Professional Continuous Glucose Monitoring Before Starting Insulin Pump Therapy

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1.0 BACKGROUND AND HYPOTHESIS

Frequent blood glucose monitoring is the cornerstone of intensive diabetes management, and has been shown to decrease long-term complications of diabetes (1,2). Continue glucose monitoring has been a promising technology, providing patients and physicians with additional blood glucose data and a more detailed and accurate look at glycemic trends throughout the day, than can be achieved with SMBG alone, which may miss post-prandial and nocturnal variability (3-7). Continuous glucose monitors (CGM) can be divided into two groups: retrospective CGM and real-time CGM. Retrospective CGM devices are owned by the physician or clinic (i.e. iPro Professional CGM), and allow for blood glucose data to be collected over 3-7 days and then to be downloaded by the physician. The data are blinded to the patient during collection, and the downloaded data is used retrospectively to identify glycemic patterns and assist with insulin dose adjustments. Real-time CGM devices are owned by the patient, and provide minute-to-minute blood glucose values and trends, which are then used immediately to adjust insulin doses. Real-time CGM devices require intensive training and rely on the frequency of use, and have been found to be most effective when worn consistently (7,8).

The insulin pump has been a useful vehicle to manage glycemic variation throughout the day. With the ability to titrate insulin doses to glycemic demand, insulin pump therapy has been shown to improve glycemic control and decrease hypoglycemic events, when compared to multiple daily injections (MDI) alone (9,10). Insulin pumps are now integrated with real-time CGM technology, which has improved glycemic control with consistent use (7,11). Sensor-augmented pump (SAP) therapy has demonstrated reductions in HbA1c and decreased glycemic variability (7,11). Though, one of the major limitations found with SAP is that it must be used consistently by highly motivated families to achieve significant reductions in hemoglobin A1c (8,12). Furthermore, patients are infrequently started on both insulin pump and real-time CGM at the same time, due to the degree of training required to master two technologic devices. However, retrospective CGM data may be used to capture glycemic patterns, without the need for extensive education or training for the patient.

It has been the experience at our institution that patients are rarely started on both insulin pump and CGM simultaneously, primarily because learning two devices can be overwhelming for families. If a CGM is desired, the sensor is typically added about 1-2 months after initiation of pump therapy. It has also been our experience that patients starting on pump therapy require frequent dose adjustments before achieving tight glycemic control. Many studies have tried to identify variations in insulin requirements throughout the day (13-15), as well as variations based on age and pubertal stage (16). From these studies, as well as clinical experience, physicians understand that most children on pump therapy need less total daily insulin and higher basal rates in the early morning. These studies have provided a

general knowledge for initial insulin pump doses. However, an individualized regimen that provides tight glycemic control does not evolve until later, after many dose adjustments.

Though there has been much research looking at glycemic control when CGM is used with pump, there is little research looking at the utility of using CGM prior to initiation of insulin pump therapy. CGM has been used as a tool to monitor variations in blood glucose during the initiation of pump therapy (17,18), but not yet studied as means to tailor initial insulin pump doses.

We hypothesize that using retrospective CGM data in youth with type 1 diabetes mellitus to inform starting insulin doses at the initiation of pump therapy will result in the selection of more physiologic starting doses resulting in an improved time within target BG within the first 6 weeks of pump therapy.

2.0 OBJECTIVES AND PURPOSE

The primary objective of this study is to demonstrate that the use of retrospective CGM before insulin pump initiation will decrease glycemic variability, as measured by an increase in percentage time within target blood glucose range, in the first 6 weeks of pump therapy when compared to standard care, which in turn may change the standard of practice for how endocrinologists approach insulin pump initiation. By using CGM in the weeks before pump initiation, an accurate glycemic profile can be created, and then used to fine tune the starting insulin pump doses. Insulin doses can be adjusted to account for patterns of glycemic excursion, therefore decreasing glycemic variability at the onset of insulin pump therapy, leading to a smoother transition between subcutaneous insulin injections and insulin pump therapy. No studies have been performed to date that have studied the use of CGM in this way.

2.1 Primary Objective:

- To determine whether the use of retrospective CGM data to inform starting doses prior to insulin pump initiation will:
    - Increase the percentage time within target blood glucose range (BG: 70-180 mg/dL)

2.2 Secondary Objectives:

- To determine whether the use of retrospective CGM data to inform starting doses prior to insulin pump initiation will improve secondary outcomes:
    - Other measures of glycemic variability:
        - Mean BG and BG standard deviation
        - Mean amplitude of glycemic excursion.
    - Insulin doses:
        - Percentage change in total daily insulin dose
        - Percentage change in percent basal insulin used
    - Frequency of insulin dose adjustments:
        - Total number of insulin dose adjustments,
        - Total number of phone calls to clinic hotline

        - Number of insulin dose adjustments made per phone call
    - Adverse effects:
        - Episodes of hypoglycemia
        - Episodes of diabetic ketoacidosis
    - Participant/parent satisfaction with transition to insulin pump therapy

2.3 See sections 3.8 for details of measurement.

3.0 STUDY DESIGN

This is a randomized controlled study of the use of continuous glucose monitoring prior to insulin pump initiation in children with type 1 diabetes mellitus.

3.1 Participant Recruitment

- Participants with type 1 diabetes from Children's Hospital Los Angeles (CHLA), who have been referred by their primary endocrinologist for initiation of insulin pump therapy will be approached to participate in the study.
- Recruitment would be in person or by telephone once referral to start insulin pump has been made. Nurses will receive referral, and contact investigator. Investigator will contact subjects either in person or by telephone.
- Recruitment will take place in the CHLA Endocrinology and Diabetes clinic, at CHLA, Los Angeles, California.

3.1.1 General criteria for starting pump

- At CHLA, patients must be referred for pump initiation by their primary endocrinologist. In general, to qualify for pump therapy, patients need to be testing blood glucoses levels 4-6 times daily, come consistently to scheduled follow-up appointments, and be willing to participate in comprehensive diabetes education.

3.2 Inclusion/Exclusion Criteria

- Listed in section 5.0.

3.3 Consent:

- Written consent will be obtained from the participant or participant's parent(s) or guardian(s). Written assent will be obtained from the participant if less than 18 years of age, but at least 7 years of age. Consent and assent will be obtained by the primary investigator.

3.4 Securing Participant Identity

- All participants will be assigned a sequential study identification (ID) number in the order of enrollment. The key linking study identification number to patient's identifying information will be kept in a separate and secure location, and only be accessible to the investigator. All documents and data collection will use only the study identification number.

3.5 Randomization

- Participants will be randomized to either have their CGM data used to inform initial pump doses, or standard insulin start using our clinic's protocol.
- See section 6.3 for details of randomization process.

3.6 Study Procedures

3.6.1 Initial visit – approximately 2±1 weeks prior to insulin pump initiation. This is a study visit, and not standard of care. Visit will last approximately 45 minutes.

3.6.1.1 Baseline characteristics will be collected on all participants enrolled by review of CHLA medical records and/or by completion of the CGM Participant Source Document and CGM Baseline Participant Information forms by participant/parent. A baseline physical exam will be performed.

- See section 6.2 for details.

3.6.1.2 All participants will have an iPro®2 (Medtronic MiniMed Inc., Northridge, CA, USA) placed by the investigator or a trained nurse in the CHLA diabetes clinic. The iPro®2 will collect baseline data and glycemic trends on all participants.

- Participants will be provided with log sheets ("CGM Participant Log Sheet") and they will be instructed to check and record blood glucose levels a minimum of four times a day (before meals and before bed), as well as record carbohydrate intake and significant activity or exercise.
- Participants will wear the iPro®2 for 5 days.
- The iPro®2 and log-sheets will then be mailed back to the investigator in a pre-paid envelop.

3.6.1.3 Appointments for all future clinic encounters associated with the study will be made during the initial visit.

3.6.2 iPro2 data will be downloaded by the investigator.

- See section 4.1 for device details.

3.6.3 Insulin pump doses determination

- All participants will have insulin doses determined by "standard practice." Standard practice for pump initiation in the CHLA clinic involves the following: 1-2 weeks prior to the scheduled pump class, the participant's latest blood glucose log is reviewed by the participant's diabetes nurse. A worksheet ("CGM Pump Dose Worksheet") is then filled out by the nurse, which includes insulin daily totals (total rapid-acting insulin/day, total basal insulin/day, total daily dose (TDD), and total units of insulin/kilogram/day) and insulin pump calculations, including recognition of the honeymoon phase, the stage of puberty, the dawn phenomenon, and/or specific trends in high or low blood glucoses. In general, the total basal dose is reduced by 10-20% of the current dose, with the use of multiple basal rates being at the discretion of the provider. In general, the correction scale is calculated by dividing 1800 by the TDD, and the insulin to carbohydrate ratio is

calculated by dividing 450 by the TDD. The proposed starting insulin regimen is reviewed and approved by the participant's primary endocrinologist

- For those participants randomized to have "informed" starting insulin pump doses (study group), the iPro®2 data will be made available only to the nurse or physician responsible for determining starting insulin pump doses, so that further dose adjustments may be made.
- For participants randomized to "standard practice" (control group), iPro®2 data will remain blinded until the end of the study and kept in a secure location.

3.6.4 Initial Pump Class

A. STANDARD OF CARE PROCEDURES

1. All participants will attend a standardized CHLA pump initiation class. This is a 6-8 hour class held on a single day. The class is taught by a CHLA certified diabetes educator nurse. The class teaches basic pump features, clinical care on pump, identification and treatment of hypoglycemia and hyperglycemia, as well as sick-day management.
2. Participants will have a hemoglobin A1c (HbA1c) collected. HbA1c will be determined by DCA Vantage Analyzer (Siemens, Malvern, PA).
3. Participants will be instructed to perform blood glucose checks (capillary finger-stick on home meter) at least 6-8 times per day, including before meals, at bedtime, midnight and 3 a.m. Participants will be instructed to use the pump bolus calculator when giving an insulin bolus for correction and/or carbohydrates and to give insulin before eating. Participants will be instructed to keep a written log of blood glucose results, carbohydrates consumed, and insulin units given.

B. RESEARCH PROCEDURES

1. All participants will have the iPro2 placed by the investigator or trained nurse to collect data in the immediate period of transition to insulin pump. The device will be worn for 5 days and then mailed back to the investigator in a pre-paid envelope. Data will be downloaded and kept blinded and secure until data analysis is performed.
2. Participants will be instructed to keep a written log ("CGM Participant Log Sheet") of blood glucose results, carbohydrates consumed, and insulin units given.

3.6.5 Follow up

- All participants will be asked to report blood glucoses to a CHLA diabetes nurse by phone on a daily basis for the first 4 days after starting on the insulin pump, and then once weekly for 5 weeks. This nurse will not have been previously involved with the initial dose determination and thus will remain blinded to the participant's study group designation. Participants may also call at additional times, as needed. Insulin pump doses may be adjusted as needed, per routine, by CHLA diabetes nurses and/or physicians.

- Changes to pump settings will be documented in the electronic medical record, and the frequency, type of adjustments made, and ease of the phone call will be documented in a written log ("CGM Telephone Call Log").

3.6.6 Advanced Pump Class

A. STANDARD OF CARE PROCEDURES

1. All participants will attend a standardized advanced pump class, which will occur approximately 6±1 weeks after pump therapy initiation.
2. Insulin pumps and blood glucose meters will be downloaded.
3. Participants will have a hemoglobin A1c (HbA1c) collected.

B. RESEARCH PROCEDURES

1. All participants/their parents will be asked to complete a follow-up questionnaire ("Follow-up Participant/Parent Questionnaire"). This questionnaire will take approximately 10 minutes to complete and will be administered at the end of the class. The questionnaire consists of 10 questions, which will ask about brand of insulin pump, number of blood glucose checks per day, episodes of DKA (defined by emergency room visit or hospital admission), episodes of severe hypoglycemia (defined by loss of consciousness, coma, or seizure), and 6 questions regarding participant/parent satisfaction with the transition to insulin pump.
2. All participants will have the iPro2 placed by the investigator or trained nurse and it will be worn for 5 days. The iPro2 will be mailed back to the investigator using a pre-paid envelope. Data will be downloaded and kept blinded and secure until data analysis is performed.

3.6.7 Clinic Follow-up Visit

A. STANDARD OF CARE PROCEDURES

1. All participants will have a follow up visit with their primary endocrinologists 3 months (±2 weeks) after starting on insulin pump therapy.
2. All participants will have a hemoglobin A1C collected.

B. RESEARCH PROCEDURES

1. A brief, three question survey ("Provider Post-study Survey") will be given to diabetes nurses and physicians who were involved in using the CGM data to write initial insulin pump doses. An information sheet will be provided and verbal consent will be obtained. This survey will be distributed after all participants have completed the study. The survey will take approximately 5 minutes to complete.

3.7 Subject retention:

This study is of short duration, 3 months, and all visits after the initial visit are standard clinic visits for all patients who start insulin pump therapy (initial pump class, advanced pump class, and regular follow up with endocrinologist). This should

limit the number of participants lost to follow up. Participants will also be compensated with a $20 gift card at the 3 visits that an iPro2 is placed (Initial Visit, Initial Pump Class, Advanced Pump Class).

3.8 Main Variables:

3.8.1 Predictor variables: CGM data used to inform starting doses (yes/no). Blood glucose data provided by iPro®2 download.

3.8.2 Outcome variables:

- Primary Outcome:
  - Percentage time within target BG
    - Target BG: 70-180 mg/dL
    - The time spent within the target BG ranges indicated glycemic stability and adequate insulin dosing. Persistent blood glucose readings above or below this target range would necessitate a change in insulin pump doses. The goal of this study is to minimized glycemic variability and frequency of insulin pump dose adjustments.
    - The following data will be collected by iPro®2 (Medtronic Minimed, Inc., Northridge, CA, USA). This is a retrospective continuous glucose monitor, which will be placed per device instructions in the CHLA diabetes clinic by the investigator, be worn for 5 days, mailed back to the investigator, and then downloaded to collect data over that time period. This is an FDA approved device. Data will be collected via iPro®2 and downloaded at three times points, once prior to pump start, one week after pump start, and again 6 weeks after pump start.

- Secondary Outcomes:
  - Other measures of glycemic variability. Data will also be collected by iPro®2 at three points in time, baseline, one week, and six weeks.
    - Mean blood glucose (BG), BG standard deviation
    - Mean Amplitude of Glycemic Excursion
  - Insulin Doses: The following data will be collected at two time points, 6 weeks apart. Data will be collected once prior to pump start and will be based on current parental report. Data will be collected a second time 6 weeks after pump start, and will be collected from data downloaded from the insulin pump.
    - Total daily insulin dose (TDD)
    - Percentage basal insulin
  - Changes to Insulin Doses: The following data will be collected over the 6 weeks following pump initiation. Data will be collected on standardized printed logs (“CGM Telephone Call Log”), by a diabetes nurse.

  - Total number of insulin dose adjustments
  - Total number of phone calls to clinic hotline
  - The number of insulin dose adjustments made per phone call
- Adverse Effects: The following data will be collected over the 6 weeks following pump initiation. Data will be collected by patient interview and/or review of medical record and documented on source document ("CGM Participant Source Document"):
  - Episodes of severe hypoglycemia (loss of consciousness, seizure, coma)
  - Episodes of diabetic ketoacidosis (pH < 7.3, Bicarbonate < 15, hospital admission)
- Glycemic Control:
  - Hemoglobin A1c collected at pump start, the advanced pump class at 6±1 weeks, and the 3-month follow visit at 3 months ±2 weeks.
- Patient/parent satisfaction: The following data will be collected via survey (Participant/Parent Questionnaire) given to patients/parents/guardians at the end of the advanced pump class. The survey will use a Likert Scale (strongly agree, agree, neutral, disagree, strongly disagree) to respond to six questions addressing patient/parent impressions of the process of transitioning to insulin pump therapy.
- Nursing/physician Satisfaction: Data will be collected via the "Provider Post-study Survey," which will be completed by nurses and physician directly involved with insulin pump dose decisions. Survey will be three questions, which will address utility and feasibility of using CGM data to write pump doses.

4.0 DEVICE INFORMATION

4.1 iPro®2 Professional Continuous Glucose Monitor (Medtronic MiniMed Inc., Northridge, CA, USA).

The iPro®2 was approved by the FDA for all ages in 2011 for the continuous recording of blood glucose levels in persons with diabetes mellitus. The iPro®2 is composed of a disposable glucose sensor and the reusable digital recorder, which stores blood glucose data. A portion of the sensor is placed subcutaneous. The device measures blood glucose levels every 10 seconds and records blood glucose measurements every 5 minutes. Upon completion of data acquisition, the device is removed and the data from the digital recorder is uploaded to the CareLink iPro software program, which is a web-based, HIPAA compliant software program.

4.2 Supplier of the iPro®2: Medtronic MiniMed Inc.

Concurrent with IRB submission, a formal request will be made to Medtronic for product support. This study will request that Medtronic provide the necessary iPro®2 devices, Sof-Sensors, and related equipment including the Sen-serter for sensor placement,

Smart Dock device for uploading iPro®2 data, and CareLink Clinical Software (internet based).

4.3 Other supplies: Alcohol swabs. Tegaderm to secure the iPro2.

5.0 SELECTION AND WITHDRAWAL OF SUBJECTS

5.1 Inclusion Criteria:

1. Males and Females aged 2-24 years
2. Clinical diagnosis of Type 1 diabetes mellitus
3. Duration of diabetes: At least 6 months
   - This will ensure some glycemic stability prior to study, and most children do not start on an insulin pump until about 6 months into their diagnosis.
4. Basal/bolus insulin regimen using long-acting and rapid-acting insulin
   - This will provide a uniform method of insulin therapy.
5. Willingness to perform at least 4 capillary blood glucose tests per day while wearing the iPro®2
6. Willingness to wear the iPro®2 for 5 days continuously per insertion
7. Participant agrees to comply with the study protocol requirements
8. Informed Consent, Assent, HIPAA Authorization, and California Experimental Subject Bill of Rights signed by the participant and/or parent guardian

5.2 Exclusion Criteria:

1. Comorbid conditions, including but not limited to cystic fibrosis, oncologic processes, other systemic diseases that may affect overall glycemic control
2. Glucocorticoid use within 2 weeks of study enrollment
3. Concurrent use of other medications that may affect glycemic control
4. Prior CGM use in the past 6 months
5. The participant has any skin abnormality (e.g. psoriasis, rash, staphylococcus infection) in the area of iPro®2 placement that has not been resolved at the time of enrollment and would inhibit the participant from wearing the iPro®2.
6. Non-English speaking

5.3 Withdrawal Criteria:

1. A participant has the right to discontinue participation in the study at any time without affecting future management and treatment. If a participant decides to withdraw from the study, they must notify the investigator immediately. It is the intention to replace subjects that do not complete the study in order to obtain complete data sets.
2. An investigator has the right to discontinue a participant's participation in the study at any time, and the participant may be within drawn from the study if:
   - There is deterioration in the participant's signs/symptoms and/or the subject develops a disease or condition that in the opinion of the

investigator would compromise the subject's safety in continuing the study
- The participant develops a significant skin condition that prevents the participant from wearing the iPro®2.
- The participant is unwilling or unable to comply with the required study procedures
- The participant discontinues insulin pump therapy during the duration of the study

6.0 STRATIFICATION/DESCRIPTION FACTORS/RANDOMIZATION SCHEME

6.1 Stratification Factors

Participants will not be stratified or receive different treatments based on pretreatment clinical characteristics.

6.2 Descriptive Factors

At initial visit, baseline characteristics will be collected on all participants enrolled by review of CHLA medical records with documentation recorded on the participant's source document and/or by completion of printed form (CGM Participant Source Document" and CGM Baseline Participant Information ") by participant/parent:

Age, gender, race/ethnicity, age at diagnosis of diabetes, diabetes diagnosis date, location of diabetes diagnosis, type of insulin used, baseline frequency of blood glucose monitoring, brand of blood glucose meter used, history of diabetic ketoacidosis (DKA) (requiring hospitalization), history of severe hypoglycemia (resulting in loss of consciousness, coma, or seizure), history of prior CGM use, last available hemoglobin A1c, average blood glucose level and standard deviation, total daily insulin dose (TDD) averaged over one week, percentage of daily basal insulin, insurance type, weight, height, body mass index (BMI), tanner stage.

6.3 Randomization Plan

Upon obtaining informed consent, subjects with be randomized to either have their CGM data used to inform initial pump doses in addition to standard of care (subject) or to receive standard of care alone (control). Simple 1:1 randomization will be used. A computer will randomly assign groups to a numbered list. The list will be kept secure in our clinic. As subjects are enrolled, clinic assistants not directly involved in the study will use the list to assign study groups in numeric order. The patient ID number will be logged on the list. Randomization will help reduce introduction of confounding variables.

7.0 CLINICAL AND LABORATORY EVALUATIONS AND STUDY CALENDAR

Parameter	Initial Encounter	Initial Pump Class	Advanced Pump Class	3-month Follow-up
Targeted History & Directed Physical Examination	X			
Baseline Questionnaire	X			
Follow-up Questionnaire			X	
Hemoglobin A1c		X	X	X
iPro®2 placement	X	X	X	

8.0 CRITERIA FOR EVALUATION AND ENDPOINT DEFINITIONS

8.1 Study Endpoint

The three-month follow-up visit with the participant's primary endocrinologist will be the final visit of the study, after which no additional participation in the study will be required. Total duration of participation not to exceed 6 months.

8.2 Study Closure

The study will be closed after 40 enrolled participants have completed the study; specifically, all devices have been returned and uploaded, and all 3 month follow up visits with primary endocrinologists have been completed.

9.0 DATA COLLECTION AND MONITORING

9.1 Data Handling

Data collection for this study will be captured using paper Case Report Forms (CRF).

iPro®2, glucometer, and insulin pump data will be collected via device download. The iPro®2 data will be downloaded using Medtronic MiniMed CareLink Clinical. This system uses Secure Sockets Layers (SSL) technology, which encrypts all data it stores. Glucometer and insulin pump data will be downloaded using the approved software for each device.

All data will be manually entered by the investigator into a password-protected, secure database. Microsoft Excel 2010 (Microsoft Office Professional Plus 2010; Microsoft Corporation) will be used.

The investigator will ensure that all CFRs are completed and entered into the database promptly, completely, and accurately.

10.0 STATISTICAL CONSIDERATIONS

The primary outcome of this randomized controlled study comparing youth with type 1 diabetes starting on an insulin pump who either have their starting pump doses informed by CGM or by standard of care is the difference in pre/post change in mean percent time within target blood glucose range between the two groups. A sample size of 40

participants will be enrolled and randomly allocated to the two groups. Assuming a 20% dropout rate, a sample size of 16 per group will achieve the desired power of 80% to detect a 10% difference between groups, which corresponds to an effect size of 0.918. A significance level of 0.05 is used throughout this design. These calculations assume the standard deviation is approximately a quarter of the mean percent time within target blood glucose on both pre and post evaluation with correlation of 0.5 between pre and post measurements within each group. Data will be analyzed using one-sided t tests. A one-sided test was selected because this study is based on an existing technology, and only a finding of blood glucose improvement would be clinically relevant.

11.0 BIOHAZARD CONTAINMENT

Biohazard materials will include sharps from the sensor insertion. Universal precautions will be followed at all times. All sharps will be disposed of in a sharps container. iPro®2 digital recorder devices will be disinfected per manufacturer recommendations.

12.0 ETHICAL AND REGULATORY CONSIDERATIONS

All institutional and Federal regulations concerning the Informed Consent form will be fulfilled. The study will be conducted in adherence to ICH Good Clinical Practice.

12.1 Institutional Review Board

This protocol, and any subsequent amendments to this protocol, the Informed Consent, Assent, HIPAA Authorization, California Experimental Subject Bill of Rights, Participant Information Sheets, and any form of participant recruitment information relating to the study will be approved by the responsible IRB. The study will not start until IRB approval has been granted.

12.2 Informed Consent/Assent

Informed consent/assent will be obtained. Prior to entry into the study, the investigator will explain the purpose and duration of the study, requirements of the participant during the study, as well as potential risks involved with participation in this study. The IRB-approved written Informed Consent form/Assent form will be given to the participant/parent/guardian to read. The HIPAA Authorization will be also be given to the participant/parent/guardian. Participants/parents/guardians will be informed that the participation is voluntary. After all the subject's/parent's/guardian's questions have been answered, and if participation in the study is desired, they will sign and date the Informed Consent, Assent, HIPAA Authorization, and California Experimental Subject Bill of Rights. Only after these documents have been properly completed can the study procedures commence. The consenting process will be documented in the participant's study file. A copy of the signed Informed Consent, Assent, HIPAA Authorization, and California Experimental Subject Bill of Rights will be provided to the subject/parent/guardian.

12.3 Potential Risks

Serious adverse effects during past studies with continuous glucose monitoring were relatively rare. Usually side effects occurred with the glucose sensor and were often limited to reactions at the site of insertion on the skin, or related to adhesive tapes used to secure the device. These potential adverse effects include:

- Skin irritation
- Bruising
- Redness
- Bleeding
- Discomfort
- Tenderness
- Pain
- Rash
- Infection
- Irritation from tapes
- Feeling faint or syncope with sensor insertion

The possibility of infection is minimized by aseptic technique of sensor insertion. An insertion device (Sen-Serter) will be used to insert the sensor, which will ensure correct sensor placement and minimize discomfort.

There is potential for adverse effects of hypo-/hyperglycemia related to the disease state of diabetes. A telephone number will be provided to all participants, which will be staffed 24 hours daily by a diabetes nurse or diabetes/endocrine physician. Participants will be calling this number daily for the first 4 days, and then weekly, to report blood glucose numbers, so insulin dose adjustments can be made before significant episodes of hypo-/hyperglycemia occur. Participants may also call this number as needed for any additional concerns.

12.4 Benefits

There may be no direct benefit to the participant, but possible benefits of the participant electing to participate in the study include, but are not limited to:

- Possible reduction in glycemic variability, swings in blood glucose values
- Possible reduction in frequency of insulin pump dose adjustments
- Possible reduction in hypo-/hyperglycemic episodes based on more accurate insulin doses.

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