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Standardized Procedure for the Assessment of new-to-market Continuous glucosE monitoring systems

Submission date
25/06/2012

Recruitment status
No longer recruiting

Registration date
02/08/2012

Overall study status
Completed

Last Edited
20/06/2014

Condition category
Nutritional, Metabolic, Endocrine

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Patients with type 1 diabetes must perform frequent blood glucose measurements to prevent unacceptable rises and falls in blood glucose. Traditionally, finger prick blood tests must be done to determine blood glucose and these finger pricks are uncomfortable for patients. Scientists have been looking for a way to automate the measurement of blood glucose and reduce the number of finger pricks. The device that does this is known as a continuous glucose monitoring device (CGM). The CGM consists of a glucose sensor that measures glucose levels, which is inserted just under the skin in the subcutaneous fat. The subcutaneous fat is the same tissue in which patients normally would inject insulin. Further elements of the CGM include a wireless transmitter which sends glucose readings to a pager-like receiver on which patients can see the current glucose values, a history of glucose values and an indicator showing whether glucose is rising, falling or stable. The device is calibrated two times a day with a regular finger prick, which allows the CGM to compare its readings to self-measured blood glucose and adjust the CGM readings accordingly. Calibration is necessary because, unlike a regular blood glucometer, CGM devices measure glucose levels in the bodily fluids in the subcutaneous fat. Glucose levels in these fluids lag behind the blood glucose by about 15 minutes. Dealing with this delay is one of the major areas of research. Currently there are several manufacturers of CGM systems, and they all use slightly different types of sensors. It is important to know which of these CGM systems is most accurate and most reliable. This is not only relevant for patients with type 1 diabetes who might want to use a CGM and need to make a choice, but also because a good CGM is important for the development of an artificial pancreas, a future device which automatically measures glucose levels and adjusts insulin dose. In this study we want to compare three currently available CGM devices to see how accurate and reliable they are. The medical devices which are examined in this study are the Animas Vibe, the Abbott Navigator CGM and the Medtronic Paradigm CGM. All CGM systems consist of a sensor, a transmitter and a receiver. These are currently available and approved products.

Who can participate?
Patients aged 18 years or above with type 1 diabetes mellitus for at least 6 months with a body mass index not higher than 35 and an HbA1c level below 10%.

What does the study involve?
Patients visit the clinical research center a total of three times. At visit 1, three CGM systems will be attached to the body, patients will be instructed on their use and will then return home and come back to the clinical research unit the following day (day 2) for visit 2. At visit 2, patients are served breakfast. During the admission glucose levels will be tested frequently for 4.5 hours. At the end of this visit one CGM system is removed at random. Patients go home and continue to wear the remaining two CGM devices as long as possible. Patients will be asked to perform five fingersticks per day and note down the values in a diary. Patients will continue to do this until the sensors of both CGM systems have stopped working. When both sensors have failed patients will return to the clinical research unit for visit 3 to have the sensors removed. All sensor values will be downloaded from the CGM devices and the patient diary will be collected.

What are the possible benefits and risks of participating?
There are no direct health benefits to be gained by participation in this trial. While wearing the glucose monitor patients may gain insight into the way their body reacts to a meal and to insulin. There may be bruising, inflammation or skin irritation at the insertion site of the intravenous catheter or the subcutaneous glucose sensors.

Where is the study run from?
This is a multinational research performed within the following medical centres in the European Union:
1. Academic Medical Center Amsterdam, Netherlands
2. Medical University of Graz, Austria
3. University of Montpellier, France
4. Profil Institute for Metabolic Research, Germany
5. University of Padua, Italy

When is the study starting and how long is it expected to run for?
The study ran from September 2011 to August 2012.

Who is funding the project?
European Union.

Who is the main contact?
Dr J.H. de Vries
Academic Medical Centre, Amsterdam, Netherlands

Contact information

Type(s)
Scientific

Contact name
Dr J Hans DeVries

Contact details
Academic Medical Centre
Room F4-215
PO Box 22660

Amsterdam
Netherlands
1100DD

Additional identifiers

Protocol serial number
WP1.1/SPACE

Study information

Scientific Title
Standardized Procedure for the Assessment of new-to-market Continuous glucosE monitoring systems: an open-label study

Acronym
SPACE

Study objectives
For the development of a closed loop system, continuous glucose monitoring (CGM) systems with an acceptable accuracy and reliability need to be available. It has been shown that the accuracy of needle-type CGM systems can be poor, especially in the hypoglycemic range. As of yet, there is no standardized procedure to assess the accuracy and reliability of CGM systems that are introduced into the market. Most pre-market assessments of CGM systems have been done by means of Clarke Error Grid Analysis and assessment of correlation between CGM-reported glucose values and reference blood glucose values. We want to evaluate a more comprehensive method for CGM system assessment.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Medical Ethics Review Academic Medical Center Amsterdam (Medisch Ethische Toetsingscommissie Academisch Medisch Centrum Amsterdam), 18/07/2010, reference number 2010_336
2. Ethics Committee of the Medical University of Graz (Ethikkommission der Medizinischen Universität Graz), 02/08/2011
3. Committee to Protect People southern Mediterranean IV (Comité de Protection des Personnes Sud Méditerranée IV), 10/08/2011
4. Hospital and University of Padua Ethics Committee for Experimentation (Azienda Ospedaliera e Università degli Studi di Padova Comitato Etico per la Sperimentazione), 24/08/2011
5. Ethics Committee of the Medical Association of North (Ethikkommission der Ärztekammer Nordrhein), 07/07/2011

Study design
Multinational open-label study

Primary study design
Interventional

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Diabetes Mellitus Type 1

Interventions
The study will use three marketed CGM systems (Animas Vibe [Animas Corp, USA and Dexcom Inc, USA], Abbott Navigator [Abbott Diabetes Care, USA] and the Medtronic Minimed Guardian /Paradigm system [Medtronic, USA]). All three CGM sensors will be worn by the participant during the visit to the clinical research center (CRC). This visit will have a duration of 4 hours.

Blood will be drawn for the determination of glucose levels. The patient will receive his usual breakfast and postpone his usual morning insulin injection. A delayed and increased insulin bolus (aiming at 5 IU or 60% in excess of the patients calculated mealtime dose) will be administered to correct the breakfast glucose excursion with the aim of inducing a period of minor hypoglycaemia. Blood sampling will continue until the end of the admission. Pressure will be applied to the sensors during the last 2 hours of the CRC visit to determine the effect of pressure on CGM accuracy. At the end of this CRC part, the patient will continue to wear two of the three sensors at home; which ones will be determined by randomization. Sensors will be worn until the end-of-life of the sensor. Patients will be asked to perform at least five fingersticks per day for blood glucose measurements with the study glucometer. If the sensor has reached its manufacturer-specified lifetime end, the sensor will remain in situ and it will be attempted to re-activate the sensor within the CGM system to assess the sensor beyond its manufacturer-specified lifetime. The study will end when the sensors cannot be reactivated anymore. In case of sensor failure, patients will return to the CRC to have the sensor removed and their CGM sensor and blood glucometer data downloaded from the devices.

Intervention Type
Other

Phase
Not Applicable

Primary outcome(s)
1. Blood glucose values
2. Sensor glucose values
3. Duration of sensor life

From the sensor glucose values the Mean and Median Absolute Relative Difference (MARD) compared to blood glucose values will be determined. Blood glucose values will consist of Yellow Springs Instruments (YSI) values during the CRC period and fingerstick values thereafter

Key secondary outcome(s))
1. Accuracy of the sensor in the hypoglycaemic and hyperglycaemic area
2. Analysis to assess sensor performance and accuracy per day of sensor life, before and after approved time of use

Completion date
01/08/2012

Eligibility

Key inclusion criteria
1. Aged 18 years or above
2. Diagnosed with Type 1 diabetes mellitus (DM) at least 6 months according to the WHO definition
3. Body Mass Index (BMI) <35 kg/m²
4. Willing and able to wear a CGM device for the duration of the study and undergo all study procedures
5. HbA1c <10%
6. Signed informed consent form prior to study entry

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Patient is pregnant or breastfeeding during the period of the study
2. Patient is using a medication that significantly impacts glucose metabolism (oral steroids) except if stable for at least the last 3 months and expected to remain stable for the study duration
3. Has severe medical or psychological condition(s) or chronic conditions/infections that in the opinion of the investigator would compromise the patients safety or successful participation in the study
4. Patient is actively enrolled in another clinical trial or took part in a study within 30 days
5. Known adrenal gland problem, pancreatic tumour or insulinoma
6. Inability of the patient to comply with all study procedures
7. Inability of the patient to understand the patient information
8. Patient donated blood in the last 3 months

Date of first enrolment
01/09/2011

Date of final enrolment
01/08/2012

Locations

Countries of recruitment

Austria

France

Germany

Italy

Netherlands

Study participating centre
Academic Medical Centre
Amsterdam
Netherlands
1100DD

Sponsor information

Organisation
Academic Medical Centre (Netherlands)

ROR
https://ror.org/03t4gr691

Funder(s)

Funder type
Government

Funder Name
The European Commission (EU) - FP7 Program (Belgium), ref: 247138

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/08/2013		Yes	No