Journal of Anesthesia (2021) 35:586–590
https://doi.org/10.1007/s00540-021-02965-1

CLINICAL REPORT

Glucose control using an artificial pancreas in a severe COVID-19 patient on extracorporeal membrane oxygenation: a case report

Takuya Hinoue[1] · Tomoaki Yatabe[2] · Himuro Fujiwara[1] · Osamu Nishida[1]

Received: 18 May 2021 / Accepted: 22 June 2021 / Published online: 24 June 2021

Abstract

The usefulness and safety of continuous glucose monitoring (CGM) systems in adult patients with severe coronavirus disease (COVID-19) have been reported. Using CGM might reduce the exposure patients and healthcare workers to COVID-19 and limit the use of personal protective equipment during the pandemic. CGM devices measure glucose in the subcutaneous interstitial fluid, but the accuracy of this technique has not been established in critically ill patients. The artificial pancreas, STG-55 (Nikkiso, Tokyo), is a closed-loop device that conducts continuous blood glucose monitoring using a peripheral vein. We used the STG-55 for glucose control in a 60-year-old woman with severe COVID-19 admitted to the intensive care unit. Due to severe respiratory failure, the patient was intubated, and extracorporeal membrane oxygenation was introduced. Because she had hyperglycemia despite high-dose intravenous insulin therapy, we decided to use STG-55 for glucose control. The STG-55 safely titrated the insulin infusion and monitored glucose levels. Fifty-six hours after adopting the STG-55, it was removed because the blood sampling failed. No episodes of hypoglycemia were observed despite deep sedation during this period. In conclusion, this case demonstrates the potential utility of an artificial pancreas in patients with severe COVID-19.

Keywords Artificial pancreas · Continuous glucose monitoring · COVID-19 · Extracorporeal membrane oxygenation

Introduction

In patients hospitalized with coronavirus disease (COVID-19), dexamethasone use has been reported to yield lower 28-day mortality among those who received either invasive mechanical ventilation or oxygen alone [1]. The use of glucocorticoids can lead to severe hyperglycemia, associated with increased mortality in hospitalized patients with COVID-19 [2]. Constant glucose monitoring can potentially increase the exposure of healthcare workers to COVID-19. To avoid this situation, studies have evaluated and reported the usefulness and safety of continuous glucose monitoring (CGM) systems [3–7]. CGM devices measure glucose in the subcutaneous interstitial fluid; however, this measurement is affected by several factors in critically ill patients [8]. The artificial pancreas, STG-55 (Nikkiso Co. Ltd., Tokyo, Japan), is a closed-loop device that performs continuous blood glucose monitoring using a peripheral vein and maintains a target blood glucose level by administering insulin and glucose intravenously [9]. Herein, we report the case of a critically ill patient with COVID-19 for whom this device—STG-55—was used for monitoring and maintenance of glucose levels.

Case presentation

Written informed consent was obtained from the patient's husband for the publication of this case report.

A 60-year-old woman with chief complaints of fever, dyspnea, and changes in smell and taste perception was admitted to a local hospital. She was diagnosed with COVID-19 and received intravenous steroid injections (dexamethasone, 6.6 mg/day) and favipiravir. Because hypoxic respiratory failure progressed rapidly, she was intubated and transferred to our hospital.

✉ Tomoaki Yatabe
yatabe.tomoaki@katch.ne.jp

[1] Department of Anesthesiology and Critical Care Medicine, Fujita Health University School of Medicine, 1-98 Dengakugakubo, Kutsukake-cho, Toyoake, Aichi 470-1192, Japan

[2] Department of Anesthesiology and Intensive Care Medicine, Nishichita General Hospital, 3-1-1, Nakanoike, Tokai, Aichi 477-8522, Japan

She was started on parenteral nutrition therapy on day 1 of hospitalization at our institution and on enteral nutrition therapy the following day. The total calories of nutrition provided was gradually increased. Blood glucose levels were measured by nurses eight times a day. In our hospital, blood samples from COVID-19 patients are obtained via the arterial line in the isolation room, and the samples were then transferred outside the isolation room to measure blood glucose levels using an arterial gas analyzer. The patient's blood glucose levels began to increase steadily and peaked at 321 mg/dL on day 3, after which intravenous insulin therapy was initiated.

On day 8, due to poor oxygenation on mechanical ventilation, we established right atrial drainage via the right femoral vein and a right atrial return through the right internal jugular vein, and veno-venous extracorporeal membrane oxygenation (ECMO) was introduced. The patient received intravenous midazolam (10 mg/h), dexmedetomidine (52 μg/h), and fentanyl (75 μg/h) for sedation. The Richmond Agitation-Sedation Scale (RASS) score was − 5. At this point, she received 707 kcal of parenteral nutrition and 509 kcal of enteral nutrition per day. Her glucose level was 223 mg/dL despite insulin therapy at a dose of 3.8 U/h. Thus, we decided to use the STG-55 for glucose control.

A 20-gauge peripheral catheter was inserted into an arm vein under ultrasound guidance because the peripheral vein was invisible due to edema. The STG-55 was then connected, and continuous blood glucose measurement and automatic glucose control were started (Fig. 1). Intensivists and nurses were able to confirm the patient's blood glucose level by looking at the monitor of the STG-55 through the window of an adjacent room. Insulin was infused from the STG-55 automatically when the blood glucose level reached 180 mg/dL or higher, and glucose was infused from the device when the level fell to 100 mg/dL or lower. The patient's blood glucose levels were generally controlled between 150 and 220 mg/dL because insulin was administered at a maximum dose of approximately 10 U/h from the STG-55. Blood glucose level measured by arterial blood gas analyzer was almost similar to that measured by the STG-55. The average percent difference between STG-55 and arterial blood gas analyzer measurements was 9.2% (Fig. 2).

On day 11, the STG-55 was removed because blood sampling failed frequently. During the 3 days that the artificial pancreas was used, hypoglycemia did not occur despite deep sedation. After the removal of the STG-55, intravenous insulin therapy was initiated again at a dose of 1.8 U/h. The insulin dose was appropriately titrated by the intensivist, targeting a blood glucose level of 100–200 mg/dL. However, her blood glucose level began to increase steadily and peaked at 275 mg/dL despite insulin therapy (4 U/h) on day 3 after removing STG-55.

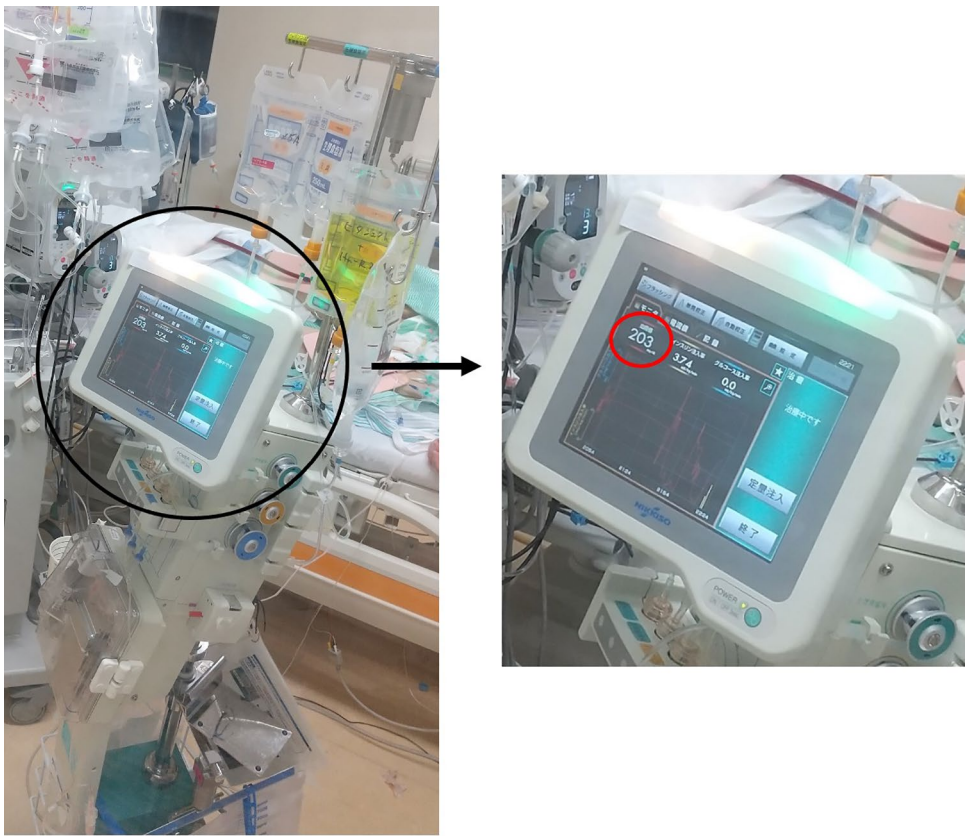

Fig. 1 Bedside artificial pancreas with a closed-loop system (STG-55). This photograph was taken from an adjacent room through a glass window. Blood glucose levels are continuously monitored and displayed (red circle)

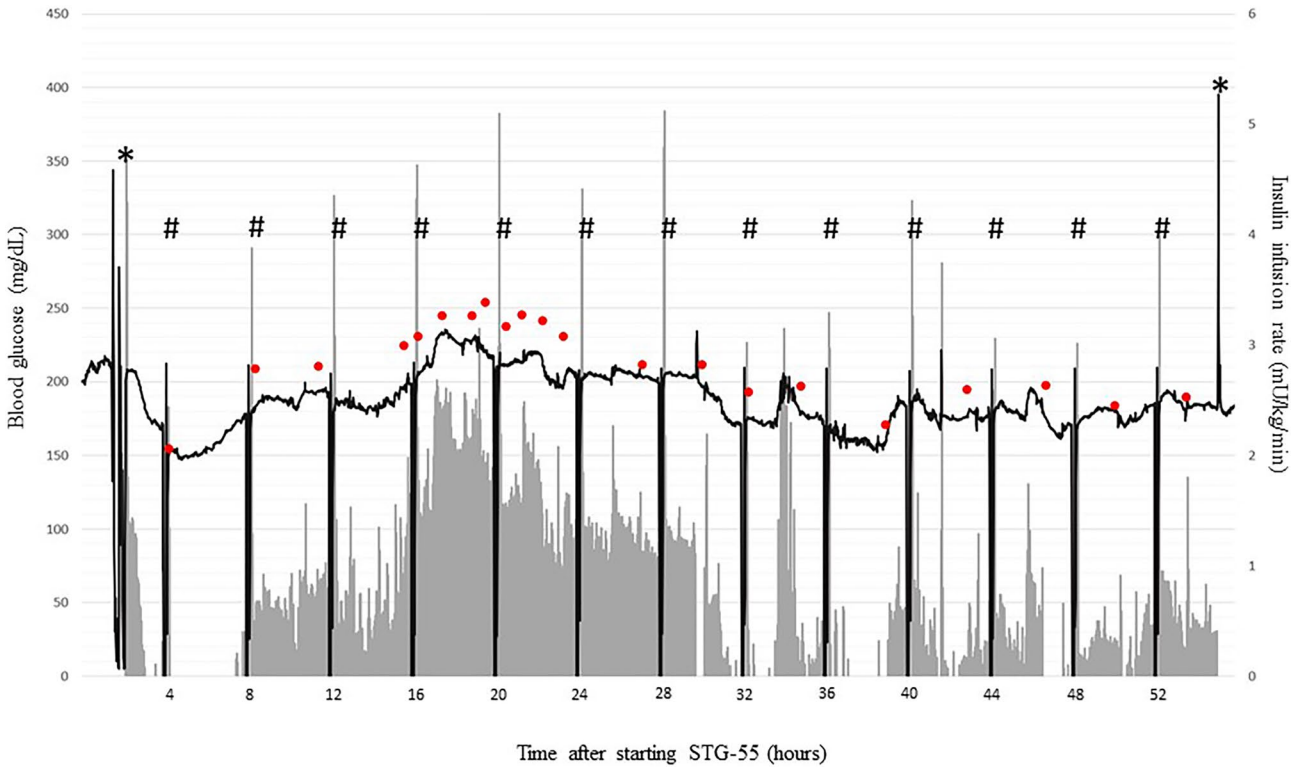

Fig. 2 Blood glucose levels controlled by the artificial pancreas (STG-55). The black line indicates blood glucose levels as measured by the STG-55, and the black dot indicates blood glucose levels as measured by blood sampling via an arterial line. The vertical gray line indicates insulin infusion rate. Continuous blood glucose monitoring was interrupted when blood sampling temporarily became impaired due to peripheral vein collapse or catheter tip occlusion (*). Automatic calibration was performed every 4 h (#). The STG-55 was eventually removed because of repeated blood sampling failure

Discussion

The United States Food and Drug Administration issued a policy to expand the availability and capability of noninvasive remote monitoring devices during the pandemic [10]. Previous studies have shown that CGM use might be feasible and reliable in reducing the frequency of point-of-care glucose testing, patient and healthcare worker exposure, and personal protective equipment (PPE) use during the pandemic [3, 4]. Although the usefulness of CGM has been reported, the measured glucose levels have been inaccurate because they are often influenced by agents commonly used in critically ill patients, such as severe COVID-19 patients [8]. In fact, van Hooijdonk et al. conducted a prospective study to assess the point accuracy and reliability of a device designed for continuous real-time monitoring of the interstitial glucose level in a mixed medical-surgical ICU [11]. They concluded that the device had relatively low accuracy for glucose measurements in critically ill patients and that an interstitial glucose sensor system could not replace blood glucose level measurements in these patients. Several guidelines have described that subcutaneous blood sampling should be interpreted with caution [12, 13].

In contrast, when using STG-55, a 20-G catheter was placed into a peripheral vein and a measurement tube for the artificial pancreas was inserted into the lumen of the catheter. Continuous blood sampling was performed through the tube at a rate of 2 mL/h. The collected blood samples were passed through a glucose sensor, which displayed glucose levels in real-time after measuring them using the glucose oxidase method [14]. In addition, by achieving the target blood glucose levels preemptively, the optimal doses of insulin and/or glucose were determined every minute based on the device's algorithm, and the management of blood glucose levels was performed by the artificial pancreas pump, which injected insulin and/or glucose automatically. Previous studies have shown that STG-55 improves hyperglycemia and glycemic variability without causing hypoglycemia after cardiac surgery [15, 16]. Mibu et al. showed that adopting the use of an artificial pancreas for the management of blood glucose in the ICU reduces the number of blood samples and overall workload for nurses when compared to using the sliding-scale method [17]. Previous studies have suggested that the use of CGM in critically ill patients with COVID-19 might reduce the frequency of blood sampling required and limit COVID-19 exposure risk to patients and

healthcare workers [3, 4]. From these viewpoints, adopting the STG-55 for COVID-19 patients with deep sedation, such as those requiring ECMO, might reduce the number of admissions in the isolation room, exposure of healthcare workers to COVID-19 infection, and usage of PPE.

Interrupted blood sampling is a major problem when using the STG-55; its incidence is reported to be 5.2% [18]. This problem occurred in our case due to collapse of the peripheral vein and occlusion of the catheter, both of which can occur in some patients admitted to the ICU. Insertion of a new intravenous catheter is required in such cases. Furthermore, the STG-55 cannot be used for blood glucose control if a catheter cannot be placed into a peripheral vein because of edema or obesity. Central venous (CV) catheters cannot be used because the length of the measurement tube of the STG-55 is too short when compared to the length of the CV catheter. In the present case, the peripheral vein was invisible due to edema, and the catheter had to be inserted under ultrasound guidance. Therefore, improved measurement methods, such as blood sampling from a CV catheter, are required.

This case report had several limitations. First, we did not measure the time or frequency of contact between healthcare workers and patients for blood glucose control. In addition, there was no change, at least, in the frequency of arterial blood sampling before, during, and after the use of STG-55 because arterial blood gas analysis was performed every 4 h during ECMO in our hospital. Therefore, it is not clear whether the introduction of the STG-55 reduced contact between patients and healthcare workers. Second, the STG-55 was only used for 3 days. Thus, we could not conclude whether the introduction of the STG-55 will improve the prognosis of patients with COVID-19. Finally, it was difficult for us to manage blood glucose control after removing STG-55. We recognize blood glucose management after STG-55 removal, such as utilizing insulin infusion rate information obtained while using the STG-55, as a future issue.

In conclusion, this case demonstrates the potential utility of an artificial pancreas in patients with severe COVID-19.

References

1. Horby P, Lim WS, Emberson JR, Mafham M, Bell JL, Linsell L, Staplin N, Brightling C, Ustianowski A, Elamahi E, Prudon B, Green C, Felton T, Chadwick D, Rege K, Fegan C, Chappell LC, Faust SN, Jaki T, Jeffery K, Montgomery A, Rowan K, Juszczak E, Baillie K, Haynes R, Landray MJ. Dexamethasone in hospitalized patients with Covid-19. N Engl J Med. 2021;384:693–704.
2. Zhu L, She ZG, Cheng X, Qin JJ, Zhang XJ, Cai J, Lei F, Wang H, Xie J, Wang W, Li H, Zhang P, Song X, Chen X, Xiang M, Zhang C, Bai L, Xiang D, Chen MM, Liu Y, Yan Y, Liu M, Mao W, Zou J, Liu L, Chen G, Luo P, Xiao B, Zhang C, Zhang Z, Lu Z, Wang J, Lu H, Xia X, Wang D, Liao X, Peng G, Ye P, Yang P, Yuan Y, Huang X, Guo J, Zhang BH, Li H. Association of Blood Glucose Control and Outcomes in Patients with COVID-19 and Pre-existing Type 2 Diabetes. Cell Metab. 2020;31:1068–77.
3. Sadhu AR, Serrano IA, Xu J, T Nisar T, Lucier J, Pandya AR, Patham B. Continuous glucose monitoring in critically Ill patients with COVID-19: results of an emergent pilot study. J Diabetes Sci Technol. 2020;14:1065-73
4. Agarwal S, Mathew J, Davis GM, Shephardson A, Levine A, Louard R, Urrutia A, Perez-Guzman C, Umpierrez CE, Peng L, Pasquel FJ. Continuous glucose monitoring in the intensive care unit during the COVID-19 pandemic. Diabetes Care. 2021;44:847–9.
5. Davis GM, Faulds E, Walker T, Vigliotti D, Rabinovich M, Hester J, Peng L, McLean B, Hannon P, Poindexter N, Saunders P, Perez-Guzman C, Tekwani SS, Martin GS, Umpierrez G, Agarwal S, Dungan K, Pasquel FJ. Remote continuous glucose monitoring with a computerized insulin infusion protocol for critically Ill patients in a COVID-19 medical ICU: proof of concept. Diabetes Care. 2021;44:1055–8.
6. Chow KW, Kelly DJ, Gupta R, Miller JD. Use of continuous glucose monitoring to assess parenteral nutrition-induced hyperglycemia in an adult patient with severe COVID-19. JPEN J Parenter Enteral Nutr. 2021;45:208–11.
7. Ushigome E, Yamazaki M, Hamaguchi M, Ito T, Matsubara S, Tsuchido Y, Kasamatsu Y, Nakanishi M, Fujita N, Fukui M. Usefulness and safety of remote continuous glucose monitoring for a severe COVID-19 patient with diabetes. Diabetes Technol Ther. 2021;23:78–80.
8. Scrimgeour LA, Potz BA, Sellke FW, Abid MR. Continuous glucose monitoring in the cardiac ICU: current use and future directions. Clin Med Res (N Y). 2017;6:173–6.
9. Tsukamoto Y, Kinoshita Y, Kitagawa H, Munekage M, Munekage E, Takezaki Y, Yatabe T, Yamashita K, Yamazaki R, Okabayashi T, Tarumi M, Kobayashi M, Mishina S, Hanazaki K. Evaluation of a novel artificial pancreas: closed loop glycemic control system with continuous blood glucose monitoring. Artif Organs. 2013;37:E67-73.
10. U.S. Department of Health and Human Services, Food and Drug Administration, Center for Devices and Radiological Health. Enforcement Policy for Non-Invasive Remote Monitoring Devices Used to Support Patient Monitoring During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency (Revised) Guidance for Industry and Food and Drug Administration Staff. https://www.fda.gov/media/136290/download. Accessed June 14, 2021.
11. van Hooijdonk RT, Leopold JH, Winters T, Binnekade JM, Juffermans NP, Horn J, Fischer, van Dongen-Lases EC, Schultz MJ. Point accuracy and reliability of an interstitial continuous glucose-monitoring device in critically ill patients: a prospective study. Crit Care. 2015;19:34.
12. Rhodes A, Evans LE, Alhazzani W, Levy MM, Antonelli M, Ferrer R, Kumar A, Sevransky JE, Sprung CL, Nunnally ME, Rochwerg B. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock: 2016. Intensive Care Med. 2017;43:304–77.
13. Nishida O, Ogura H, Egi M, Fujishima S, Hayashi Y, Iba T, Imaizumi H, Inoue S, Kakihana Y, Kotani J, Kushimoto S. The Japanese clinical practice guidelines for management of sepsis and septic shock 2016 (J-SSCG 2016). J Intensive Care. 2018;6:7.
14. Mibu K, Yatabe T, Yamasaki F, Kitagawa H, Munekage M, Namikawa T, Hanazaki K. Questionnaire survey on the use of a novel artificial pancreas by intensive care unit nurses. J Artif Organs. 2015;18:162–5.
15. Aizawa K, Muraoka A, Kurumisawa S, Akutsu H, Sugaya A, Uesugi S, Kawahito K. Artificial endocrine pancreas with a closed-loop system effectively suppresses the accelerated hyperglycemic status after reperfusion during aortic surgery. Gen Thorac Cardiovasc Surg. 2021;69:14–8.

16. Shin U, Naoko H, Michinori T, Yuya K, Yuka S, Yuki N, Motoharu K, Soichiro H, Mitsuo K, Yu Y, Tokito K, Satoru K, Kazuki D, Tetsuya O, Hirohisa M, Nobuhiko M, Takeshi O. Utility of bedside artificial pancreas for postoperative glycemic control in cardiac surgery. J Artif Organs. (in press)
17. Mibu K, Yatabe T, Hanazaki K. Blood glucose control using an artificial pancreas reduces the workload of ICU nurses. J Artif Organs. 2012;15:71–6.
18. Yatabe T, Yamazaki R, Kitagawa H, Okabayashi T, Yamashita K, Hanazaki K, Yokoyama M. The evaluation of the ability of closed-loop glycemic control device to maintain the blood glucose concentration in intensive care unit patients. Crit Care Med. 2011;39:575-8