MINISTRY OF HEALTH
NATIONAL HEALTH SCIENCES RESEARCH COMMITTEE

IMPORTANT ELEMENTS IN AN INFORMED CONSENT FORM

Study title: A feasibility CGM trial for patients with type 1 diabetes followed at a rural, first-level hospital in a low-income country

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NHSRC Contacts

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Introduction

Treatment for Type 1 diabetes (T1D) is currently reaching very few of those affected in low-income countries. Mostly care is restricted to national or regional centers. Recent efforts have begun to increase access and lower the costs of care by decentralizing services to primary hospitals through nurse-led integrated delivery models (Package of Essential Noncommunicable Disease Interventions/PEN-Plus). These care delivery models are in the process of being codified in collaboration with the World Health Organization. At this stage, it is critical to establish viable strategies to improve glycemic control for patients with T1D as PEN-Plus is adapted and scaled throughout Africa.

New advancements in blood glucose monitoring and management technology, namely real-time continuous glucose monitoring (rtCGM), allow for patients' glucose levels to be automatically measured and recorded throughout the day and then reviewed by the patient at home or uploaded for the clinician to review at the clinic. Additionally, some CGM systems have built in alarms that are set to alert patients if their glucose levels fall below or rise above a certain number, and some even predict hypoglycemic episodes minutes before they even happen. This technology has been shown to significantly reduce HbA1c values and median duration of hypoglycemia by allowing uniform tracking of the glucose concentrations in the body's interstitial

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fluid and alerting patients when or before they experience hypoglycemia by allowing them to treat low blood sugars. This near real-time glucose data can be used to inform and direct precise diabetes management. Cochrane review of CGM systems for the management of patients with T1D across all age groups showed a statistically significant average decline in HbA1c levels six months after baseline for patients who started on CGM therapy at the time of the study. While this study indicates significant benefits CGM therapy can achieve in the management of patients with T1D, all of the studies included in the review were conducted in high income countries where robust health systems and a higher familiarity with technology and data informed self-management are more common. Additionally, many of the studies included patients utilizing CGM sensor augmented insulin pump therapy, a therapy not largely available in low resource settings at this time.

Currently, no data exist on the feasibility and clinical impact of rtCGM for patients with T1D managing with multiple daily injections in rural, low resource settings especially in areas that experience a lack of electricity, literacy and data informed self-management. In one RCT study on the clinical benefits of CGM technology in the management of women with gestational diabetes at an urban tertiary facility in Malaysia, 22 of the 81 eligible participants refused to participate in the study due to inconvenience (n=6) and refusal of the CGM intervention (n=16) (4). Even at this urban facility in a middle-income country, there are potential barriers to the feasibility of delivering CGM technology. This study aims to assess the feasibility and clinical impact of CGM use among largely illiterate, patients with T1D receiving care at rural first-level hospitals in a low-income country, namely Malawi.

Purpose

This proposed research will help us understand the feasibility and clinical effectiveness of continuous glucose monitor (CGM) use among a largely illiterate rural population of patients with T1D, and the feasibility of CGM technology in rural health facilities and homes to explore viable strategies to improve glycemic control for patients with T1D in Malawi. This study is a 3-month, 2:1 parallel arm closed randomized study of any patient with a T1D diagnosis that is enrolled in the NCD program at two district hospitals in Neno District, Malawi.

Procedure

Training of NCD clinicians: Prior to the start of data collection, the NCD clinicians at the four country sites will be trained on the study protocol as it applies to the use of CGM and SMBG by subjects and clinicians as well as use of glucose meter and logbooks.

Participants in the study will be randomized into two groups: those who will be using home glucometers to measure their blood sugars and those who will be using CGM technology to measure their blood sugars. Participants will be randomly assigned based on chance to either group while ensuring that two-

thirds of all participants are in the CGM group and one-third of all participants are in the home glucometer group. Both the control and treatment groups will be expected to have monthly follow-up clinic visits. Clinicians will use the CLARITY-based data on the computer as one of the tools for managing type 1 diabetes. Additionally, during the monthly follow-up clinic visit, the clinician and/or study staff will download the last month's data from the Dexcom 6 Receiver to be analyzed via the CLARITY software. If deemed medically necessary, the clinician will recommend any dose adjustments on the day of reviewing the data.

For those in the control group, subjects will be required to carry along their glucose meter machines and logbooks. During these visits the study staff will assess the utilization of the log book by checking completeness as per the expected number of recordings. The utilization of the glucose meter will be assessed by assessing the historical memory. To check the validity of the log book records, the records in the log book will be compared by study staff to those in the glucose meter memory including the time and readings of the glucose levels.

For all study subjects, patients will receive routine T1D care including regular blood tests for HbA1c every 3 months. Thus, all patients will receive HbA1c testing at enrollment and upon conclusion of the study period.

Baseline and endline assessments will be conducted in both arms and will include:

a. Complete the intake form: This will include information on duration since diagnosis with T1D, marital status and education level.

b. Complete the WHO quality of life questionnaire

c. Point of care test for the HbA1c (to be performed by clinical staff)

d. Qualitative interviews will be performed on a sample of subjects to assess their baseline diabetes management prior to study. The interviews will be facilitated by trained study staff.

The following data collection methods are described by outcomes:

- *Clinical outcomes:*

  HbA1c: measured at point of care every at baseline and three months.

  All-cause mortality: This will be conducted by endline surveys with subjects; if the subject is not available, then the clinical team will be asked to provide last known subject status

  % Time in range: Measured using logbooks and CGM reports

Quality of Life: WHO QoL survey will be conducted by trained research staff

Severe adverse events: These will be measured from logbooks and self-reports

- *Implementation outcomes:*

  Appropriateness and acceptability: We will conduct semi-structured interviews with 12 purposefully selected participants in each arm (3 from each site) at baseline and endline. In both baseline and endline interviews we will ask questions about their experiences with T1D, self-management, and experiences with adverse events.

  In endline interviews we will ask about their experiences with filling out logbooks, and their experiences with the home glucometers and CGM.

  Fidelity: Fidelity will be measured by logbooks (control arm) and from the CGM and SBGM (intervention arm). We will assess to see:

  a) % of expected blood glucose readings logged

  b) % of participants who brought log book to clinic during study period

  c) % of expected times blood sugar test was performed (based on logbooks, home glucometers, numbers of strips, CGM)

  d) % of expected times CGM and SBGM information was used to inform lifestyle adjusted interventions.

Benefits

Participants in the study could experience a reduction in HbA1c level, a decrease hypoglycemic events, increased detection of blood glucose trends, better informed treatment decisions and insulin dose adjustments, a better understanding the effects of diet, exercise, stress, illness, etc., on blood glucose, a decrease in the need for finger sticks, increased awareness of hypoglycemia and hyperglycemic events via predictive alarms, increased peace of mind for caregivers and patients, especially at night.

Risks

Participants in the study could experience a slight discomfort with application of the sensor, discomfort with the device being on the body, frustration with the sensor falling off, minor skin irritation from the adhesive, missed blood glucose information if the signal is lost or the receiver is not working, inaccurate blood glucose readings compared to venous blood glucose, or feeling overwhelmed from the increased data.

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Privacy and Confidentiality

*S*ubjects' data will be entered on an electronic database using study specific identification numbers to maintain patient's confidentiality. Computerized data will be accessible only by password and stored in a secure office setting. No subject identifiers will be used in data analysis or dissemination of reports. Data will be reported in aggregate measures that cannot be linked back to any individual participant. Recorded interviews and study records that identify participants will be kept in a secure cabinet that can only be accessed by the study staff.

Each study hospital will have a password-protected laptop with CLARITY application installed. This application will house data that was obtained via sync with the subjects' receiver-based data with physical cable. At the end of the study period, de-identified data will be exported from the laptops (CLARITY application) as a Microsoft Excel file. All computers will be encrypted.

Study Approval

Harvard Medical School Institutional Review Board, Boston, MA, USA

National Health Sciences Research Committee, Malawi

Consent and Signature

Indicate where the participant, data collector and witness should sign

Participant Signature_____

Data Collector Signature_____

Witness Signature_____

Study site

Two District Hospitals in Neno, Malawi

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