Remote Glucose Monitoring System in Hospitalized Patients With Diabetic Ketoacidosis (DKA)

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Remote glucose monitoring using the Dexcom G6 Continuous Glucose Monitoring (CGM) System in hospitalized patients with diabetic ketoacidosis (DKA)

Study Purpose and Rationale:

We propose to study use of Continuous Glucose Monitoring (CGM)for glucose monitoring in patients with DKA which would enable the treatment of hemodynamically stable DKA patients outside of intensive care units (ICU) thereby saving ICU beds a precious resource which have become extremely scarce resource during COVID-19 pandemic (1). In most hospitals, protocols for treatment of patients with diabetic ketoacidosis (DKA) require capillary point of care (POC) glucose testing every 1-2 hours (2) . Often, patients need to be transferred to the intensive care units (ICU) for frequent fingerstick glucose monitoring in order to safely administer intravenous insulin to treat the DKA. During the COVID-19 pandemic, this need to transfer patients to the intensive care unit (ICU) for treatment of DKA and the requirement for nurses to enter the room every 1-2 hours has contributed to scarcity of critical care unit beds and shortage personal protective equipment (PPE) Additionally, COVID-19 patients have been prone to develop DKA which has further increased the need for ICU beds (3, 4). Therefore, methods to safely and effective treat patients with DKA outside of ICU setting represent a common and pressing need.

Continuous glucose monitoring (CGM) is widely used in the outpatient setting but its use is still investigational in the inpatient setting. Several studies showed improvement in detection of hyperglycemic and hypoglycemic episodes with the use of CGM when compared to fingerstick point of care (POC) glucose testing in both the ICU and non-ICU setting (5-8). The FDA has allowed use of DEXCOM G6 CGM in hospitalized patients during the COVID-19 pandemic (9). In a recent pilot study performed during the COVID-19 pandemic done in hospitalized patients in the perioperative period, DEXCOM G6 CGM showed a mean absolute relative difference (MARD) of 9.4% compared to point of care (POC) glucose measurements (10). Use of continuous glucose monitoring has not been reported in hospitalized patients with DKA. The DEXCOM G6 CGM (https://www.DEXCOM G6.com/) provides glucose levels in real time, as well as glucose trends, and alarms if glucose levels are in hypoglycemic or hyperglycemic range. These safety features can decrease the risk of hypoglycemia when patients with DKA are being treated with insulin infusion. Furthermore, the DEXCOM G6 CGM is labeled as an “integrated continuous glucose monitoring system” which can reliably and securely transmit glucose data to digital devices allowing remote monitoring of glucose levels by multiple care team members without entering patient’s room and thus reducing the number of healthcare contact and use of personal protective equipment (PPE). If CGM is shown to be non-inferior to fingerstick glucose monitoring (measured by time to resolve DKA, incidence of hypoglycemia) in patients with DKA, then hemodynamically stable non-intubated DKA patients would not have to be transferred to the ICU for frequent fingerstick glucose testing as is now being done. Instead, these patients could be treated and monitored with CGM on the stepdown unit. This would help reallocate critical care unit beds, save time and effort for the nurses and help conserve PPE.

Study Design:

Retrospective Quality Improvement Data

In January 2021 during COVID 19 pandemic, we launched a quality improvement project with goal to treat non-critically ill DKA patients outside of ICU setting in order to reallocate ICU beds for critically ill patients at New York Presbyterian Hospital /Columbia University Irving Medical Center. Before this quality improvement project, DKA patients were treated in the ICU setting because the DKA protocol requires hourly fingerstick glucose monitoring, which is considered higher level of care and not appropriate for stepdown unit or medical/surgical wards. During this quality improvement project, we monitored glucose levels remotely with continuous glucose monitoring (CGM) device DEXCOM G6 thus eliminating the need for hourly fingerstick glucose testing. Therefore, patients with DKA whose glucose levels have been monitored via DEXCOM G6 CGM have been treated in the stepdown unit instead of the ICU setting where glucose levels are monitoring hourly via fingerstick point of care glucose testing. We enrolled 48 patients (with additional 2 patients who had glucose levels monitored with CGM but were treated in the ICU setting therefore will not be used for this analysis).

Study participants were not being recruited and asked for their participation; non-critically ill DKA patients who presented in DKA had glucose levels monitored via CGM. Given that the recommended hourly fingerstick checks needed for treatment could not be performed on the stepdown unit and only in the ICU, the Dexcom G6 CGM device eliminated the need for hourly fingerstick checks and thus removed the barrier for patients being admitted to stepdown. Once the number of COVID cases decreased and ICU beds were more readily available, the hospital returned to practicing the pre-COVID standard of care, which was admitting DKA patient to the ICU for hourly glucose monitoring and we stopped enrolling patients for this retrospective quality improvement project

We propose to study outcomes of DKA patients who had glucose levels monitored with DEXCOM G6 CGM treated in the stepdown unit. The primary outcome is time to resolution of metabolic acidosis. Secondary outcomes are length of ICU stay, length of hospital stay, frequency of hypoglycemic episodes defined as glucose level <70 mg/dl and cost savings

Prospective Study

The prospective part of this study will involve recruiting patients in the Emergency Department and offering them the opportunity to use DEXCOM G6 CGM instead of hourly fingerstick point of care glucose testing . We will enroll additional 50 non-critically ill DKA patients who will have glucose levels monitored via DEXCOM CGM and be treated in the stepdown unit. The primary outcome is time to resolution of metabolic acidosis. Secondary outcomes are length of ICU stay, length of hospital stay, frequency of hypoglycemic episodes defined as glucose level <70 mg/dl and cost savings.

Inclusion Criteria:

age >18, AG>20 (normal is 5-17) with bicarbonate <19 (normal is 19-27), positive urine ketones or beta hydroxybutyrate >0.3 (normal is <0.27)

glucose level >250 mg/dl on presentation to the ED

Exclusion criteria:

hypotension (BP below 80/60), require pressor therapy, or have any contraindication for utilizing Dexcom CGM ,, altered mental status, lack of decision making capacity, mechanical ventilation or non-invasive ventilation, chronic kidney disease with GFR <30 including patients with hemodialysis, pregnancy, other clinical reason for admission to the intensive care unit (ICU) , are excluded from study participation

Provider Survey/nurses satisfaction

We will study nurses' satisfaction evaluating remote glucose monitoring in DKA patients using DEXCOM G6 CGM by administering an anonymous online survey. We will evaluate nurses' satisfaction only for the prospective part of the study.

Statistical Procedures:

The primary outcome for this study is the time to resolution of DKA. We will compare time to resolution of the DKA of patients who had glucose levels monitored via DEXCOM G6 CGM and treated in the stepdown unit (both those enrolled in the retrospective study and those who will be enrolled in the prospective study) to DKA patients who had glucose levels monitored hourly via fingerstick (and not CGM) and treated in the ICU setting.

We will perform a non-inferiority trial to study whether monitoring glucose levels via CGM in DKA patients treated in the stepdown unit is not inferior to DKA treated patients in the ICU setting with hourly fingerstick glucose monitoring.

For a noninferiority trial, based on what we have previously observed for the time to resolution of DKA, and a noninferiority margin of 1/2 the SD, we estimate that a sample size of 98 patients per group will have a 90% power to determine noninferiority at an alpha level of 0.05. Since we enrolled 48 patients in the retrospective part of the study, we will need additional 50 patients enrolled in the prospective part of the study to have 90% power and a noninferiority at an alpha level of 0.05. We plan a conservative approach where we will enroll additional 50 DKA patients who will have glucose levels monitored via CGM. We will compare with the historical control using 1:1 matching, thus will collect historical control data which include DKA patients treated for DKA in the ICU setting with hourly fingerstick glucose monitoring.

We will perform linear regression (for patients enrolled in both retrospective and prospective part of the study) to learn what clinical factors are associated with length of time to the DKA resolution. Then we will use propensity matching for historical control group (DKA patients treated in the ICU setting with glucose levels monitored via hourly fingerstick glucose levels).

To study the frequency of hypoglycemic episodes (<70 mg/dl) in patients from both prospective and retrospective study; we will use CGM glucose data stored manufacture's web based software : Clarity.

We will also evaluate frequency of hypoglycemic episodes (glucose level <70%) in historical control patients who were treated for DKA in the ICU and had hourly glucose level monitoring.

We will evaluate potential cost savings comparing treatment of DKA patients in the stepdown unit using DEXCOM G6 CGM (both retrospective quality improvement project and prospective study vs treatment of DKA patients in the ICU setting using hourly point of care glucose testing (historical controls). We will include variables such as daily cost of ICU stay vs stepdown unit, cost of DEXCOM CGM.

We will calculate satisfaction scores from nursing surveys for the prospective part of the study.

There are no validated surveys assessing provider satisfaction as use of CGM in the inpatient setting is still a novel approach. We will use a modified CGM survey used for patient/caregivers (11)

Study Procedures:

Retrospective Quality Improvement Project

We will search electronic medical records (EMR) for laboratory data and clinical notes to estimate time to resolution of the DKA. Laboratory data and patient's characteristics which can contribute to time to resolution of DKA will be needed to match historical controls (DKA patients treated in the ICU setting with and glucose levels monitored via hourly fingerstick) . All relevant data will be gathered from chart review and stored in Excel format on a secure Department of Surgery server. All statistical analysis will be conducted in cooperation with Center for Innovation and Outcomes Research of the Department of Surgery.

Prospective Study

Patients who have glucose levels monitored by the CGM will be treated in the Stepdown Unit instead of intensive care unit (ICU) setting. Glucose levels from the CGM will be transmitted to the smartphones devices which will be provided to the provider and nurse taking care of the patient by the study team.

We provided extensive training for the ED staff and Stepdown Unit staff regarding the use of CGM in patients with DKA. Additionally, we will provide information sheet describing provider and nurses' role when DKA patients are monitored via CGM.

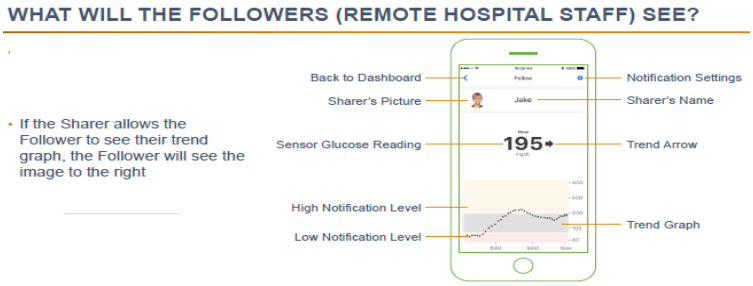
Once provider and the nurse in the ED give verbal consent for the study, and patient gives a written consent, a research coordinator will attach CGM DEXCOM G6 device (which consists of sensor and transmitter) on patient's arm and set up smartphone devices (study patient smartphone, study provider smartphone and study nurse smartphone) to receive glucose levels from the CGM device.

Description of the remote glucose monitoring via CGM device and workflow:

1. A research coordinator will apply sensor (which senses glucose levels just below the skin from the interstitial fluid) and transmitter (which gets glucose information from the sensor and send glucose information to the DEXCOM G6 app via Bluetooth to the smart phone provided by the study team) on the patient. The Dexcom CGM will be attached to the upper arm or lower abdomen. The patient will be asked for their preference. The Dexcom CGM should not be placed where the patient is lying down or sleeps. CGM will not be placed on scars, hair, tattoos, irritated areas, areas where the sensor can be rubbed (waist band, seat belt), and insulin injection sites. The patient may already be wearing their own personal CGM, which should not be removed. If the patient's personal CGM is on the arm, the study Dexcom CGM will be attached to the lower abdomen. If the patient's personal CGM is on the lower abdomen, the study Dexcom CGM will be attached to the patient's upper arm. The study patient smartphone receiving glucose level data needs to be placed on the patient's IV pole next to the insulin bag.

In order to have glucose levels sent from the transmitter to the DEXCOM app, each patient needs to have a user name and a password. A user name and password for each patient is created by the research team. Patient's information is coded when transmitted to these phones, meaning that instead of referencing any PHI such as MRN to identify the patient, the patient is labeled via a unique study-specific identifier ("study participate 001"). If the phones were to get lost, there will be no concern for improper release of PHI. The " study smartphone for the patient " is placed on the IV pole next to insulin infusion bag.

2. A study coordinator will set app DEXCOM follow apps (which are necessary for glucose to be sent from the patient study phone) on the study smartphones given to the nurse and provider for remote glucose monitoring.



There is a 2 hour "warm up" period until glucose levels are transmitted the study patient smartphone and during that time glucose levels should be checked via hourly fingerstick as per the DKA protocol.

3. Once glucose levels are transmitted to the study smartphone devices, glucose levels from the CGM to guide insulin adjustments. Check fingerstick glucose if CGM glucose levels are <100 mg/dl and >350 mg/dl to guide treatment decisions. Note that CGM device will have audible alerts if glucose level are < 100 mg/dl and >350 mg/dl. If there are NO glucose levels transmitted to the phone please check q 1 fingerstick glucose levels and contact Dr Magdalena Bogun (347 831 28 41). If CGM glucose data cannot restored and patient needs q 1 hour fingerstick glucose testing, patient will be transferred to the ICU. If patient is moved to the ICU the CGM will be removed. Although CGM data will be transmitted to the study smartphone devices continuously, please monitor CGM glucose levels every 1 hour and make treatment decisions based on q 1-hour CGM readings or more frequently when glucose levels are <70 mg/dl (confirmed with a fingerstick glucose). If patient's glucose levels are <100 mg/dl on the CGM, fingerstick glucose testing will be performed to ensure that fingerstick glucose level is not in hypoglycemic range (<70 mg/dl). If patient's glucose levels are in hypoglycemic range (<70 mg/dl) , fingerstick glucose levels testing will be performed as per hospital protocol until hypoglycemia resolves. Once hypoglycemia resolves, then glucose levels from the CGM can be used for further insulin adjustments. In the Emergency Department, document glucose levels q 2 hours as per the research protocol or more frequently as per provider request treating the patient. When patient is transferred to the stepdown unit, glucose levels should be recorded every 3 hours in hospital electronic medical record system.
4. If the patient condition worsens and patient requires the ICU care, patient will be transferred to the ICU. Also, if patient needs to get MRI or CT, sensor and transmitter will be removed prior to the imaging.
5. Smartphones which are receiving glucose data (study provider smart phone, study nurse smart phone and the study patient smart phone which receives glucose level from the sensor and is next to the IV insulin bag) should be transferred to the Stepdown Unit nurse when patient is arrives at the Stepdown Unit.
6. Sensors and transmitters are removed on the day of transfer to the hospital ward from the stepdown unit or 10 days from insertion (whichever comes first). The reason the sensors are not be removed at the resolution of DKA is that in case anion gap (AG) reopens (which indicates that patient is in DKA) then we can continue to monitor glucose levels using the sensor in place. Both sensors and transmitters will be removed by the primary nurse. The study smart phones are be returned to the research team (research coordinator) once DKA resolves.

The same process of abstracting data and demographic information described for the retrospective study from the patient's medical records for analysis will be used.

Provider Survey

We will identify nurses via EMR who took care of DKA patients who had glucose levels monitored via DEXCOM G6 CGM. We will then send them e-mail asking to voluntarily participate in the survey. The link to the anonymous QUALITRIC survey will be included in the e-mail.

Potential Risks:

The potential risks of this prospective study include a breach in confidentiality given information will be shared across technology platforms. This breach of confidentiality is highly unlikely as all PHI will be stored in encrypted devices and on encrypted endpoints to which only the study investigators and those directly involved in patient care will have access

Risks associated with use of the system may include hypoglycemia (low blood sugar) or hyperglycemia (high blood sugar) in cases where information provided by the device is inaccurate and used to make treatment decisions or where hardware or set-up issues disable alarms and alerts.
There may be slight pain or bruising in the insertion site of the sensor. There is also a small risk of infection at the insertion site. We will use only skilled individuals to insert the device.

Patients may also experience skin irritation or redness around the device's adhesive patch

Potential Benefits:

Subjects will likely not directly benefit from the study

Alternatives:

If patients decide not to take part of in this study, they will have glucose levels monitored hourly via fingerstick glucose testing.

Data and Safety Monitoring:

PHI will be stored in encrypted devices and on encrypted systems to which only the study investigators will have access.

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