OpT2mise glucose control in type 2 Diabetes Mellitus (DM) with insulin pump therapy

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

Summary

ID

NL-OMON38266

Source
ToetsingOnline

Brief title
OpT2mise

Condition

- Glucose metabolism disorders (incl diabetes mellitus)
- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
Sugardisease

Research involving
Human

Sponsors and support

Primary sponsor: Medtronic B.V.
Source(s) of monetary or material Support: industrie

Intervention

Keyword: Insuline pump, Type 2 diabetes mellitus

Outcome measures

Primary outcome

Primary Endpoint:

* Between group difference in average HbA1c changes from baseline to 6 months, when comparing CSII to MDI

Secondary outcome

Secondary Endpoints:

* Change in glycemic parameters calculated from blinded CGM data such as:

* Average glucose/day

* AUC in hypo- (*70mg/dL or 3.9 mmol/l) and in hyperglycemia (*180 mg/dL or 10.0 mmol/l)

* Time spent in hypo- (*70mg/dL or 3.9 mmol/l) and hyperglycemia (*180 mg/dL or 10.0 mmol/l)

* Mean Amplitude of Glycemic Excursions (MAGE) the most commom measure of the volatility of blood glucose levels

* Standard deviation of glucose/day

* Change in mean postprandial hyperglycemia 0 to 2 hours post meal, defined as *180 mg/dl or 10.0 mmol/l

* Safety:

* Severe hypoglycemia incidence: defined as an episode absolutely requiring assistance from another person and preferably accompanied by a confirmatory blood glucose by finger stick of less than 50mg/dL (2.8 mmol/L), (i.e., subject

is unable to treat self and requires carbohydrate, glucagon or other

resuscitative actions to prevent further clinical deterioration)

* Hospitalizations

* Diabetic Ketoacidosis (DKA) an acute metabolic complication of diabetes,

characterized by hyperglycemia, hyperketonemia, and metabolic acidosis

* Within group difference in HbA1c from 6 months to 12 months

* Change in weight or BMI

* Change in Lipids : T-Cholesterol * high density lipoprotein (HDL) * low

density lipoprotein (LDL) - Triglycerides

* Change in blood pressure

* Number of SMBG/day

* Insulin Dosage Changes

* Medication

* Treatment satisfaction : Diabetes Treatment Satisfaction Questionnaire

status and change version (DTSQs and DTSQc)

* Montreal Cognitive Assessment (MoCA).

* Medical resource utilization

Study description

Background summary

The use of external pumps in patients with type 2 diabetes is a recent practice compared with that in type 1 diabetes and only few studies have been published at this time.
Continuous subcutaneous insulin infusion (CSII) using an external pump is proposed as another treatment option to multiple daily injections (MDI) for insulin therapy in type 2 diabetes. Indeed, the use of external pumps is an

alternative strategy of insulin therapy intensification in these patients. In several countries, reimbursement of insulin pumps for type 2 diabetes is granted however, guidelines for choosing between these treatments are still lacking. In contrast with the widely documented use of CSII in type 1 diabetes, only few studies on the use of CSII in T2DM haven been published and their results are conflicting

Study objective

The purpose of this study is to evaluate the comparative the efficacy of insulin pump therapy versus multiple daily injections in insulin*taking type 2 DM who are sub optimally controlled with MDI.

Primary objective:
To evaluate between groups change in glycemic control (HbA1c) from baseline to 6 months of insulin pump therapy in patients with type 2 DM, as compared to patients on MDI therapy over the same time period.

Secondary objectives:
To evaluate between group change in glycemic variability parameters and diabetes clinical outcomes after 6 months in patients with type 2 DM. PROs will be measured after 6 Months of therapy.
To evaluate within group difference in the single cross-over sequence in the study continuation at 12 months and the change for the CSII arm in the continuation phase

Study design

This study has been designed to be prospective randomized controlled parallel-group, with a single-arm cross-over in the continuation phase, comparing group A on Continuous Subcutaneous Insulin Infusion (CSII) with group B on MDI therapy (see below *randomization*)
After a run-in phase of 8 weeks, the first 6-months phase (2-arms parallel) will be followed by another 6-months continuation phase (single cross-over of the MDI arm alone switching to CSII).
Total study duration per patient: 15 months, including the follow-up phase.
This study has an adaptive design: a Data Safety Monitoring Board (DSMB) will perform an interim evaluation of the sample size.

Objectives of the 8 weeks run-in period:
1. The primary objective of the run-in period is to ensure subjects are on an optimal MDI regimen. A titration protocol will be provided to the Investigator as a guide to help ensure appropriate insulin doses are used. The investigators should perform an insulin titration of the patients whose glycemia is not within the target range, defined as pre-meal glycemia between 70 and 130 mg/dl (3.9 and 7.2 mmol/l) and post prandial glycemia below 180 mg/dl (10.0 mmol/l).

2. A secondary objective of the run-in period is to demonstrate subject compliance with Self Monitoring Blood Glucose (SMBG) and a visit schedule. Medical attempts to improve glycemic control during the run-in period while on MDI therapy will consist of:
* nutrition counseling
* diabetes education (effect of insulin, basal/boluses principles, effect of diet, activity etc.)
* titration of insulin in order to improve glycemic control safety, minimizing hypoglycemia and weight gain

Start or continue taking metformin, to a maximum dose of 3000 mg/day or as tolerated. Metformin is an oral anti-diabetic drug in the biguanide class. It is the first-line drug of choice for the treatment of type 2 DM. Metformin should be continued during the entire duration of the study, unless it is not tolerated.

Use of all other Oral Anti Diabetics (OADs) will be suspended.

Insulin administration dosage with MDI should be at a minimum of 0.5 U/kg/day at screening. At the end of the run-in period (visit C), insulin dosage should be at minimum 0.7 U/kg/day, and at maximum 1.8 U/kg/day or a maximum of 220U/day.

At the end of the run-in phase, all patients who do not meet inclusion criteria or exhibit exclusion criteria will be screened out.

Randomization: Once the Investigator has received and reviewed lab results, patients who successfully pass randomization inclusion and exclusion criteria are randomized (at a 1:1 ratio) to group A or B in the study database. The randomization will be done within 1 week after visit C. Subjects will be notified by the investigator via a phone call.

Visits following randomization:

Visit 1: Start of treatment and pump training (for pump group, and continuation of optimization of treatment for MDI group); this visit must occur between 3 weeks following randomization. Visit 1 initiates a period of 2 weeks during which visits or phone calls may occur in order to train the patient on appropriate use of the pump, according to each center*s routine practice.

Further study visits will be planned after 1 month (Visit 2), 2 months (Visit 3), 3 months (Visit 4) and 6 months (Visit 5).
Blinded Continuous Glucose Monitoring (CGM) data, using iPro2 will be collected for a 6 days period before randomization (Visit C), at 6 months (Visit 5) and at 12 months (Visit 10). A sensor connected to an iPro2 will be inserted during those visits.

The first 6-months phase (2-arms parallel) will be followed by a 6-month continuation phase (single cross-over of the MDI arm patients, who will be switching over to CSII).

Further visits are planned after 6 months (Visit 6), 7 months (Visit 7), 8 months (Visit 8), 9 months (Visit 9) and 12 months (Visit 10).

Total study duration per patient: 15 months, including the follow-up phase. Recruitment is anticipated to be completed by each center within 10 months. Total study duration expected to be 3 years.

Intervention

group A on Continusous Subcutaneous Insulin Infusion (CSII) , group B on MDI therapy

Study burden and risks

The risk associated with an adaptive design is that there is a possibility that the sample size needs to be increased.
All devices used in this study are released for distribution at the moment of study start. Medtronic is not aware of any significant problems with these products. In the study, the products will be used in accordance with their labeling, therefore no risks other than the risks typically associated with devices routine usage are anticipated.
Due to the use of rapid-acting insulin, potential adverse events related to insulin infusion pumps, due to either intensive management of diabetes or interruption in insulin delivery, may include:
* Hypoglycaemia,
* Hyperglycemia,
* Diabetic Ketoacidosis.

The patient will be instructed to keep an emergency kit with him/her at all times in the event of the pump malfunction.

Potential adverse events related to insulin pump infusion sets may include: localized infection, skin irritation, bruising, discomfort, redness, bleeding, irritation, pain, and rash. The patient will be trained to use aseptic technique when inserting the infusion set and to change sites frequently to minimize the possibility of infection. If an infusion site becomes irritated or inflamed, the infusion set will be removed.
Possible additional risks include the possible side effects related to the use of iPro2 (although others are possible): skin irritation, bruising, discomfort, redness, bump, bleeding, irritation, pain, rash, infection, appearance of a small *freckle-like* dot where the sensor needle was inserted, local infection at sensor site and allergy to sensor components or dressing. The possibility of

infection is minimized, because the sensor will be inserted aseptically and will be worn for a short time. If irritation of the insertion site is noted, then the sensor will be removed. It is recommended to wear the iPro2 glucose sensor for 6 days.
Potential adverse events associated with frequent finger sticks include discomfort and ecchymosis at tips of fingers.
Potential adverse events associated with drawing blood include discomfort and bruising.

Possible benefits
The use of the Veo pump constitutes an alternative to multiple daily injections. It may also help patients adjust insulin treatment and therapy management.

Overall, the potential benefits for the patient to participate in this study include:
* Flexibility of using an insulin pump
* Easier adjustment of insulin doses
* Improved glycemic control.

The information gathered in this study may help physicians to determine the best treatment option for patients.

Results from this study may support the development of new devices and therapies, and may facilitate reimbursement of insulin pumps in countries where it is not currently reimbursed for type 2 diabetic patients.

Contacts

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Criteria for Inclusion at screening
1. Diagnosed with type 2 DM, as per Investigator diagnosis.
2. HbA1c (DCCT-standard) must be * 8.0% and *12% as evidenced by central lab value taken at screening.
3. Insulin resistance defined as required daily dose between 0.5-1.8 U/Kg or a maximum of 220 units insulin per day.
4. Age between 30-75 years old inclusive.
5. On MDI regimen (basal/bolus regimen with long-acting insulin and rapid acting analogs) defined as * 3 injections per day for at least 3 months prior signing the informed consent.
6. Ability to comply with technology, according to Investigator*s judgment.
7. Patients must be willing to undergo all study procedures.
8. Female patients of child-bearing potential must be using adequate contraception means as assessed by Investigator.;Criteria for Inclusion at randomization
1. Diagnosed with type 2 DM, as per Investigator diagnosis.
2. HbA1c (DCCT-standard) must be * 8.0% and *12% as evidenced by central lab value.
3. Insulin resistance defined as required daily dose between 0.7-1.8 U/Kg or a maximum of 220 units insulin per day.
4. On MDI (basal/bolus regimen with long-acting insulin and rapid acting analogs) defined as * 3 injections per day.
5. Ability to comply with technology, according to Investigator*s judgment.
6. * 2.5 SMBG per day on average, as reported in Carelink Clinical during the run-in period.
7. Patients must be willing to undergo all study procedures.
8. Female patients of child-bearing potential must be using adequate contraception means as assessed by Investigator.

Exclusion criteria

Criteria for Exclusion (screening and randomization)
1. Subject has a history (* 2 events) of hypoglycemic seizure or hypoglycemic coma within the last 6 months
2. Subject is pregnant as assessed by a pregnancy test with central laboratory, or plans to become pregnant during the course of the study
3. Participation in another interventional clinical study, on-going or completed less than 3 months prior to signature of Patient Informed Consent.
4. Subject has proliferative retinopathy or sight threatening maculopathy
5. Subject has
- an acute coronary syndrome (myocardial infarction or unstable angina) within 12 months OR
- coronary artery revascularization by bypass surgery or stenting within 3 months OR
- a transient ischemic attack (TIA) or cerebrovascular accident (CVA) within 3 months OR
- hospitalization for heart failure within 3 months or current New York Functional Class III or IV OR
- current 2nd or 3rd degree heart block OR
- symptomatic ventricular rhythm disturbances OR
- thromboembolic disease within the last 3 months OR
6. Subject with renal impairment expressed as estimated glomerular filtration rate (eGFR) using the Modification of Diet in Renal Disease (MDRD) formula < 30 ml/min as demonstrated by the screening central laboratory value at the time of enrollment
7. Subject has taken oral or injectable steroids within the last 30 days
8. Systolic blood pressure on screening visit is > 180 mmHg
9. Diastolic blood pressure on screening visit is > 110 mmHg
10. Any other disease (eg active cancer under treatment) or condition including abnormalities found on the screening tests, that in the opinion of the Investigator, may preclude the patient from participating in the study
11. Taking any medication prescribed for weight loss
12. Alcohol or drug abuse, other than nicotine, at the Investigator*s discretion
13. Use of a GLP-1 agonist or pramlitide (Symlin®). GLP-1 slows gastric emptying, thereby decreasing the rate of glucose absorption. Pramlitide (Symlin®) is a commercially available analogue of amylin, a synergistic partner to insulin.

Study design

Design

Study phase:	4
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):	31-05-2011
Enrollment:	60
Type:	Actual

Medical products/devices used

Generic name:	Medtronic Minimed Paradigm® Veo insulin pump and infusion sets.
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	25-03-2011
Application type:	First submission
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	21-10-2011
Application type:	Amendment
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	12-10-2012
Application type:	Amendment
Review commission:	METC Maxima Medisch Centrum (Veldhoven)

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	NCT01182493
CCMO	NL33620.015.10