THE EFFECTS OF REAL-TIME CONTINUOUS GLUCOSE MONITORING ON GLYCEMIA AND QUALITY OF LIFE IN PATIENTS WITH TYPE 1 DIABETES MELLITUS AND IMPAIRED HYPOGLYCEMIA AWARENESS

Published: 22-01-2013
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Primary objective: To assess the mean difference in time spent in the euglycemic range (interstitial glucose >3.9-

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Diabetic complications
Study type	Interventional

Summary

ID

NL-OMON41465

Source
ToetsingOnline

Brief title
IN CONTROL

Condition

- Diabetic complications

Synonym
diabetes mellitus type 1, insulin-dependent diabetes

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Diabetescentrum VUmc en industrie (Medtronic;Eli Lilly),Eli Lilly,Medtronic B.V.,Sanofi-aventis

Intervention

Keyword: Glycemic control, Hypoglycemia unawareness, Real-time glucose monitoring, Type 1 diabetes mellitus

Outcome measures

Primary outcome

The mean difference in time spent in the euglycemic range (interstitial glucose >3.9-<10.0 mmol/L), expressed as hours/day (primary endpoint) between the two 16-week intervention periods, i.e. RT-CGM versus masked CGM in patients with T1DM and IHA.

Secondary outcome

1) (Diabetes-specific) markers of QoL, as assessed with questionnaires, covering diabetes-related distress (PAID-5), fear of hypoglycemia (HFS-2), self-efficacy (CIDS), health status (EQ5D) and emotional well-being (WHO-5)

2) Other glycemia variables, including HbA1c and time spent in hypo- and hyperglycemia ranges, expressed in hours/day, averaged over 16 weeks of data gathering during the intervention period, spent as or below an interstitial glucose level of 3.9 or above an interstitial glucose level of 10.0 mmol/L, respectively, as determined by (RT-)CGM data during the respective intervention periods.

3) The incidence and duration of hypoglycemic episodes, expressed in hours/day, averaged over 16 weeks of data gathering during the intervention period, during

which the patients* (RT-)CGM-measured interstitial glucose values are 3.9

mmol/L or below 3.9 mmol/L, according to (RT-)CGM data during the respective

intervention periods.

4) Changes in hypoglycemia awareness score according to Gold et al.

Study description

Background summary

Intensive insulin therapy in patients with type 1 diabetes (T1DM) reduces microvascular and macrovascular complications but is also associated with an increased rate of hypoglycemia. Recurrent hypoglycemia may lead to the development of impaired hypoglycemia awareness (IHA) or hypoglycemia unawareness (HU). Meticulous avoidance of hypoglycemia can restore the concomitantly attenuated hypoglycemia counterregulatory mechanisms. The recently developed technology of real-time continuous glucose monitoring (RT-CGM) may help patients with T1DM to achieve better glycemic control with less hypoglycemic episodes. Accordingly, one may hypothesize that particularly T1DM patients with IHA will profit most from this novel technology as it may be expected to lead to improvements in their quality of life. However, to date there are no studies using RT-CGM specifically in T1DM patients with IHA.

Study objective

Primary objective:
To assess the mean difference in time spent in the euglycemic range (interstitial glucose >3.9-<10.0 mmol/L), expressed as hours/day, between the two 16-week intervention periods, i.e. RT-CGM versus masked CGM, in patients with T1DM and IHA.

Secondary objectives:
To measure:
1. (Diabetes-specific) markers of QoL, as assessed with questionnaires, covering diabetes distress (PAID-5), fear of hypoglycemia (HFS-2), self-efficacy (CIDS), health status (EQ-5D) and emotional well-being (WHO-5)
2. other glycemia variables, including HbA1c and time spent in hypo- and hyperglycemia ranges, expressed in hours/day, averaged over 16 weeks of data gathering during the intervention period, spent as or below an interstitial glucose level of 3.9 or above an interstitial glucose level of 10.0 mmol/L, respectively, as determined by (RT-)CGM data during the respective intervention periods.

3. the incidence and duration of hypoglycemic episodes, expressed in minutes/day, averaged over 16 weeks of data gathering during the intervention period, during which the patients* (RT-)CGM-measured interstitial glucose values are 3.9 mmol/L or below 3.9 mmol/L, according to (RT-)CGM data during the respective intervention periods.
4. changes in hypoglycemia awareness score according to Gold et al. (reference: Gold AE, MacLeod KM, Frier BM. Frequency of severe hypoglycemia in patients with type I diabetes with impaired awareness of hypoglycemia. Diabetes Care 1994 Jul;17(7):697-703.)

Exploratory objectives
To explore:
1. RT-CGM derived measures of glucose variability
2. the autonomic nervous system balance
3. the duration of wear of the RT-CGM device
4. patients* therapy adjustments during the interventions
5. hypoglycemia awareness scores according to Clarke et al. (reference: Clarke WL, Cox DJ, Gonder-Frederick LA, Julian D, Schlundt D, Polonsky W. Reduced awareness of hypoglycemia in adults with IDDM. A prospective study of hypoglycemic frequency and associated symptoms. Diabetes Care 1995 Apr;18(4):517-22.)
6. satisfaction with use of CGM (reference: Youth and parent satisfaction with clinical use of the GlucoWatch G2 Biographer in the management of pediatric type 1 diabetes. Diabetes Care 2005 Aug;28(8):1929-35.)
7. the number of contact moments not planned according to the study schedule
8. absence of work of patient (and spouse)
9. the global estimated costs of use of health care (hospital admissions, ambulance- and house calls, etc.)

Study design

This is a randomized, two intervention periods, separated by a 12-week wash-out period, cross-over study. After a 5-week run-in period, during which patients receive global diabetes education and training in using CGM, patients will be randomized to either 16 weeks of use of RT-CGM or a 16-week period of CGM. Both interventions are additional to usual care and to performing self-measurements of blood glucose (SMBG) according to the protocol. Depending on the order of intervention, after the wash-out period patients will cross over to 16 weeks of the other intervention.

Intervention

Depending on the order, 16 weeks of use of real-time continuous glucose monitoring (RT-CGM) and a 16-week period of masked continuous glucose monitoring (CGM),.Both interventions are additional to usual care and to performing self-measurements of blood glucose (SMBG) according to the protocol.

Study burden and risks

There will be 14 visits, 1 optional visit and13 telephone consultations in a total study duration of 45 weeks. The duration of visits ranges from approx. 45 minutes (for follow-up visits) to approx. 2 hours (in case of endpoint measurements).

A total amount of 45 mL blood will be collected for hematological and biochemical (safety and end-point) assessments during the entire study period. The maximum blood volume to be obtained during one visit is 13 mL. The venipuncture may be painful.

During the screening, subjects will receive an extensive physical examination (incl. e.g. length and weight measurement, vital parameters, examination of heart, lungs and abdomen), during follow-up physical examination will be limited to measuring vital parameters.

Four times cardiovascular autonomic functioning tests will be performed (each time 20 min in total), and participants will be asked to fill out questionnaires (approx. 30-50 min in total).

Participants will be asked to fill out questionnaires five times (taking approx. 30-60 minutes). These concern hypoglycemia awareness or quality of life. Two times participants will be asked to complete a 5-day diary concerning intake, insulin use and sports.

Wearing of the continuous glucose monitors may case discomfort. Inserting a sensor may cause bleeding, swelling, irritation and/or infection at the site of insertion. Real-time glucose information will not be visible when participating in the CGM-phase. Alarms from the RT-CGM may be perceived to be inconvenient.

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

- Type 1 diabetic patients
- Use of multiple daily injections of insulin (with a basal insulin injection and bolus injections) or continuous subcutaneous insulin infusion
- Any HbA1c
- Age between 18 and 70 years old (inclusive)
- IHA according to the questionnaire by Gold et al. (Diabetes Care 17:697-703, 1994)
- Performing at least 3 SMBG/day or 21 SMBG/week

Exclusion criteria

- Type 2 diabetes mellitus
- History of (recent) major renal, liver, or (ischemic) heart disease (including cardiac conduction disorders)
- Current untreated unstable diabetic retinopathy
- Current (treatment for) malignancy
- Current use of non-selective beta-blockers
- Current psychiatric disorders, including schizophrenia, bipolar disorder, anorexia nervosa or bulimia nervosa
- Substance abuse or alcohol abuse (men >21 units/week, women >14 units/week)
- Current pregnancy or intention to conceive
- Current use of RT-CGM other than for short term (i.e. diagnostic use or use shorter than 3 consecutive months)
- Hearing or vision impairment hindering perceiving of glucose display and alarms, or otherwise incapable of using a (RT-)CGM, in the opinion of the investigator
- Poor commandment of the Dutch language or any (mental) disorder that precludes full

understanding of the purpose and instructions of the study
- Participation in another clinical study
- Known or suspected allergy to trial product or related products

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	04-03-2013
Enrollment:	52
Type:	Actual

Medical products/devices used

Generic name:	MiniMed Paradigm® Veo□-system;Enlite iPro2 system
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	22-01-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-06-2014

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-04-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

No registrations found.

In other registers

Register	ID
ClinicalTrials.gov	NCT01787903
CCMO	NL41199.029.12