Continuous Glucose Monitoring in Hospitalized Patients With Diabetes Mellitus

NCT#04653454

12August2020

IRB Minimal Risk Protocol Template

Note: If this study establishes a human specimen repository (biobank) for research purposes, do not use this template. Use the Mayo Clinic Human Specimen Repository Protocol Template found on the IRB home page under Forms and Procedures at [redacted]

First-time Use: Use this template to describe your study for a new IRB submission.

1. Complete the questions that apply to your study.
2. Save an electronic copy of this protocol for future revisions.
3. When completing your IRBe application, you will be asked to upload this document to the protocol section.

Modification: To modify this document after your study has been approved:

1. Open your study in IRBe. Click on the study 'Documents' tab and select the most recent version of the protocol. Save it to your files.
2. Open the saved document and activate "Track Changes".
3. Revise the protocol template to reflect the modification points , save the template to your files
4. Create an IRBe Modification for the study and upload the revised protocol template.

General Study Information

Principal Investigator: Adrian G. Dumitrascu, M.D.

Study Title: CGM use in hospitalized patients with diabetes mellitus.

Protocol version number and date: Version 1.0, 8/12/2020

Research Question and Aims

Hypothesis: Patient's own CGM (continuous glucose monitor) used in the hospital will be as accurate as POC (point of care) glucose monitors and acknowledgement by providers of high and low glucose trends will prevent episodes of hyper and hypoglycemia.

Aims, purpose, or objectives:
1. To determine if patient's own CGMs worn in the non-ICU hospital setting have adequate accuracy for blood glucose monitoring when compared to point-of-care capillary glucose measurement.
2. To determine if alerts given by CGMs worn in the non-ICU hospital would prevent episodes of hyperglycemia and hypoglycemia.

Background (*Include relevant experience, gaps in current knowledge, preliminary data, etc.*):

Diabetes Mellitus (DM) affects approximately 34.2 million (10.5%) Americans. Hyperglycemia and hypoglycemia in hospitalized patients have been associated with unfavorable clinical outcomes, including higher rates of sepsis, deconditioning, mortality and longer hospital stay. Untreated

hypoglycemia may lead to neurological damage, cognitive decline, seizures and coma. Additionally, the management of the diabetic complications doubles the inpatient cost per capita compared to non-diabetic patients.

Current standard of care in the hospital recommended by the national guidelines is the bedside point-of-care (POC) glucose capillary testing performed before meals and at bedtime. This approach however does not provide continuous 24-h glucose measurement and fails to detect nocturnal or asymptomatic hypoglycemia or hyperglycemia, all of which are common insulin therapy complications.

Continuous Glucose Monitoring (CGM) represents an alternative with the potential to assist making personalized therapy decisions. It measures levels of interstitial glucose every 5-15 min, which provides better assessment of nocturnal or asymptomatic hypoglycemia or hyperglycemia and shows glycemic patterns following treatment interventions. The ability to monitor glucose more frequently will also allow for timely interventions, and thus hyperglycemia and hypoglycemia episodes can be reduced. There have been studies demonstrating improved glycemic control in insulin-treated DM patients using CGM in outpatient setting, and even a few studies describing the use of CGM in non-ICU hospitalized patients.

Prospective studies evaluating the use of the newer CGMs in non-critically ill hospitalized patients are lacking. The aim of our study therefore was to compare the accuracy of patient's own CGM monitor worn in the hospital in detecting blood glucose levels by comparing them with those measured by a POC blood glucose capillary test.

Study Design and Methods

Methods: *Describe in lay terms, completely detailing the research activities that will be conducted by Mayo Clinic staff under this protocol.*

All patients admitted to the hospital in inpatient or observation status and having a CGM monitor attached will be screened and identified by providers and nurses. An order will be placed by providers to continue patient's home CGM monitor use in the hospital. A CGM patient agreement describing the hospital policy for use of CGMs will be provided to the patient for signature. (see attached agreement) Patients will be encouraged to continue to wear their CGMs in the hospital unless their presence interferes with patients' medical care. CGM presence will be recorded by nursing in patient chart under LDA (lines, drains, airway) section. A daily report will be run and these patients identified. Patients will be approached by research staff and asked to be enrolled in the study. A research consent will be reviewed with the patients and will be provided to patients for signature. Patients will be asked to continue to use their home CGMs in the hospital. If the sensor will reach the end of life patients have the option to place a new sensor and follow manufacturer recommendations for calibration and setting. Patients are responsible to provide their own sensors, transmitters, readers during the hospitalization period. If it is determined that the current sensor will interfere with the in-hospital medical and surgical care (MRI testing, procedure at the site, etc.), patient will be asked by their providers to remove the sensor and transmitter. Patients will have the option to replace the sensor after the procedure if they so desire. Patients will continue to monitor their glucose via CGM and their approved devices. For flash sensors, patients will be asked to scan their sensor at least every 8 and as needed. CGMs that require calibration will be calibrated by patients using hospital POC glucose meter readings. .

Patients alerted by their CGM about low glucose levels or fast downward or upward trending will be asked to notify their nursing staff. A POC blood glucose check will be done by nursing staff to confirm the alert or the trend. Treatment decisions will be made based on POC readings.
During hospitalization patients will continue to have their blood glucose checked with POC glucose monitor per hospital policy.
Treatment of the DM and associated complications, dosing of the insulin, change from PO to insulin treatment and back to PO medications during hospitalization or at discharge will be guided by the admitting team with as needed help from the inpatient Endocrinology Consultation Service.
Decisions about insulin dosing or other medication use designed to treat hyper or hypoglycemia episodes or underlying diabetes mellitus will be made based on hospital POC blood glucose meters and not based on CGM readings alone.
Patients will be asked to give the research team "provider access" to their cloud CGM software, or to allow the team to download their CGM data prior to discharge if their reading devices do not automatically synchronize with the cloud software.
CGM data will be compared with POC blood glucose monitoring obtained in the hospital. Different patient variables (demographics, comorbidities, labs and vitals, administered medications) will be collected from electronic health record and will be evaluated to determine if they would interfere with CGM readings. The accuracy of CGM for glucose measurement in the hospital will be calculated.

Outcomes measured:
CGM accuracy when compared with POC monitors.
CGM accuracy at detection of hypo or hyperglycemia episodes when compared with POC monitors.
Number of CGM alarms and the clinical result of these alarms: nurse notification, treatment of hypo or hyperglycemia episodes, treatment for rapid declining glucose alarms.

Materials:
CGMs (sensors, transmitters and readers) belong to patients
Provider access to cloud CGM program will be granted to the research team by the patient.

Personnel:
A research assistant that will identify the patients and enroll them into the study.

Subject Information

Target accrual is the proposed total number of subjects to be included in this study at Mayo Clinic. A "Subject" may include medical records, images, or specimens generated at Mayo Clinic and/or received from external sources.

Target accrual: 150

Subject population (children, adults, groups): Admitted adult medical and surgical patients with Diabetes Mellitus type I or II that have their own CGM monitor present on admission or able to be placed after admission.

Inclusion Criteria:
Patients with Type 1 or 2 Diabetes Mellitus,
Patients 18 years of age or older,
Patients admitted under medical or surgical services.
Patients treated with diet alone, insulin (SQ, insulin pump) or oral hypoglycemic medications.

Exclusion Criteria:

COVID-19 infection,
Infection of the skin at the CGM site requiring removal of the sensor.
Patients with altered Mental Status,
Patients unable to scan their flash CGMs at least every 8 hours.
Inability to provide written consent.
Hospitalized for less than 24h

Biospecimens

Collection of blood samples. When multiple groups are involved copy and paste the appropriate section below for example repeat section b when drawing blood from children and adults with cancer.

a. **From healthy, non-pregnant, adult subjects who weigh at least 110 pounds**. For a minimal risk application, the amount of blood drawn from these subjects may not exceed 550ml in an 8 week period and collection may not occur more frequently than 2 times per week.
   Volume per blood draw: _____ml
   Frequency of blood draw (e.g. single draw, time(s) per week, per year, etc.) _____

b. **From other adults and children considering age, weight, and health of subject.** For a minimal risk application, the amount of blood drawn from these subjects may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period, and collection may not occur more frequently than 2 times per week.
   Volume per blood draw: _____ml
   Frequency of blood draw (e.g. single draw, time(s) per week, per year, etc.) _____

Prospective collection of biological specimens other than blood: _____

MAYO CLINIC

Review of medical records, images, specimens

Check all that apply (data includes medical records, images, specimens).

☐ Only data that exists before the IRB submission date will be collected.

Date Range for Specimens and/or Review of Medical Records:
Examples: *01/01/1999 through 12/31/2015*, or all records through *mm/dd/yyyy*.
01/01/2010 through 01/01/2022

Note: The Date Range must include the period for collection of baseline data, as well as follow-up data, if applicable.

☒ The study involves data that exist at the time of IRB submission **and** data that will be generated after IRB submission. Include this activity in the Methods section.
Examples

- The study plans to conduct a retrospective chart review and ask subjects to complete a questionnaire.
- The study plans to include subjects previously diagnosed with a specific disease and add newly diagnosed subjects in the future.

☐ The study will use data that have been collected under another IRB protocol. Include in the Methods section and enter the IRB number from which the research material will be obtained. *When appropriate, note when subjects have provided consent for future use of their data and/or specimens as described in this protocol.*

Enter one IRB number per line, add more lines as needed

☐ Data ☐ Specimens ☐ Data & Specimens _____

☐ Data ☐ Specimens ☐ Data & Specimens _____

☐ Data ☐ Specimens ☐ Data & Specimens _____

Data Analysis

Power analyses may not be appropriate if this is a feasibility or pilot study, but end-point analysis plans are always appropriate even if only exploratory. Provide all information requested below, or provide justification if not including all of the information.

Power Statement:

Data Analysis Plan:

Data will be described as percentages or means. Pearson $\chi 2$ and Kruskal Wallis tests will be used to compare categorical and continuous variables respectively. Odds ratios, 95% confidence intervals and p-values will be reported for each model. All tests of significance will be 2-sided and the level of statistical significance will be set at p-value < 0.05.

Mean Absolute Relative Differences will be calculated between matched pairs of POC monitors and the closest CGM reading (within 5 minutes of POC). Additionally, level of agreement between the two devices will be examined with Bland-Altman plots, with particular attention focused on detection agreement in range (70-180 g/dl). Poisson or negative binomial regression will be utilized to assess count variables such as number of alarms, nurse notification, and hypo or hyperglycemia events adjusting for patient characteristics. Finally, longitudinal analysis will be conducted to determine differences associated with medications, clinical parameters or diagnosis. Analysis will seek to define if there are any differences between CGM and POC measurement based on these changes.

Endpoints
Primary: CGM accuracy - mean absolute relative difference (MARD)

Secondary:

- CGM accuracy at detection of hypo or hyperglycemia episodes when compared with POC monitors. (MARD for readings <70g/dl, >180g/dl, >250g/dl)
- CGM accuracy for detecting time in range (70-180 g/dl MARD).
- Number of CGM alarms and the clinical result of these alarms: nurse notification, treatment of hypo or hyperglycemia episodes, treatment for rapid declining glucose alarms.
- Time in therapeutic range for glucose as measured by CGM and POC glucose monitor.
- Detection of medications, clinical parameters or diagnoses that would interfere with CGM reading.
- Effect of CGM use on length of hospital stay, post-surgical duration of hospitalization

Clinical safety measures:

- Number of sensors with failure.
- Number of sensors removed for procedure.
- Number of sensor related skin reaction (contact dermatitis, infection)