Early Observation and Mitigation of Challenges in Diabetes Management of COVID-19 Patients in Critical Care Units

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Clinical studies of patients with coronavirus disease 2019 (COVID-19) have found diabetes to be a major risk factor for disease severity and mortality (1,2). One new study showed that COVID-19 patients with diabetes and/or uncontrolled hyperglycemia had a longer length of stay and markedly higher mortality than patients without diabetes or uncontrolled hyperglycemia (3). Given rising numbers of cases of patients with COVID-19 and diabetes, understanding their interaction on insulin requirement and glycemic control is prudent. As seen in other infections, blood glucose starts to rise with the beginning of clinical symptoms. By the time the patient is admitted to the intensive care unit (ICU), insulin requirement is at its highest, and blood glucose remains high if not properly managed. Treating physicians face several challenges that need careful attention. Here are some of the potential issues that we encountered in our ICUs and their suggested mitigating plans. We thought that sharing them at this early stage is important.

Continuous tube feeding in patients on artificial ventilation. Continuous tube feeding is the ideal nutrition method for intubated patients with COVID-19. Typically, this has been managed by a combination of continuous intravenous insulin infusion and frequent glucose testing to improve glycemic control and reduce glucose variability to the minimum in order to reduce mortality in ICU (4). However, this method significantly increases contact frequency by health care providers, especially ICU nurses. The other common challenge of continuous tube feeding is the looming risk of hypoglycemia when tube feeding is interrupted, a frequent situation in patients with COVID-19 treated in ICUs. The main aims of a safe and effective insulin regimen are to reduce contact frequency, reduce glucose variability, minimize risk of severe hypoglycemia, and improve overall glycemic control. Table 1 shows the pros and cons of several insulin regimens that have been tried in ICUs and their mitigation protocols to optimize insulin coverage in patients on continuous tube feeding. Hospitalists are advised to pick the right insulin plan that fits their prime target. As shown, if the prime target is to reduce contact frequency, an NPH-Regular insulin regimen is preferred. However, if the goal is to reduce glycemic variability to its minimum, intravenous insulin infusion with a relaxed target is preferred. To reduce high insulin exposure for a prolonged period when long-acting insulin regimen is selected, part of insulin coverage may be given as fixed doses of Regular insulin every six hours.

Intravenous corticosteroids. Many critical care units are using a protocol of injecting hydrocortisone 400 mg b.i.d. for the first day followed by 200 mg b.i.d. for 4 days to suppress inflammation in the mildly symptomatic cases. When severe shortness of breath occurs and hypoxemia requires oxygen by nasal canula at a rate of ≥4 L per min, a loading dose of methylprednisolone 80 mg is usually given followed by 40 mg every 12 h for at least 7 days or, alternatively, hydrocortisone 50 mg every 6 h is given with the aim of dampening the cytokine storm that frequently occurs in COVID-19 (5,6). Such high doses of steroids raise blood glucose even higher, with readings as high as 400–500 mg/dL. In our hospital, we found that adding NPH insulin in a dose of 20–30 units in the morning in addition to the current insulin regimen is frequently sufficient to minimize the impact of steroids on blood glucose values. This dose is usually stopped when steroid therapy is discontinued.

Factitious high glucose readings by finger sticks. Several ICUs, including ours, are using high doses of intravenous vitamin C, which was shown in several studies to have beneficial effects on blood pressure, infections, bronchoconstriction, atrial fibrillation, and acute kidney injury and to shorten the length of

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Table 1—The pros and cons of several insulin regimens used in the ICU for patients with diabetes and COVID-19 on continuous tube feeding

	Insulin infusion, i.v.	Basal insulin q12h + Regular insulin q6h for correction	NPH insulin q8h + Regular insulin q8h for correction	Regular insulin q6h
Contact frequency/day	24	4	3	4
Glycemic control	++++ (best)	+++	++	+
Glycemic variability	+ (lowest)	++	+++	++++
Risk of hypoglycemia upon TF interruption	—	++++	+++	++
Mitigation protocol	Relax the target blood glucose and test q2–4h	Reduce doses of basal insulin and add fixed doses of Regular insulin q6h plus correction by Regular insulin q6h Infuse D10W at same rate if TF is interrupted for >2 h	No mitigation is required Infuse D10W at same rate if TF is interrupted for >2 h	No mitigation is required

D10W, dextrose 10% in water; TF, continuous tube feeding.

stay in the ICU (7). The common protocol is to inject 3 g of vitamin C intravenously every 6 h for 7 days. Such a high dose of ascorbic acid was shown to factitiously increase blood glucose values measured by glucose meters (8). This may mislead treating physicians and may result in overestimation of insulin doses and possible hypoglycemia. Testing plasma glucose at the same time as finger sticks for 1–2 times may explore the excursion difference between the two values that may be considered when making insulin decisions.

Interference of hypoxemia, acetaminophen, and albuterol with continuous glucose monitoring. Continuous glucose monitoring (CGM) with or without insulin infusion pumps or hybrid closed-loop insulin delivery systems was tried successfully in ICUs (9). However, hypoxemia and possible reduction in peripheral perfusion as seen in COVID-19 may shed some doubt on the reliability of measuring glucose in interstitial fluid. Acetaminophen is a commonly used antipyretic in COVID-19 patients, and albuterol is a frequently used bronchodilator in these cases. It is known that paracetamol and albuterol interfere with CGM readings, so great precaution is needed when interpreting glucose values from CGM (10,11).

Use of hybrid closed-loop insulin infusion system. We have observed two cases of patients with type 1 diabetes who were previously treated with insulin through t:slim Control IQ hybrid closed-loop system prior to ICU admission. We decided to continue using it in the ICU since glucose calibration is not required and patients' feeding is always continuous without boluses, with the aim of reducing contact frequency and glucose variability. We noticed optimal glycemic levels with minimal variability, but since these cases are limited and considering CGM interference, it is difficult and too early to draw any solid conclusion on continuation of using it in patients with COVID-19 managed in ICUs.

Although it is a challenge to manage diabetes in COVID-19 patients admitted to ICUs, good glycemic control is possible and may help in reducing complications, length of stay in the ICU, and possibly mortality. These observations may draw our attention to several knowledge gaps that may need further studies.

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