Case Report

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Interference of high dose intravenous vitamin C with blood glucose testing in a patient with COVID-19 infection

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ABSTRACT

Flash glucose monitoring system (FGMs) is an option for patients to monitor their glucose however, the presence of interfering substances can result in false blood glucose readings. The COVID-19 (SARS-2-Cov) pandemic has resulted in substantial damage to the public and currently, no effective treatment is available for this deadly disease. Intravenous vitamin C (VC) has been shown to attenuate the cytokine storm in COVID-19 infection. Studies suggest that vitamin C supplementation reduces blood glucose in diabetic patients. On the other hand, VC can affect glucose readings obtained by devices in varying degrees. Here, we present a diabetic patient diagnosed with COVID-19 infection, who had false increased blood glucose readings on FGM after VC treatment. A 45-year-old woman with T2DM was diagnosed with a COVID-19 infection. Intravenous VC at a dose of 2500mg five times was added to the standard treatment protocol due to COVID-19 pneumonia. Her flash glucose levels were consistently elevated during intravenous VC infusion and returned to her normal average values after cessation of infusion. Insulin was not given at the time of fluctuations in blood glucose readings because both fingerstick and venous blood glucose measurements at the time of VC infusion were not consistent with the FGM readings. False increase in blood glucose readings due to interfering substances should be kept in mind since correction with insulin or antidiabetics may lead to a potential for dangerous life-threatening hypoglycemic events.

Keywords: Flash glucose monitoring system, COVID-19, interference, high dose vitamin C

INTRODUCTION

Continuous glucose monitoring (CGM) is a new method that depends on interstitial glucose measurement via a subcutaneous sensor. CGM has been shown to reduce risks of hypoglycemia and hyperglycemia, glycemic variability, and improve HbA1c and patient's quality of life (1). Flash Glucose Monitoring system (FGMs), a subset of CGM, is designed as an alternative to traditional blood glucose monitoring, which allows patients to get individual blood sugar readings on demand. However, understanding the limitations of flash glucose monitoring (Abbott Freestyle Libre) due to the presence of interfering substances and the clinical status of the patient can be significant, and need to be considered when interpreting the glucose values provided. Dehydration, using high dose vitamin C (VC) or salicylic acid may lead to false readings with the system (2). The COVID-19 (SARS-2-Cov) pandemic, first reported in Wuhan, China, spreads to many countries, has resulted in substantial damage to the public. Currently, no effective treatment is available for this deadly disease. Coronaviruses increase oxidative stress that promotes cellular malfunction and ultimately results in organ failure. This process finally leads to serious cellular injury, organ failure, and death (3,4). The administration of anti-oxidizing agents along with proven conventional supportive therapies is believed to have an important role in controlling these medical situations. VC shows its antioxidant properties by the elimination of harmful reactive oxygen species, thus defending the cells from oxidative damage (5,6). It is known that high-dose VC provides a certain protection against viral infection. Intravenous VC may also attenuate the cytokine storm in the COVID-19 infection besides its antiviral properties (7). High-dose vitamin C is an example of a substance that has proven to alter blood glucose measurements on glucose devices. Here, we will discuss a type 2 diabetic patient diagnosed with COVID-19 infection, who had false increased blood glucose readings on FGM after VC treatment.

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CASE REPORT

A 45-year-old woman with T2DM was diagnosed with a COVID-19 infection. She was on metformin/sitagliptin and empagliflozin treatment and her last HbA1c and C-peptide were 8.2% and 1 ng/mL, respectively. She was on FGMs to improve her glycemic control. After diagnosed with a COVID-19 infection, she was admitted to the hospital since she had pulmonary infiltrations. Empagliflozin treatment was discontinued as recommended by the guidelines. She has started standard hydroxychloroquine (800 mg loading dose, 400 mg/day for 4 days), azithromycin (500 mg loading dose, 250 mg/day for 4 days), and oseltamivir (75 mg/day for 5 days) treatment and later inhaler treatment and, intravenous VC at a dose of 2500 mg for five times was added to the treatment protocol due to COVID-19 pneumonia. Following this, her flash glucose levels (Freestyle Libre) were consistently elevated with intravenous VC and returned to her normal average values after cessation of infusion (**Figure 1-2**). Both fingerstick and venous blood glucose measurements at the time of VC infusion were not consistent with the FGM readings. Dextrose or some other dextrose-containing fluid was not administered during hospital admission. Her diabetes medication dose was not increased and insulin was not given at the time of fluctuations in blood glucose readings. Her glucose levels returned to her normal average levels after discontinuation of VC treatment. She did not need an intensive care unit for COVID-19 infection. She was discharged on the 6th day of admission after recovery of COVID-19 infection.

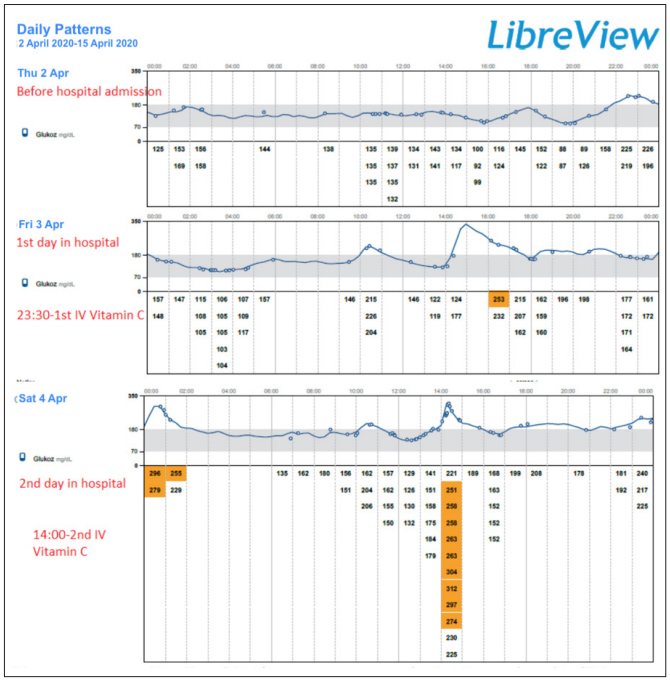

Figure 1. Flash glucose levels before hospital admission and 1st and 2nd days of hospital stay

DISCUSSION

Currently, no suitable vaccine or specific antivirals are available for COVID-19. Acute respiratory distress syndrome (ARDS) is considered as the virtual reason for mortality (7). Coronaviruses may lead to significant lung damage and death from ARDS via the activation of pulmonary capillary endothelium, infiltration by neutrophils, and enhanced oxidative stress as a result of "cytokine storm" (3,4). Enhanced oxidative stress is an important trigger in lung damage leading to acute lung failure with remarkably increased morbidity and mortality (8).

FGMs (Abbott Freestyle Libre) mechanically measures and constantly reads the glucose concentration in the interstitial fluid glucose collected by an inserted sensor filament just beneath the skin and record changes in an individual's glucose levels up to 14 days; this process reduces the necessity for countless and painful finger pricks currently used for glucose monitoring. FGMs are delicate and tolerable, which efficiently improve glycemic control (2). FGM systems can be exposed to heterograde interference from various drugs and nondrug compounds, such as acetaminophen, salicylic acid, and VC (9,10). It is known that vasopressor drugs and severe acute illness may also interfere with glucose readings, however, the patient was not admitted to the intensive care unit.

VC shows its antioxidant properties by the elimination of harmful reactive oxygen species, thus defending the cells from oxidative damage. VC at high concentrations (1,000–5,000 mmol/L) is administrated by intravenous access. According to a randomized cross-over study, supplementation with vitamin C tablets two times a day (2×500 mg/d, quite higher than the daily recommended dose) decreased postprandial hyperglycemia in diabetics

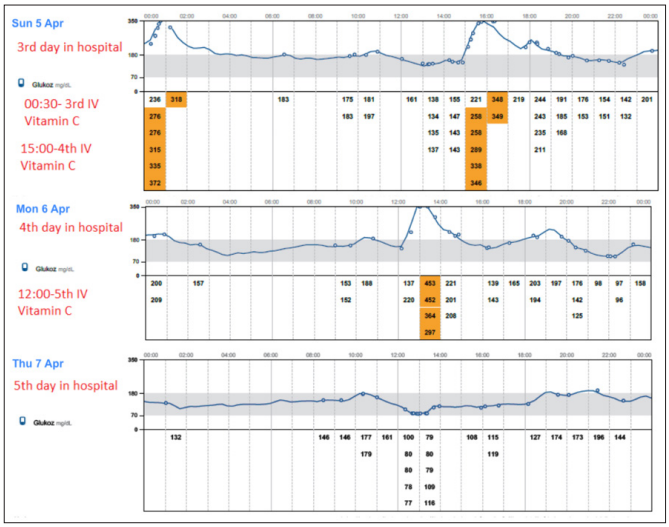

Figure 2. Flash glucose levels at the 3rd, 4th, and 5th days of hospital admission

(11). A meta-analysis showed vitamin C supplementation has beneficial effects on glycaemic control in diabetic patients (12). On the other hand, VC can variably affect glucose devices. The oxidization of ascorbic acid at the electrode surface, leading to more electrons and current production, which leads to a false increase in blood glucose reading (5). The antiviral activities of VC were known for decades and high-dose intravenous VC treatment was shown to be effective in patients with sepsis, ill with severe influenza, receiving mechanical ventilation (7). In addition to direct antiviral properties, intravenous VC may also attenuate the cytokine storm in the COVID-19 infection. Pneumonia caused by COVID-19 may lead to severe lung injury and prevent sufficient pulmonary oxygen enter that results in ARDS, with increased morbidity and mortality rate. Oxidative stress-induced by COVID-19 leads to cellular dysfunction and finally results in organ failure. ARDS is considered the main trigger of COVID-19's induced lung failure. An increase in oxidative stress by the production of free radicals and cytokines eventually causes critical cellular damage, organ dysfunction, and death. Anti-oxidants use with proven supportive therapies is considered to play a significant role in disease control. Intravenous VC and other antioxidant agents can be used for ARDS. Additionally, high dose intravenous VC is well-tolerable and effective (6).

In most cases of mild COVID-19 infection, antidiabetic medications should be followed as usual, except for sodium-glucose co-transporter-2 (SGLT2) inhibitors, which can lead to an increase in the risk of dehydration and diabetic ketoacidosis, necessitating careful renal function monitoring. Since there is a risk for lactic acidosis with metformin, discontinuation is suggested during hospitalization in case of moderate or severe disease (13). Our patient had mild disease and only empagliflozin treatment was discontinued.

Because no vaccine or specific antiviral medicine is available presently for this mortal disease, high-dose VC is safe and may be an option to mitigate COVID-19 associated pulmonary involvement. Correction of false increase in blood glucose readings as a result of high-dose VC may create a potential for dangerous life-threatening hypoglycemic events. Clinicians and patients need to be aware of the susceptibility of the blood glucose monitoring system to interfering substances.

ETHICAL DECLARATIONS

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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