Title

No deleterious effect of lockdown due to COVID-19 pandemic on glycaemic control, measured by glucose monitoring, in adults with type 1 diabetes

Running title: Impact of lockdown on glycaemic control in type 1 diabetes

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Manuscript word count: 2289

Abstract word count: 255
Abstract

Background. The COVID-19 pandemic has forced the health public authorities to impose extraordinary policies to limit the virus spread. Lockdown has been recognized as an effective measure to minimize the risk of infection. The effect of this extreme and prolonged situation on glycaemic control in people with type 1 diabetes (T1D) is unknown. Continuous glucose monitoring (CGM) and Flash glucose monitoring (FGM) allow health care professionals to remotely monitored sensor glucose levels. The aim of the study was to evaluate the effect of lockdown on glycaemic control in adults with T1D.

Methods. People with T1D on multiple daily insulin injections and using CGM or FGM were included. Sensor data from the 2 weeks before the start of the COVID-19 lockdown and from the 2 weeks after 5 weeks of consecutive lockdown were compared.

Results. 147 subjects were selected (age: 39±14 years (15-80), 54% male (n=80), diabetes duration: 18±11 years). Forty six percent (n=68) were CGM users and 54% (n=79) FGM users. Estimated HbA1c was reduced from 57±11 mmol/l to 55±11 mmol/l (7.38±1.0% to 7.16±1.0%), (p<0.001). Time 70-180 mg/dl was increased from 60.3±16.0 to 62.8±17.0 (p=0.009). Time >180 mg/dl and >250 mg/dl were reduced from 36.0±17.2 to 32.6±17.5 (p<0.001) and from 11.9±11.8 to 9.4±10.3%, (p=0.001), respectively. Time in hypoglycaemia remained unchanged. Estimated HbA1c and time in range 70-180 mg/dl showed an improvement in 62% (n=91) of the subjects. Sensor use (93%) and coefficient of variation (36%) remained unchanged.

Conclusion. No deterioration in glycaemic control was found as a result of lockdown due to the COVID-19 pandemic.

Keywords: type 1 diabetes, COVID-19, CGM, FGM.
Introduction

The spread of the SARS-CoV-2 coronavirus (COVID-19) has reached pandemic dimensions in most of the countries in the world. Exceptional and drastic public health measures have been imposed by the authorities to minimise the spread of the virus. Enforced lockdown of the whole population has been established as an effective tool to limit the transmission of the disease.

Lockdown policies due to the COVID-19 outbreak have forced a tremendous distortion in people's daily routines. In Spain, as in many countries, a national state of emergency was established at the beginning of the COVID-19 pandemic. During the lockdown, people's movement outside their houses has been restricted to provide for food or medications and work from home has been encouraged. No outside exercise or leisure activities have been allowed for any group of age.

There are no data on how these unprecedented changes in daily routines could affect glycaemic control in people with type 1 diabetes (T1D). Continuous glucose monitoring (CGM) and Flash glucose monitoring (FGM) allow to remotely monitor, in real-time, changes in glycaemic control in large groups of people with T1D. The evidence in favour of CGM and FGM in people with T1D on multiple daily insulin injections has led to the increasing use of these devices in routine clinical practice (1-6).

The aim of the study was to evaluate the impact of prolonged lockdown due to the COVID-19 pandemic on glycaemic control in adults with T1D, evaluated by changes in sensor glucose levels.

Material and Methods

People with T1D on multiple daily insulin injections and using CGM and FGM were included in the analysis. All the subjects were routinely followed-up at the Endocrinology and Nutrition Department in a general hospital in Extremadura, a region situated in southwestern Spain. No general practices participated in the study.
Data from the 2 weeks before the state of emergency declaration, between the 1st of March 2020 and the 14th of March 2020, were compared with data from the 2 weeks after 5 weeks of consecutive lockdown, between the 4th of April 2020 and the 17th of April 2020.

The sensor data were downloaded from the available web-based software (Clarity®, Eversense Pro® and Libreview®). Only people with T1D who had their sensor data uploaded in real-time were included. People using a Dexcom receiver or a FreeStyle libre receiver, instead of their mobile phones, were excluded. Estimated HbA1c, mean sensor glucose, standard deviation and coefficient of variation were recorded. Time in range 70-180 mg/dl, time in hypoglycaemia < 70 mg/dl and < 54 mg/dl and time in hyperglycaemia > 180 mg/dl and > 250 mg/dl were analysed, according to previous reports and international consensus (7-9). Sensor use was recorded and only people with a sensor use ≥ 70% were included in the analysis. The number of scans per day, in users of FGM, was also analysed.

Data analysis was conducted using SPSS statistics software v22. Results are presented as mean ± SD values. A paired Student’s t-test was used for the analysis of differences. A p-value < 0.05 was considered statistically significant. All the individuals had given written permission to access remotely their data and use them for research purposes when they started using the CGM or FGM devices.

Results

A total of 147 people with T1D were included in the analysis. Eighteen people with T1D were from the analysis excluded because of a sensor use < 70% before lockdown. Demographic characteristics of the 147 subjects included in the analysis were as follows: age 39 ± 14 years (15-80), 54% male (n = 80), diabetes duration 18 ± 11 years, 17% (n = 25) with chronic diabetes complications. Forty six percent of the people (n = 68) were using CGM (Dexcom G6®: 41% (n = 61), Eversense XL®: 5% (n = 7), while 54% (n = 79) were users of the FGM device FreeStyle libre®.

According to the electronic records, 10% (n = 14) of the subjects had attended the clinic, as a routine visit, during the 2 weeks, included in the analysis, before the lockdown was established. Also, 5% (n = 7) of the subjects were virtually attended during the lockdown, as part of their routine follow-up, none of them specifically during the 2 weeks included in
the analysis. No proactive phone or email contact was requested by the patients during any of the periods. None of the subjects were hospitalised during the analysed period.

Table 1 shows the comparison between the period before the lockdown and the period during the lockdown in the variables included in the analysis. Time in different glycaemic ranges is represented in Figure 1. Only 5 of the 147 subjects showed a sensor use < 70% during the lockdown period.

The changes during the lockdown period, compared to baseline, in estimated HbA1c and time 70/180 mg/dl. Considering relevant a change in HbA1c ≥ 0.4%, 37% (n = 55) of the subjects had an improvement in HbA1c and 16% (n = 23) of them had a deterioration in HbA1c. Similarly, regarding time 70-180 mg/dl, there was no change in 3% (n = 5) of the people, and there was an improvement > 1% in 62% (n = 91), and a deterioration > 1% in 35% (n = 51) of them.

When analysed separately, CGM users (n = 68) showed an increase in time 70-180 mg/dl from 61.2 ± 16.7 to 64.1 ± 17.2 (p = 0.021) and their estimated HbA1c decreased from 57 ± 12 mmol/l to 55 ± 12 mmol/l (7.38 ± 1.08% to 7.22 ± 1.06%) (p = 0.036). FGM users (n = 79) increased their time 70-180 mg/dl from 59.5 ± 15.4% to 62.4 ± 15.7% (p = 0.012) and their estimated HbA1c from 57 ± 11 mmol/l to 54 ± 11 mmol/l (7.39 ± 0.96% to 7.12 ± 0.96%) (p = 0.001). Time in hypoglycaemia < 70 mg/dl and < 54 mg/dl remained unchanged in CGM users but time < 70 mg/dl increased slightly in FGM users, from 4.1 ± 4.1% to 5.2 ± 4.4% (p = 0.022), while time < 54 mg/dl remained unchanged. Also, no relevant gender differences were observed in the outcomes when males and females were evaluated separately.

Discussion

The COVID-19 pandemic is posing an enormous challenge to the population and the governments. Also, our clinical practice is being challenged and new ways of delivering care to people with diabetes are being explored (10,11). Telemedicine and remote access to sensor data have been proven to be useful tools in the management of T1D during the COVID-19 pandemic (10). Besides, diabetes has been found to be a risk factor for medical complications related to COVID-19 infection and good glycaemic control could have a
beneficial effect on clinical outcomes in individuals with diabetes and COVID-19 infection (12-14).

The physical and mental consequences of lockdown, as a way of limiting the spread of the virus, are not known in the general population or in people with specific conditions (15). Specifically, T1D is known to be rapidly affected by changes in daily routines. People with T1D experience fluctuations in their blood glucose control as a result of changes in physical activity, work activity and mental stress. Knowledge of this effect could help us to better understand the effect of daily routines on diabetes control and to better direct our efforts to help people with T1D during the current COVID-19 pandemic.

From our data, we did not find a deterioration in glycaemic control related to the prolonged lockdown in people with T1D. Time in hypoglycaemia remained unchanged, while time in the range of normoglycaemia, mean glucose and estimated HbA1c improved, as a result of a reduction in time in hyperglycaemia, both moderate and severe. Also, glycaemic variability was maintained below the established target of 36% (8).

It could be hypothesized that staying at home has given the people with T1D the opportunity to better take care of their glucose control, maintaining healthier food choices and regular and more convenient schedules than normally. People with T1D could also have been able to maintain a certain level of physical activity at home to avoid deterioration in their glucose levels.

The main limitation of the study is that it only reflects changes in sensor data, with no direct information from the people with T1D, regarding their particular changes in work situation or level of physical activity. Also, although we could confirm that none of the subjects included in the analysis were hospitalised during the analysed period, we could not state if they had suffered from COVID-19 infection or not. Also, these data refer to an adult cohort that generally was under good control, and results may not be generalizable to those under poorer control or not using CGM.

In conclusion, a negative impact of lockdown due to the COVID-19 pandemic could not be demonstrated, by remote analysis of sensor data, in adult people with type 1 diabetes.
References


### Table 1. Comparison between the period before lockdown (PRE) and after 5 weeks of consecutive lockdown (POST).

<table>
<thead>
<tr>
<th></th>
<th>PRE</th>
<th>POST</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean sensor glucose (mg/dl)</td>
<td>165 ± 29</td>
<td>159 ± 29</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Estimated HbA1c (mmol, %)</td>
<td>57 ± 11</td>
<td>55 ± 11</td>
<td>&lt; 0.001</td>
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<tr>
<td></td>
<td>7.38 ± 1.0</td>
<td>7.16 ± 1.0</td>
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<tr>
<td>Time &lt; 54 mg/dl (%)</td>
<td>0.59 ± 0.97</td>
<td>0.64 ± 1.21</td>
<td>0.6</td>
</tr>
<tr>
<td>Time &lt; 70 mg/dl (%)</td>
<td>3.7 ± 3.8</td>
<td>4.2 ± 4.1</td>
<td>0.1</td>
</tr>
<tr>
<td>Time 70-180 mg/dl (%)</td>
<td>60.3 ± 16.0</td>
<td>62.8 ± 17.0</td>
<td>0.009</td>
</tr>
<tr>
<td>Time &gt; 180 mg/dl (%)</td>
<td>36.0 ± 17.2</td>
<td>32.6 ± 17.5</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Time &gt; 250 mg/dl (%)</td>
<td>11.9 ± 11.8</td>
<td>9.4 ± 10.3</td>
<td>0.001</td>
</tr>
<tr>
<td>Sensor use (%)</td>
<td>92.9 ± 11.2</td>
<td>93.2 ± 9.2</td>
<td>0.699</td>
</tr>
<tr>
<td>Coefficient of variation glucose (%)</td>
<td>36.4 ± 6.0</td>
<td>35.9 ± 6.9</td>
<td>0.3</td>
</tr>
<tr>
<td>Standard deviation of glucose (mg/dl)</td>
<td>60 ± 16</td>
<td>57 ± 16</td>
<td>0.001</td>
</tr>
<tr>
<td>Scans (number per day)*</td>
<td>10.0 ± 6.7</td>
<td>9.5 ± 6.7</td>
<td>0.2</td>
</tr>
</tbody>
</table>

n = 147 (*only users of FreeStyle libre, n = 79). Data are expressed as mean ± standard deviation.

Bold values mean a significant difference.
No deleterious effect of lockdown due to COVID-19 pandemic on glycaemic control, measured by glucose monitoring in adults with type 1 diabetes (DOI: 10.1089/dia.2020.0184)

This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

Figure 1. Time in different glycaemic ranges before the start of COVID-19 lockdown (PRE) and after 5 weeks of lockdown (POST).