Official Title: A Trial of CGM Technology in Preoperative Assessment Clinic
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Study Title: A Pilot Trial of CGM Technology in Preoperative Assessment Clinic

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Background, Rationale and Context

In the past, many subjects with diabetes on insulin pump therapy have utilized continuous glucose monitoring (CGM) technology in the outpatient setting. Recent advancements in CGM technology have led to an increase in the subject population utilizing this innovative technology as calibrations with fingerstick blood glucose values are no longer required with CGM technology. CGM technology is now being used frequently in subjects with diabetes mellitus who are not on insulin pump therapy, with either professional CGM studies ordered by providers for a two-week duration or personal CGM technology that subjects utilize on a daily basis to facilitate managing their diabetes. The use of CGM technology has recently been granted emergency use authorization by the U.S. Food and Drug Administration (FDA) for use in the inpatient setting but has not been extensively studied in the perioperative period.

CGM technology aids tremendously in data collection with recognition of glycemic patterns, as well as evaluating prediction of blood glucose changes including both hyperglycemic and hypoglycemic events. The availability of such a large volume of glycemic data has been shown to make a tremendous impact in subject care, resulting in statistically significant reductions in hemoglobin A1c, a decrease in hypoglycemia, a decrease in hospital admissions for diabetes complications, and improved overall quality of life and fear of hypoglycemia in subjects using CGM technology.[1,2]

Prior studies of use of CGM in the inpatient non-ICU setting have indicated that CGM is effective in evaluating glycemic trend and allowing for interventions to prevent hypoglycemia based on studies utilizing professional CGM technologies compared to fingerstick blood glucose values.[3] Furthermore, a recently conducted study of 8 critically ill subjects with diabetes that wore Freestyle Libre CGM's during their ICU stay demonstrated high test–retest reliability and acceptable accuracy when compared with arterial blood glucose measurements.[4] However, there is currently very limited data regarding the use of CGM technology in the perioperative setting. Current standards of care by the American Diabetes Association advise monitoring blood glucose while subjects are taking nothing by mouth and that rapid or short acting insulin be administered to target perioperative blood glucose of 80-180 mg/dL.[5] Standard of care protocol during surgery includes blood glucose checks at 60 minute intervals and when clinically indicated. A dose of correction insulin is recommended to be administered if blood sugar is greater than 180 mg/dL.

A recent small study evaluated use of Dexcom G6 CGM technology in the OR and Cardiac ICU in 13 subjects without diabetes mellitus undergoing coronary artery bypass surgery.[6] In some subjects

intermittent signal loss was noted during operative time with some sensors continuing to function in the postoperative setting. We recently studied CGM technology in the OR in 76 subjects at Wake Forest University School of Medicine undergoing noncardiac surgery.[7] We compared current standard of care blood glucose fingersticks to CGM data utilizing both the Dexcom G6 CGM and the Freestyle Libre 2.0 CGM.

Additional studies are needed to further evaluate the possible benefits and potential limitations of CGM technology in the perioperative setting. We are interested in how CGM technology could improve glycemic management in the preoperative setting. We aim to evaluate utilization of CGM technology in the preoperative setting by enrolling a total of 220 subjects with diabetes mellitus. The original feasibility study included 20 subjects who all were wearing the Freestyle Libre Pro CGM device in an effort to determine the feasibility of wearing the device for up to 14 days prior to their scheduled surgery. No randomization was involved in that initial cohort. This expanded study will now randomize subjects to utilization of the Freestyle Libre Pro device versus Freestyle Libre 2 device. Subjects will be enrolled during the preoperative appointment and have a 50% chance of have a Freestyle Libre Pro CGM device vs Freestyle Libre 2 device placed during the preoperative appointment. Current standard of care with monitoring glycemic range utilizing point of care blood glucose fingersticks, serum glucose, as well as arterial glucose as indicated will be utilized for all subjects. Additionally, patients randomized to the Freestyle Libre 2 device will be instructed to scan the sensor every 8 hours at home.

Objectives

1-Investigate time in range during preoperative period prior to the day of surgery in patients wearing CGM;

2-Compare average glucose from holding room in patients wearing Freestyle Libre Pro CGM vs. patients wearing Freestyle Libre 2 CGM

- To evaluate use of CGM technology in the preoperative setting: evaluate feasibility of placement of CGM during preoperative clinic visit
- To assess how CGM technology could improve glycemic management in the perioperative setting

Methods and Measures

Design

- This is a prospective analysis of a cohort study of subjects with diabetes mellitus undergoing surgery.
- Prospectively, subjects will be undergoing surgery that does not involve the upper extremity given the potential need for CGM placement site.
- We will be analyzing data obtained from the Freestyle Libre Pro and Freestyle Libre 2, which will be placed on a randomized group (1:1) of consented subjects. 100 subjects will receive the Freestyle Libre Pro CGM and 100 subjects will receive the Freestyle Libre 2 CGM.
- Subjects will wear CGM throughout perioperative period.
- CGM will be in use for up to 14 days (total preoperative + postoperative, or until discharge, whichever comes first).
- For the Freestyle Libre 2 CGM group, an endocrinologist will review the CGM data within a week of placement of CGM, and may recommend medication changes based on CGM data to the study subject.
- Regardless of the group, all subjects will receive standard of care during surgery and hospitalization with fingerstick blood glucose checks at Atrium Health Wake Forest Baptist. It is standard of care for fingerstick blood glucose checks to occur upon arrival to preoperative holding bay and upon arrival to Post Anesthesia Care Unit. Intraoperative

and postoperative glucose checks are at the discretion of the anesthesiologist while in the recovery area, and at the discretion of the surgical team when on the postoperative floor.
- CGM device will be removed by research team prior to discharge.

Setting

The study takes place at an academic medical center, Atrium Health Wake Forest Baptist in Winston- Salem, NC.

Subjects Selection Criteria

- **Inclusion Criteria**
  -18 years of age or older
  -Diagnosed with diabetes mellitus
  -Undergoing inpatient surgery at Atrium Health Wake Forest Baptist
  -Smartphone compatible with the Freestyle Libre 2 CGM phone application
- **Exclusion Criteria**
  -Undergoing surgery that would limit the placement of CGM to the posterior aspect of the upper extremity
  -CGM devices do not pose a risk to mother or fetus, so pregnancy will not be an exclusion criteria.
  -Undergoing cardiac surgery
- **Sample Size**
  There will be a total of 220 subjects selected during preoperative evaluation appointment at Atrium Health Wake Forest Baptist. In order to get 220 evaluable subjects, a total of up to 240 subjects may be consented. This total of subjects includes the 20 pilot subjects that were previously enrolled under this protocol.

Interventions and Interactions

- Subjects will be identified at time of preoperative appointment at Atrium Health Wake Forest Baptist. Similar to our previous CGM study, the research team will review subjects scheduled for Preoperative Assessment Clinic visit for inclusion criteria and exclusion criteria. Subjects that meet criteria will be approached by research team during Preoperative Assessment Clinic visit in a private clinic room. This is a private clinic room with adequate space to discuss study participation.
- Written informed consent will be obtained from individuals that meet above inclusion criteria by a member of the research team.
- Once consent has been obtained, the subjects will be randomized to receive either the Freestyle Libre Pro or Freestyle Libre 2. CGM will be placed on the subject prior to their discharge from their preoperative assessment clinic visit with contact information for research staff being given for any issues that may arise.
- Research staff will then meet the subject in the holding room on the morning of surgery to ensure device remains in place. The subject will then be followed during the perioperative period.
- Chart review will occur to collect data on the standard of care glucose values obtained from preoperative holding bay and post anesthesia care unit.
- The CGM device will be removed prior to discharge.
- Typical standard of care blood sugar collection occurs in preoperative holding bay (before subject is taken back to the OR) and upon arrival to the post anesthesia care unit (after surgery). Intraoperative blood sugar collection is at the discretion of the anesthesiologist.

- For all consented study subjects, we will retrospectively review the CGM data to compare to 1. The time of the preoperative blood sugar collection and 2. The time of the post anesthesia care unit blood sugar collection. We will retrospectively note insulin administration in this study.
- Data collection for each subject will include subject demographics, status of diabetes mellitus diagnosis, comorbid conditions, all blood glucose values during admission, all chemistry laboratory during admission, as well as data obtained from the Freestyle Libre Pro and Freestyle Libre 2 CGM that is worn throughout the perioperative and postoperative setting.

Outcome Measure(s)

- Proportion of subjects who present on day of surgery with CGM still in place and functioning
- Comparison utilizing Freestyle Libre 2 CGM in the perioperative setting for subjects with diabetes mellitus compared with Freestyle Libre Pro CGM with current standard of care utilizing point of care blood glucose fingerstick.
- Subject satisfaction with CGM
- Comparison of number of events of hyperglycemia (>180 mg/dL) on day of surgery (preoperative holding room and post anesthesia care unit) in subjects wearing Freestyle Libre Pro CGM vs. subjects wearing Freestyle Libre 2 CGM

Analytical Plan

Results will be analyzed comparing glycemic data from point of care fingerstick blood glucose values as well as serum glucose values of patients wearing Freestyle Libre Pro CGM to patients wearing Freestyle Libre 2 CGM and will be assessed statistically. Other inferential statistical analysis will be conducted as appropriate.

Human Subjects Protection

Subject Recruitment Methods

Only those subjects who have diabetes mellitus and are undergoing inpatient surgery at Atrium Health Wake Forest Baptist will be recruited for this study. Subjects will be identified with the assistance of the Anesthesiology team on day of preoperative assessment prior to planned surgery.

Informed Consent

Signed informed consent will be obtained from each subject by the investigators listed above at time of admission to Atrium Health Wake Forest Baptist. Risks, benefits, and alternatives will be explained to each subject.

Confidentiality and Privacy

Confidentiality will be protected by collecting only information needed to assess study outcomes, minimizing to the fullest extent possible the collection of any information that could directly identify subjects, and maintaining all study information in a secure manner. To help ensure subject privacy and confidentiality, only a unique study identifier will appear on the data collection form. Any collected subject identifying information corresponding to the unique study identifier will be maintained on a linkage file, store separately from the data. The linkage file will be kept secure, with access limited to designated study personnel. Following data collection, subject identifying information will be destroyed (3 years after closure of the study by file deletion), consistent with data validation and study design, producing an anonymous analytical data set. Data access will be limited to study staff. Data and records will be kept locked and secured, with any computer data password protected. No reference to any individual subject will appear in reports, presentations, or publications that may arise from the study.

Data and Safety Monitoring

The principal investigator will be responsible for the overall monitoring of the data and safety of study subjects. The principal investigator will be assisted by other members of the study staff.

Reporting of Unanticipated Problems, Adverse Events or Deviations

Any unanticipated problems, serious and unexpected adverse events, deviations or protocol changes will be promptly reported by the principal investigator or designated member of the research team to the IRB and sponsor or appropriate government agency if appropriate.

APPENDIX:

Timeline

1. Day 1: Preoperative Assessment Clinic visit.
    a. The timing of this visit varies, but is often a few days to a week or so prior to day of surgery.
    b. Potential subject will be identified by research team (like we did for our previous CGM study)
    c. Consent by PI or clinical research staff
    d. Device placement (CGM) by research team
    e. Subject wearing Freestyle Libre 2 CGM will be given protocol to scan the sensor at least every 8 hours at home. Otherwise, subjects should follow their usual routine for their blood sugar management.
2. Day 2 – 13: Day of surgery
    a. The timing of this varies, but is often a few days after PAC visit.
    b. If the patient is wearing a Freestyle Libre 2 CGM, an endocrinologist will review the data remotely within a week of placement and may recommend medication changes prior to day of surgery.
    c. Blood sugar obtained in preoperative holding room bay by preoperative nurse (this is our standard of care at Atrium Health Wake Forest Baptist, this will not need to be protocolized, preoperative nurse should follow their usual routine for a subject with diabetes).
    d. Device checked by research team in preoperative holding room (that CGM is still in place and functional).
    e. If subject is discharged to home, CGM will be removed in PACU by research team prior to discharge.
3. Up to day 14: Post operative day 1
    a. If subject stays overnight, CGM will be removed in subject hospital room by research team prior to discharge.

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