Original article

Influence of the stage of emergency declaration due to the coronavirus disease 2019 outbreak on plasma glucose control of patients with diabetes mellitus in the Saku region of Japan

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Abstract

Objective: Because patients with diabetes mellitus (DM) were forced to stay indoors during the state of emergency, resulting in stress and a lack of physical activity, concerns about their glycemic control were raised.

Patients and Methods: The 165 patients’ glycated hemoglobin (HbA1c) levels were compared during the following periods: the 4 months that were selected as a representative condition 1 year before the COVID-19 pandemic (May 2018, March 2019, June 2019, and July 2019) and the latter 3 months as a 1-year follow-up during the COVID-19 pandemic (May 2019, March 2020, June 2020, and July 2020).

Results: The patients’ HbA1c levels were 7.32 ± 1.23, 7.44 ± 1.20, 7.16 ± 1.06, 7.01 ± 1.05, 7.23 ± 1.06, 7.45 ± 1.18, 7.15 ± 10.7, and 7.11 ± 1.17 in May 2018, March 2019, June 2019, July 2019, May 2019, March 2020, June 2020, and July 2020, respectively (expressed as mean ± standard deviation).

Conclusion: The analysis showed that HbA1c levels did not worsen during the self-restraint period.

Key words: Coronavirus disease 2019, COVID-19, Diabetes mellitus, HbA1c

Introduction

The coronavirus disease 2019 (COVID-19) pandemic poses problems that not only concern the economy but also the health of people worldwide. The disease affects everyone, especially those with underlying chronic conditions, including diabetes mellitus (DM). To protect the people from acquiring COVID-19 and prevent its spread, governments around the world enacted “lockdowns”. Despite the lockdown, not only persons with type 1 DM (T1DM) maintained good glycemic control but those with type 2 DM (T2DM) also showed improvement in glycemic control.

In Japan, despite the declaration of a “state of emergency”, no lockdown was implemented, and a request for self-restraint and avoidance of nonessential trips was issued instead. After a month, the state of emergency was lifted. Because patients with DM were forced to stay indoors during the state of emergency, resulting in stress and a lack of physical activity, concerns about their glycemic control were raised. The patients’ glycated hemoglobin (HbA1c) levels in different time periods were compared (May 2018, March 2019, June 2019, July 2019, May 2019, March 2020, June 2020, and July 2020) to determine the effect of the state of emergency on plasma glucose control.
Patients and Methods

Participants

The study protocol was reviewed and approved by the review boards of the Saku Central Hospital Advanced Care Center and was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all patients who participated in this clinical study.

The data of 165 patients with DM admitted in Saku Central Hospital Advanced Care Center and Saku Central Hospital were analyzed. These patients regularly visited the hospital between May 2018 and July 2020. Those who did not undergo a monthly regular checkup in the hospital were excluded from the study. The mean age of the participants was 67.8 ± 11.5 years; of them, 67.3% were males. The mean body weight measurements were 65.6 ± 14.6 and 66.1 ± 15.2 kg in July 2019 and July 2020, respectively. The mean body mass index (BMI) values were 24.4 ± 3.6 and 24.4 ± 3.6 kg/m² in July 2019 and July 2020, respectively. Approximately 90% of the participants had T2DM, while the rest had T1DM. The mean duration of DM was 12.0 ± 7.4 years. The laboratory examination results from July 2019 to July 2020 are summarized in Table 1. No significant differences were observed between the results in July 2019 and those in July 2020.

The proportions of patients prescribed with antidiabetic medications were as follows: metformin and dipeptidyl peptidase-4 inhibitors (DPP4i) were prescribed to 46.3% and 42.5% of the patients, respectively; insulin therapy, 22.5%; α-Glucosidase inhibitors, 18.8%; sodium glucose cotransporter 2 inhibitors, 15.0%; GLP-1 analogs, 10.0%; sulfonilureas, 7.5%; glinides, 5.0%; thiazolidines, 5.0%; and none, 5.0%. The medications prescribed remained unchanged throughout the study period. These results are summarized in Figure 1.

Consent to publish

All participants understand that the information will be published anonymously, but that full anonymity cannot be guaranteed. We understand that the text and any pictures or videos published in the article will be freely available on the Internet and may be seen by the general public. Pictures, videos, and text may also appear on other websites or in print; may be translated into other languages; or used for commercial purposes.

Study design

Study 1: To assess the effect of self-restraint on plasma glucose control, HbA1c levels during these periods were compared: 1 year before the COVID-19 pandemic (May Table 1 Participants characteristics

|                | July/2019 | July/2020 |
|----------------|-----------|-----------|
| N              | 165       | 165       |
| Sex (M/F)      | 111/54    | 111/54    |
| Age            | 67.8 ± 11.5 | 68.8 ± 11.5 |
| BL             | 162.2 ± 9.4 | 161.7 ± 8.9 |
| BW             | 65.6 ± 14.6 | 66.1 ± 15.2 |
| BMI            | 24.4 ± 3.6  | 24.4 ± 3.6  |
| SB             | 133.7 ± 18.1 | 136.2 ± 18.9 |
| DP             | 74.6 ± 12.4  | 76.4 ± 12.6  |
| AST            | 23.5 ± 11.3  | 23.7 ± 10.1  |
| ALT            | 22.4 ± 14.5  | 22.9 ± 13.4  |
| SCr            | 1.01 ± 0.65  | 1.03 ± 0.78  |
| UA             | 5.64 ± 1.94  | 5.65 ± 1.41  |
| SCr            | 58.4 ± 19.1  | 58.3 ± 18.5  |
| LDLC           | 108.6 ± 25.9 | 105.1 ± 28.7 |
| TG             | 149.9 ± 125.6 | 156.4 ± 100.5 |
| Duration with diabetes | 12 ± 7.4 | 13 ± 7.4 |

N: subject number; M: male; F: female; Age (years); BL: body length (cm); BW: body weight (kg); BMI: body mass index (kg/m²); SP: systolic blood pressure (mmHg); DP: diastolic blood pressure (mmHg); AST: aspartate aminotransferase (IU/L); ALT: alanine aminotransferase (IU/L); SCr: serum creatinine (mg/dL); UA: uric acid (mg/dL); HDL-c: high-density lipoprotein cholesterol (mg/dL); LDL-c: low-density lipoprotein cholesterol (mg/dL); TG: triglyceride (mg/dL); duration of diabetes (years).

Figure 1 Proportion of patients prescribed with antidiabetic medication.

DPP4i: dipeptidyl peptidase-4 inhibitor; insulin: insulin therapy; α-Gl: α-glucosidase inhibitor; SGLT2i: sodium glucose cotransporter inhibitor; GLP-1 RA: glucagon-like peptide-1 receptor agonist; SU: sulfonylurea; TDZ: thiazolidine; nothing: without medication.
2018, March 2019, June 2019, and July 2019) and the last three months during the COVID-19 pandemic (May 2019, March 2020, June 2020, and July 2020). March 2020 corresponded to the period prior to the request for self-restraint, while June and July 2020 corresponded to the periods right after the end of self-restraint.

Study 2: HbA1c levels between May 2019 and July 2020 were also compared by self-monitoring of blood glucose (SMBG) levels to assess the effect of SMBG on plasma glucose control during the period of self-restraint.

**Statistical analyses**

All data were expressed as mean ± standard deviation. Data were analyzed using one-factor analysis of variance to compare the means of all groups. To determine the statistical differences between the means, the Tukey-Kramer multiple-comparisons procedure from the InStat 2.00 program was used. A p value of <0.05 was considered significant. The change in HbA1c levels was analyzed using a paired t-test in the second clinical study.

**Results**

The HbA1c levels in May 2018, March 2019, June 2019, July 2019, May 2019, March 2020, June 2020, and July 2020 were 7.32 ± 1.23, 7.44 ± 1.20, 7.16 ± 1.06, 7.01 ± 1.05, 7.23 ± 1.06, 7.45 ± 1.18, 7.15 ± 1.07, and 7.11 ± 1.17, respectively. Results showed that HbA1c levels during the period of self-restraint were not significantly different from those in other periods. These values are also shown in Figure 2. Similarly, no statistically significant difference was found in the HbA1c levels between May 2019 without SMBG and May 2019 with SMBG. Additionally, no statistically significant difference was observed in the HbA1c levels between July 2020 with SMBG and July 2020 without SMBG (Figure 3).

**Discussion**

The Saku Central Hospital Advanced Care Center is located in Saku-shi, Nagano Prefecture, Japan. It has a population of around 99,000 with the following population per age group: 0–14 years, 13,000; 14–64 years, 57,000; and over 65 years, 29,000. Although the Saku-shi region has four seasons, it is extremely cold during winter season, with an average temperature of −7.5°C in mid-winter. This clinical study unexpectedly found that the request to avoid nonessential trips as a form of self-restraint during the country’s state of emergency did not affect the plasma glucose control.
in patients with DM in this city. This result could be due to the unique features of the Saku region.

First, HbA1c levels in this region tend to increase during the cold winter season as a seasonal change as it is the off-season for farmers in rural areas (Figure 2). Fortunately, for patients in the Saku region, the state of emergency was declared just after the off-season for farmers. Hence, majority of patients were able to easily adapt to avoiding nonessential trips and staying at home based on the results of the medical examination conducted via patient interview. In fact, the HbA1c levels from May 2018 to July 2019 and from May 2019 to July 2020 had similar changes, as shown in Figure 2. Therefore, this confirmed that self-restrain did not affect the plasma glucose control in individuals with DM living in the Saku region.

Second, the participants’ BMIs in July 2019 and July 2020 were 24.4 ± 3.6 and 24.4 ± 3.6, respectively, which did not fall under the obesity range and did not increase during the state of emergency. Therefore, our participants did not develop severe insulin resistance before and after the state of emergency. This may also be due to the location of our hospital, which is in a rural area where the population density is relatively low and patients can easily find a suitable place to exercise without visiting the gym compared with urban areas.

Third, the HbA1c level of the participants was within 7%. This suggested that the participants had relatively good self-control. Therefore, they were able to overcome the challenges during the state of emergency by focusing on maintaining better self-control than that during an ordinary situation, leading to good plasma glucose control. In fact, this speculation corresponded to the result that HbA1c levels were not affected by the absence or presence of SMBG, as shown in Figure 3.

These three points could explain why HbA1c levels were not elevated, despite the temporary sedentary lifestyle and lack of exercise within a period of month. However, our results need to be verified in different regions, including those regions with warmer winters and big cities.

This study also has several limitations that warrant discussion. First, the study only involved 165 participants, most of whom were older adults. The results should be verified in a larger cohort. Second, the study had a selection bias due to the differences in the ethnicity, age, and sex (115 males and 45 females), and weight of the participants. If this study is replicated in the future, it should be conducted in a wider demographic area.

**Conclusion**

In conclusion, HbA1c levels did not worsen despite the request for self-restraint during the state of emergency in the Saku region. When the effect of the state of emergency due to the COVID-19 pandemic on plasma glucose control is estimated, not only the patients’ background but also the characteristics of the residential area should be considered.

**Conflict of interest:** The authors declare that they have no conflict of interest.

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