mol) and an increase in TIR $\geq$ 5%, we found an improvement in 46.6% (n = 143) and 48.2% (n = 148) of the subjects, respectively. A relevant change in both HbA1c and TIR was found in 35.8% (n = 110) of the subjects. A relevant change in HbA1c and TIR without increasing the time in hypoglycemia was only found in 9.8% (n = 30) of the subjects.

Fig. 1 shows the comparison of times in ranges, eHbA1c and CV between baseline and after lockdown, according to baseline eHbA1c. Those subjects with higher baseline eHbA1c [>8% (64 mmol/mol)] showed a greater reduction in eHbA1c [0.6 ± 0.8% (6.6 mmol/mol ± 8.7 mmol/mol); p < 0.001] and a greater increase in TIR (8.3 ± 11.9%, p < 0.001). Subjects with baseline eHbA1c between 7 and 8% (53–64 mmol/mol) also

Table 1 – Comparison of glycemic metrics between baseline (14 days before lockdown: PRE) and after 8 weeks of lockdown (the last 14 days: POST).

FGM Metric	PRE	POST	p
Mean glucose (mg/dl)	166.9 ± 29.4	158.0 ± 29.0	<0.001
Estimated HbA1c (%)	7.4 ± 1.0	7.1 ± 1.0	<0.001
Time in range 70–180 mg/dl (%)	57.8 ± 15.8	62.5 ± 16.1	<0.001
Time < 70 mg/dl (%)	4.9 ± 4.0	5.5 ± 4.4	0.006
Time < 54 mg/dl (%)	0.8 ± 1.4	0.9 ± 1.5	0.696
Time > 180 mg/dl (%)	37.3 ± 16.9	32.0 ± 17.1	<0.001
Time > 250 mg/dl (%)	13.0 ± 11.3	10.3 ± 10.6	<0.001
Coefficient of variation (%)	38.3 ± 6.6	37.7 ± 6.7	0.081
Sensor use (%)	94.9 ± 9.5	94.2 ± 6.3	0.145
Number of scans per day	11.1 ± 6.5	11.4 ± 7.9	0.116

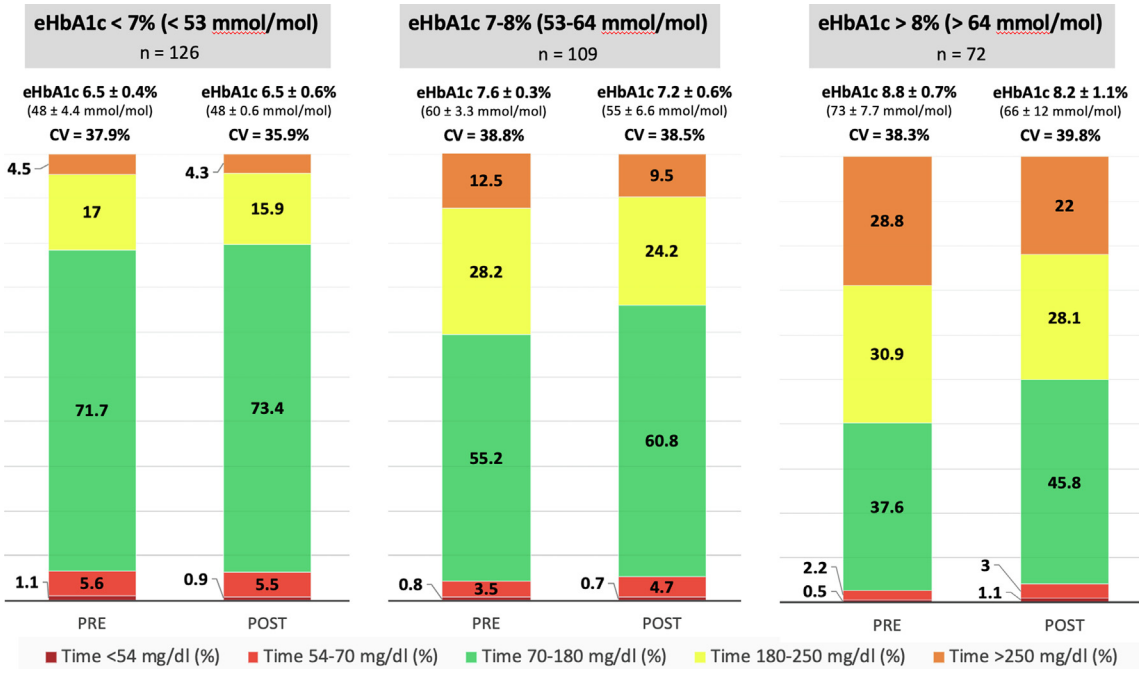

Fig. 1 – Comparison of times in ranges, eHbA1c and CV baseline (14 days before lockdown: PRE) and after 8 weeks of lockdown (the last 14 days: POST), according to baseline eHbA1c.

achieved an improvement, although inferior, in eHbA1c [0.4 ± 0.5% (4.4 mmol/mol ± 5.5 mmol/mol), p < 0.001] and an increase in TIR (5.6 ± 9.1%, p < 0.001). Those with baseline eHbA1c < 7% did not show significant changes in eHbA1c during lockdown, whereas TIR increased 1.6 ± 0.8% (p 0.030). Time in hypoglycemia < 70 mg/dL increased 1.2 ± 3.3% (p < 0.001) in those with baseline eHbA1c > 8% (64 mmol/mol) and 1.5 ± 3.4% (p < 0.001) in those with baseline eHbA1c 7–8% (53–64 mmol/mol). Time in hypoglycemia < 54 mg/dL increased 0.6 ± 1.9% (p 0.007) in those with baseline eHbA1c > 8%, whereas no significant changes were observed in the other groups. CV decreased only in those with baseline eHbA1c < 7%. No differences in the number of scans per day between baseline and after lockdown were found in any of the groups.

When analyzed according to the type of treatment, no differences were found between those on MDI and those on pump therapy in eHbA1c reduction [0.3 ± 0.7% vs 0.4 ± 0.8% (3.3 ± 7.7 vs 4.4 ± 8.7 mmol/mol); p = 0.455] or in TIR increase (4.7 ± 9.9 vs 3.1 ± 8.8; p = 0.367).

Also, no relevant differences were observed in the outcomes between those who were remotely attended during lockdown and those who were not.

4. Discussion

The current COVID-19 pandemic scenario has presented a challenge for healthcare systems. Most of the outpatient clinics have had to adapt their daily activities and have been forced to introduce the use of telemedicine. In fact, the COVID-19 pandemic has acutely stimulated the expansion of digital medicine. Telemedicine has emerged as a useful way to monitor patients with diabetes at home, especially those with T1D using CGM or FGM systems connected to the clinic via the cloud [14,15].

Lockdown policies established to avoid SARS-CoV-2 spread may favor deterioration of control in people with diabetes due to difficulties in accessing the health system, lack of physical activity and increased stress or anxiety associated with lockdown [7,16,17]. Anxiety in people with T1D has been associated with less frequent BG monitoring and suboptimal glycemic control [18]. However, our data do not show a deterioration in glycemic control as might have been expected. Instead, we found an improvement in glycemic control after 8 weeks of lockdown, especially in those with poorer baseline control. Mean glucose, eHbA1c and TIR improved, as a result of a reduction in time in hyperglycemia, and a slight increase in time in hypoglycemia < 70 mg/dL.

These results suggest that greater stability in schedules, healthier meals, and more time to make treatment adjustments may have a beneficial impact on glycemic control, at least in the short term. The main limitation for glycemic control found in our study was the increased time in hypoglycemia. A recent study found no changes in hypoglycemia in people with T1D using FGM or CGM during lockdown. However, when analyzed separately, a slight increase in time < 70 mg/dL was also found in FGM users, but not in CGM users [8]. This may be due to the presence of hypoglycemia alarms in CGM systems. The new FreeStyle Libre2, not yet available during lockdown in our region, has the possibility of setting real-time alarms for hypoglycemia. This could help T1D patients improve their glycemic control, without increasing the time in hypoglycemia.

Another factor that may have influenced the improvement in glycemic control is the fact that diabetes has been reported in the media as a risk factor for COVID-19 prognosis. This may have influenced patients' awareness and self-management. However, to date few studies have reported the impact of T1D on COVID-19. Pitocco et al. reported no cases of T1D in a sample of 1591 Italian subjects infected by SARS-CoV2. They suggested that age and adaptative immunity dysregulation could have influenced these results [19]. More recently, a study conducted in England, has evaluated the risk of death in type 1 and type 2 diabetes (T2D) patients hospitalized with COVID-19. They found that those with T1D had a higher risk than those without diabetes and those with T2D. Cardiovascular comorbidities were taken into account and people with T1D were at a higher risk of in-hospital death after adjusting for age, sex, ethnicity, socioeconomic deprivation, region and diagnosed cardiovascular comorbidities. Other comorbidities were not analyzed, which according to the authors, could have been a limitation of the study [20]. In our study only one patient (0.3%) developed COVID-19 infection confirmed by PCR during the lockdown period and none required hospital admission for this reason. This could have been influenced by the relatively young age of our sample and a selection bias, as FGM users in our clinic tend to have better glycemic control and be more adherent. Moreover, we did not check for the presence of comorbidities or long-term complications, which seems to be an important factor in the progression of COVID-19.

Furthermore, another limitation of the study might be the lack of information about changes in meals, physical activity and insulin doses, as well as changes in working routine. In addition, as aforementioned, patients included have relatively good glycemic control and correct use of FGM. Therefore, it remains unclear whether these results could be generalizable to those T1D patients with poorer control or not using FGM.

5. Conclusions

Despite the limitations of lockdown, we report an improvement in glycemic control in patients with T1D using FGM after 8 weeks of lockdown. These results suggest that having more time for self-management may help improve glycemic control, at least in the short term.

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Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: 'Elsa Fernandez has served as a consultant for, or received research support or lecture fees from Novo Nordisk. Alicia Cortazar has served as a consultant for, or received research support or lecture fees from Eli Lilly. Virginia Bellido has served as a consultant for, or received research support, lecture fees from Abbott, Sanofi Aventis, Novo Nordisk, Eli Lilly, MSD, Boehringer Ingelheim, Esteve, Novartis, and Astra Zeneca'.

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