Using Continuous Glucose Monitoring and contextual data to increase insight in glucose patterns for individuals with type 2 diabetes.

Published: 21-08-2019
Last updated: 15-05-2024

The objective of this project is to gain a better understanding of the relation between blood glucose levels and patterns, and contextual data in individuals with T2D. An enhanced understanding of this relation can provide insights on how...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Glucose metabolism disorders (incl diabetes mellitus)
Study type	Interventional

Summary

ID

NL-OMON49104

Source
ToetsingOnline

Brief title
Gluco-Insight

Condition

- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
sugar, type 2 diabetes mellitus

Research involving
Human

Sponsors and support

Primary sponsor: TNO

Source(s) of monetary or material Support: Roche B.V.,TKI Health Holland,TKI Life Sciences & Health;TNO;Roche Diabetes Care Nederland BV

Intervention

Keyword: continuous glucose monitoring, lifestyle, modeling, type 2 diabetes

Outcome measures

Primary outcome

The main outcome of this study will be the understanding and prediction of glucose levels using real life contextual data (e.g. food intake, PA, stress and sleep) as well as lifestyle interventions.

The main study parameter in this study consists of continuous measured glucose values (mmol/l) measured with the use of the Dexcom G6. The Dexcom G6 is a CE marked device for the measurement of glucose in people with diabetes. The device uses gluco-oxidase method to measure glucose levels in the interstitial fluid. It automatically measuring the glucose levels and updates it every 5 minutes.

The Dexcom G6 system is a continuous glucose monitoring system that consists of three parts, a sensor, transmitter and an inserter. The sensor is placed transdermal with the use of the inserter and remains there for 10 days. The transmitter is attached to the sensor and transmits the data from the sensor to a smartphone app. Subjects can use this app to get insight in their own glucose levels.

To improve accuracy, the Dexcom G6 system can be calibrated once a day by manually entering the blood glucose value measured by a blood glucose meter. During the study participants are asked to calibrate once every day during

monitoring days.

Recent consensus statements provide recommendations how to use CGM data in clinical care. Based on these recommendations, complemented with results from a literature search and expert opinion, CGM metrics will be selected and available corresponding ranges will be used.

Secondary outcome

In order to model and predict the glucose data, we need insight in lifestyle factors, including dietary intake, PA, sleep and wellbeing. In addition anthropometric and clinical data are collected during the three visits to the clinic, including a standardized glucose and insulin response during an OGTT.

The following data will be collected:

1. Daily food and drink intake: this will be monitored with a food intake application (Fatsecret app) which is integrated in the HowAmI app that can be accessed via a smartphone. The Fatsecret app is based on the nutrition assessment method *food diary record*. Subjects report their daily food intake, incl. breakfast, lunch, dinner, snacks and drinks, immediately after consumption. Fatsecret converts selected food items into energy and macro- and micronutrients. This allows for collecting not only types of foods consumed, but also number of calories, fat, carbs, sugar, proteins, etc. Due to integration of the Fatsecret app in the HowAmI app participants can add timestamps to all their meals/snacks to register time of consumption. The HowAmI app will send out reminders regarding registration of food intake.

2. Wellbeing: this will be measured via visual analogue scales (VAS) /

ecological momentary assessment (EMA) questionnaire, including five questions for *feeling energetic * tired*, *feeling focused * distracted*, *feeling positive * negative*, *feeling motivated * unmotivated*, *feeling relaxed * stressed*. Filling in takes max. 30 seconds. This questionnaire will be administered four times per day; once after breakfast, once after lunch, once 4 hours after lunch (end of working day) and once two hours after dinner. The HowAmI app will send out notifications regarding the wellbeing questionnaires.

3. Physical Activity: heart rate, type of exercise, onset and duration of exercise, and energy expenditure are measured using a smartwatch.

4. Sleep: sleep duration, sleep onset, awakening time, and sleep quality are measured using a smartwatch. Sleep quality is also assessed subjectively via a single-item question using the HowAmI app.

5. Anthropometric measurements: weight (kg), BMI (kg/m2), waist and hip circumference (cm), waist/hip ratio and blood pressure (mmHg) are measured by a health care professional during the start and end visits to the clinic.

6. Clinical chemistry: average glucose levels (HbA1c), c-peptide, lipid profile (total cholesterol, HDL, LDL, triglycerides, free fatty acids) and C-reactive protein (CRP in mg/l) are measured in a fasting venous blood sample that is taken together with the baseline blood sample for the OGTT during the visits to the clinic.

7. Oral glucose tolerance test: a standardized glucose and insulin response is recorded during an OGTT to evaluate the level of insulin resistance in different organs and the *-cell function. Before as well as 30, 60, 90 and 120 minutes after consumption of a sugar water solution (75gr glucose) both glucose

and insulin levels will be measured using a venous blood sample.

Study description

Background summary

Type 2 diabetes mellitus (T2D) is not a homogeneous disease; individuals with T2D might benefit from different types of lifestyle interventions, depending on the underlying physiology. Therefore, personalization is of crucial importance for clinical care, as we know that the physiological response to environmental cues (i.e. food, exercise, sleep, stress) and lifestyle interventions (e.g. low-carb or Mediterranean diet) is highly variable between individuals. Evidence shows that CGM can promote reductions in HbA1c, body weight, and caloric intake, better adherence to a personal eating plan, and an increase in physical activity (PA)12. When integrated with education, these benefits may be further enhanced. This education becomes particularly powerful when it is personalized, meaning that an individual patient is given information about his or her own glycemic pattern and how this responds to what he or she does (e.g. food intake, PA, and sleep pattern) or experiences (e.g. stress)

Study objective

The objective of this project is to gain a better understanding of the relation between blood glucose levels and patterns, and contextual data in individuals with T2D. An enhanced understanding of this relation can provide insights on how individuals with T2D can modify their lifestyle to improve glycaemic control.
Additionally, it is aimed to assess how different lifestyle interventions that are proven effective on a population level (Mediterranean diet, low-carb diet, PA) affect glucose fluctuations and specific CGM parameters for individuals.
To make sense of the generated data, a combination of traditional and novel analysis/ modelling techniques will be used.

Study design

This study is a single-arm between and within-subject, exploratory study lasting 27 weeks. The study consists of observational phases and interventional phases. After a participant gives consent, a baseline questionnaire on demographics, medical history and lifestyle behaviour is filled out. Subsequently, participants will be trained in self-monitoring, including the application and use of the Dexcom G6 continuous glucose monitor. During the three observational phases, participants are asked to monitor their habitual lifestyle with the use of the glucose monitor, an activity tracker and a smartphone application for registering food intake and wellbeing. At the end of

each observational period an OGTT is performed. During eight intervention phases participants will be subjected to lifestyle interventions for 4 days each. This is to induce short-term glycaemic variations in response to lifestyle changes including two nutrition and two exercise-based interventions that are repeated twice (see table 1 in section 6.3). Additionally, for standardisation purposes subjects are asked to refrain from eating or drinking (except water) for up to three hours after the intervention. The observational and intervention phases are separated by at least one week wash-out period.

Intervention

Several interventions are introduced to induce a glucose response. These interventions will take a total of 4 days of which 3 are week days and 1 is a weekend day. Participants will perform the intervention independently after being contacted by phone by a researcher to receive instructions, have any questions answered and to be motivated to complete the intervention. During the intervention phase all food and drink intake as well as health events are logged with the use of a smartphone application. Participants are also asked to wear their activity tracker, calibrate their CGM system once per day using a finger prick and manual blood glucose measurement device, and fill in the ecological momentary assessment on their phone throughout the day.
The following interventions are performed twice by each participant in a randomized order
1. Hourly physical activity: reducing sedentary time by being physically active for 5 minutes every hour between 09:00 and 17:00
2. After meal walk: 15-minute walk after lunch and diner
3. Low carb: A diet with a low amount of carbohydrates
4. Mediterranean diet: A healthy eating plan with high fruits, vegetable, nuts, fish, whole grain and olive oil.
The exact days at which the intervention is performed is flexible to allow participant to fit it into their daily lives, with the only limit that the different interventions must be at least a week apart as a wash-out period.

Hourly physical activity
Interrupting sitting time with short bouts of light- or moderate-intensity physical activity lowers postprandial glucose and insulin levels in overweight/obese adults. Therefore, participants are asked to be physically active for 5 minutes every hour between 09:00 and 17:00. An alarm on the activity tracker is set that will vibrate to remind participants. Before starting with the intervention, tips are given by the researchers on how to incorporate this intervention in daily life. If someone already has an occupation that requires them to be physically active, focus will be on staying active in the evenings and during the weekends.

After meal walk
This intervention also focusses on interrupting sitting time and reducing postprandial glucose and insulin levels. This time, instead of reducing

sedentary behaviour in general, participants are asked to walk for about 15 minutes after each meal to reduce the glycaemic peaks after said meal. In other words, participants are asked to walk for 15 minutes after breakfast, lunch and dinner. Smartphone notifications will be used to remind participants.

Low carb
During the low carbohydrate intervention, focus is on reducing the daily intake of sugar and starch (max. 20 grams per meal). For this purpose, participants will receive meal boxes from Ekomenu that contain recipes and ingredients for dinner for 4 days. Additionally, participants will receive meal plans for breakfast, lunch and snacks that they should buy and prepare themselves. In total, the daily food intake will contain between 50 and 100 gram of carbohydrates (sugar and starch) per day to reduce post meal glucose excursions.
As the nutritional content of the delivered dinner is known, participants only have to register the time they eat and how much they have eaten. For breakfast, lunch and snacks food intake has to be logged completely by means of compliance check with the suggested meal plans. Participants will have some freedom in choosing a menu if some of it is not to their liking. However, all food choices will adhere to the low carb diet and will be of similar glycaemic load.

Mediterranean diet
The Mediterranean diet has been shown to have potential as *lifestyle treatment* of T2D and cardiovascular disease.7 The Mediterranean diet is high in fruits, vegetables, nuts, fish, whole grain and olive oil. Also for this diet, participants will receive meal boxes from Ekomenu that contain recipes and ingredients for dinner for 4 days. Additionally, participants will receive meal plans for breakfast, lunch and snacks that they should buy and prepare themselves.
As the nutritional content of the delivered dinner is known, participants only have to register the time they eat and how much they have eaten. For breakfast, lunch and snacks food intake has to be logged completely by means of compliance check with the suggested meal plans. Participants will have some freedom in choosing a menu in the same fashion as with the low carbohydrate diet.

Study burden and risks

The burden of this study consists of the and insertion use of a glucose monitor for 11 times, 3 oral glucose tolerance tests and registering contextual factors. During the intervention phases participants are also requested to follow an intervention i.e. regular walking or eating according to the meal plan that is provided.
The risks associated with participation can be considered negligible, and are mainly associated with the glucose sensor and the OGTT. The glucose sensor provides a small risk of adverse events including skin irritation, skin infection and skin colouring. The OGTT poses a small risk of hypo- or hyperglycaemia and can lead to nausea.

Benefits include that participants can get more insight in their individual health behaviour and status by self-monitoring food intake, glucose levels, wellbeing and physical activity. Additionally, the use of continuous glucose monitoring and the prescribed interventions are associated with improved health outcome in type 2 diabetes.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

* Aged < 80 years
* BMI 25 * 40 kg/m2, with preference for < 35 kg/m2; BMI 20-25 kg/m2 is also allowed if aged 60-80 years
* Diagnosed with type 2 diabetes mellitus
* Insulin naïve

* Using either lifestyle and/or metformin for managing their diabetes
* Able to answer questionnaires in Dutch
* In possession of a Smartphone running on a recent version of iOS or Android
* Able and willing to sign the informed consent form
* Willing to comply with all study procedures

Exclusion criteria

* Insufficient motivation to be in the study
* Unavailability for more than 2 weeks in a row during the study period
* A condition that would need an MRI in the upcoming 6 months
* History of bariatric weight loss surgery
* Planned (bariatric) surgery in the upcoming 6 months
* Active cancer or chemotherapy or radiation within 2 years prior to participation
* Chronic medical condition, treatment, or medication other than diabetes that may affect glucose metabolism (HIV diagnosis, use of steroids or immunosuppressive drugs, etc.)
* Chronic anaemia (haemoglobin of 6.2 mmol/l or less)
* Use of antibiotics or fertility treatments within 3 months prior to participation
* Pregnancy or a pregnancy wish
* 4 or more alcoholic drinks per day on a regular basis or use of recreational drugs
* Skin allergy, eczema or known sensitivity for plasters
* Coeliac or Crohns* disease
* Food allergies or intolerances including, gluten, wheat, egg, (pea)nuts, celery, sesame, soy, cacao, glutamate, legumes, coriander, maize, (shell)fish, chicken, beef, pork, lamb, sulphites, lupine, milk and lactose

Study design

Design

Study type: Interventional

Masking:	Single blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	24-09-2020
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO Date:	21-08-2019
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	09-09-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	15-11-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	22-07-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	03-11-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 24321
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL70771.028.19
OMON	NL-OMON24321