Beta cell imaging in type 1 diabetes with stable near-normal and unstable glucose control using PET

Published: 24-07-2017
Last updated: 13-04-2024

The main study objective is to measure residual beta cell mass, indicated by the pancreatic uptake of Ga-68-exendin using quantitative PET, in type 1 diabetes patients with stable near-normal and unstable glucose control, to improve understanding of...

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

Summary

ID

NL-OMON49309

Source
ToetsingOnline

Brief title
GLP1-reg

Condition

- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
Diabetes mellitus type 1, diabetes type 1

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: Diabetesfonds

Intervention

Keyword: Beta cell mass, Exendin, Glycemic control, Type 1 diabetes

Outcome measures

Primary outcome

The main study objective is to determine residual beta cell mass in T1D patients with stable near-normal and unstable glucose control, as determined by measuring pancreatic uptake of Ga-68-exendin-4, to gain a better understanding of the relation between residual beta cell mass and glycemic control.

Secondary outcome

The secondary aim is to correlate the measured residual beta cell mass to the beta cell function that will be determined by a mixed-meal tolerance test.

Study description

Background summary

The change in beta cell mass in type 1 diabetes (T1D) is still poorly understood. Initially, the belief was that this could be explained by the loss of all pancreatic beta cells due to the autoimmune attack. However, recent literature suggests that a considerable number of beta cells can survive this attack. This could mean that certain beta cells survived, but have lost their function. The ratio of functional and non-functional residual beta cells might play an important role in the degree of glycemic control. It would therefore be of great interest to study residual beta cell mass in two types of T1D patients that differ in glycemic control. Although both types of patients receive treatment, one group of patients is characterized by a stable near-normal glucose control (control group) while the second group is characterized by an unstable glucose control. These groups will be defined based on their HbA1c values, number of severe hypoglycemic events and hypoglycemic awareness. In case glycemic control mostly depends on beta cell function and less on beta cell mass, novel therapies could focus on the functional reactivation of these non-functional beta cells to restore overall beta cell function. This could especially be in favour of patients with an unstable glucose control. Beta cell mass will be determined using Ga-68-NODAGA-exendin-4 positron emission

tomography (PET), which allows visualization of pancreatic beta cells as well as absolute quantification of tracer uptake, providing a measure for the pancreatic beta cell mass. The outcome of this study will lead to a better understanding of the relation between the amount of residual beta cells, beta cell function and the influence of glycemic control. This could provide new insights regarding the development of new therapies to improve beta cell function and glycemic control, which could lower disease burden and improve the patient*s quality of life.

Study objective

The main study objective is to measure residual beta cell mass, indicated by the pancreatic uptake of Ga-68-exendin using quantitative PET, in type 1 diabetes patients with stable near-normal and unstable glucose control, to improve understanding of the relation between residual beta cell mass and glycemic control.

Study design

T1D patients with stable near-normal and unstable glucose control will be recruited from the outpatient diabetes clinic of the Radboudumc in collaboration with the Department of Internal Medicine. Advertisements will be placed on the websites and social media (e.g. Twitter/Facebook) of the Radboudumc and diabetes-gerelateerde websites (Diabetes Fonds, eendiabetes, diabetestype1) for additional recruitment.
Subsequent to patient recruitment, a medical check will be performed at the Department of Radiology and Nuclear Medicine in the Radboudumc by a qualified physician. This medical check includes a medical interview and a physical examination. Blood samples will be taken to determine different laboratory parameters (C-peptide, insulin, glucose, HbA1c, creatinine, ALAT, ASAT). In addition, 2 blood samples will be taken and processed for phenotyping. The beta cell function will be determined by a mixed-meal tolerance test.
During the second visit at the Department of Radiology and Nuclear Medicine a PET/CT scan will be made. After a fasting period of 4 hours, 75 MBq of Ga-68-NODAGA-exendin-4 will be administered. The PET/CT scan will be performed 1 hour after administration. For a period of 7 days (prior to the scan) glucose profiles will be obtained by continuous glucose monitoring. This requires a single placement of a sensor that measures glucose subcutaneously. These profiles will give detailed information on the course of blood glucose levels of each subject and will provide insight into their metabolic control, which will be valuable for this study.

Study burden and risks

The participants need to visit the Department of Radiology and Nuclear Medicine twice. During both visits blood sampling will be performed. Blood sampling will

be done via an intravenous catheter, which reduces the number of required venipunctures. Due to the placement of an intravenous catheter, there is a small chance of bruising, pain and inflammation at the site of catheter placement. During the second visit a single dose of 75 MBq Ga-68-NODAGA-exendin-4 will be administered. Injection of this radiopharmaceutical may theoretically result in nausea and headache as has been reported for (much higher doses) of Byetta® in therapy studies, although this has never been observed in imaging studies so far (see section 5.4 in reseach protocol). In addition, single cases of low blood pressure and low blood glucose levels have been described after application of therapeutic or higher doses of Byetta®. Although low blood glucose levels only occurred after accidental heavy overdosing of Byetta®, patients will be closely monitored. In the period between the two visits, glucose levels will be measured subcutaneously through continuous glucose monitoring. This requires the single placement of a subcutaneous sensor (frequently used by diabetes patients). Subjects are not hindered by the sensor in terms of showering, swimming, et cetera.
In this study, we will only administer 75 MBq Ga-68-NODAGA-exendin-4 and therefore no (serious) adverse events will be expected. In case of administering 75 MBq Ga-68-NODAGA-exendin-4 followed by a PET/CT scan, the expected radiation exposure will be 3.7 mSv. The radiation exposure can therefore be considered minimal to little. Despite a low radiation exposure is needed, Ga-68-exendin PET provides a sensitive and specific visualization of the beta cell mass in vivo and allows accurate quantification of the beta cell mass, which is beneficial to improve understanding of the pathophysiology of T1D. The added clinical value of this method is that beta cell imaging using Ga-68-exendin PET, can be applied to select specific patients for future treatment options.
The participants will not benefit directly from this study.

Contacts

Public
Radboud Universitair Medisch Centrum

Geert Grooteplein-Zuid 10
Nijmegen 6525 GA
NL
Scientific
Radboud Universitair Medisch Centrum

Geert Grooteplein-Zuid 10
Nijmegen 6525 GA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Inclusion criteria: T1D patients with stable near-normal glucose control:
- Age *18 years
- T1D diagnosed *1 year at the start of the study
- HbA1c *7 (*53 mmol/mol)
- 17* BMI *30 kg/m^2
- No severe hypoglycemic events in the past year and a maximum of 2 severe hypoglycemic events in their entire life.
- Intact hypoglycemic awareness as assessed by a score of 0 or 1 on the modified Clarke*s questionnaire
- Ability to sign informed consent

Inclusion criteria: T1D patients with unstable glucose control:
- Age *18 years
- T1D diagnosed *1 year at the start of the study
- Ability to sign informed consent
- Option 1: HbA1c *8.5 (*69 mmol/mol) and in addition a minimum of 2 severe hypoglycemic events in the past year, or an impaired awareness of hypoglycemia (IHA), as assessed by a score of 2 or more on the modified Clarke*s questionnaire (subjects may comply with both criteria, but this is not a requirement). Option 2: HbA1c *8.0 (*64 mmol/mol) and in addition a minimum of 2 severe hypoglycemic events in the past year, or an impaired awareness of hypoglycemia (IHA), as assessed by a score of 3 or more on the modified Clarke*s questionnaire (subjects may comply with both criteria, but this is not a requirement)
- 17* BMI *30 kg/m^2

Exclusion criteria

Exclusion criteria:
- Previous treatment (within 6 months) with synthetic Exendin (Exenatide, Byetta®) or Dipeptidyl-Peptidase IV inhibitors
- Liver disease defined as aspartate aminotransferase or alanine aminotransferase level of more than three times the upper limit of normal range
- Renal disease defined as MDRD <40 ml/min/1.73m^2
- Pregnancy or the wish to become pregnant within 6 months after the study
- Breastfeeding
- BMI <17 kg/m^2 or BMI >30 kg/m^2
- Age <18 years
- Inability to sign informed consent

Study design

Design

Study phase:	2
Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	06-12-2017
Enrollment:	18
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	68Ga-NODAGA-[K40]-Exendin-4

Generic name:	68Ga-NODAGA-[K40]-Exendin-4

Ethics review

Approved WMO Date:	24-07-2017
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	27-07-2017
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	29-11-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	29-03-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	07-08-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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
EudraCT	EUCTR2017-002739-40-NL
CCMO	NL59582.091.17

Study results

Date completed:	21-06-2021
Actual enrolment:	16