Visualizing beta cells after Intrahepatic Islet of Langerhans Transplantation

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Primary Objective: Compare the uptake of 68Ga-NODAGA-exendin-4 in the liver between T1D patients with functional islet grafts (C-peptide > 0.8 nmol/L after mixed meal stimulation test and relevant laboratory parameters as HbA1C and exogenous...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON47855

Source
ToetsingOnline

Brief title
Visualizing beta cells after islet transplantation

Condition

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

Synonym
Intrahepatic islet transplantation in type 1 diabetes patients

Health condition

Transplantatie eilandjes van Langerhans

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: beta-cells, Islet transplantation, MRI, PET

Outcome measures

Primary outcome

The main parameters of the study are the qualitative and quantitative assessment of the uptake of 68Ga-NODAGA-exendin-4 in the liver of T1D patients who received intrahepatic islet transplantation by PET/CT with additional MRI/MRS and compare this uptake to the uptake in the liver of healthy individuals.

Secondary outcome

- The quantitative assessment of the detected signal in the liver compared to the functionality of the islet graft as assessed by clinical parameters.
- The qualitative assessment of the distribution of uptake in the liver reflecting islet distribution across the liver.
- Correlation between the distribution of uptake in the liver (PET) and structural abnormalities, such as hepatic steatosis (MRI/MRS)

Study description

Background summary

Detecting damage to islets with a reliable imaging technique could be important for improving islet survival after transplantation. This could lead to better patient outcomes which would be of great interest for the treatment of type 1

diabetes. In order to assess the possibility of visualizing transplanted islet grafts with 68Ga-NODAGA-exendin-4 PET, we aim to perform a proof-of -concept study in 10 patients with type 1 diabetes who have undergone intrahepatic islet transplantation with biochemically proven functional islet grafts and 5 patients with T1D who are on the waiting list for islet transplantation. We propose to determine the uptake of the radiolabeled tracer and compare it to functionality of the islet grafts. Furthermore, we aim to evaluate the distribution of the transplanted islets in the liver and correlate this with structural hepatic abnormalities such as steatosis. These highly relevant data will provide us with more information on the suitability of GLP-1 receptor imaging for monitoring of transplanted islet mass.

Study objective

Primary Objective:
Compare the uptake of 68Ga-NODAGA-exendin-4 in the liver between T1D patients with functional islet grafts (C-peptide > 0.8 nmol/L after mixed meal stimulation test and relevant laboratory parameters as HbA1C and exogenous insulin administration) and healthy volunteers using PET.

Secondary Objective(s):
The secondary objectives are:
- Comparing the uptake in the liver to islet graft function, defined by clinical parameters (C-peptide levels after mixed meal stimulation test, HbA1c levels and exogenous insulin usage).
- Assessing distribution of uptake across the liver (PET) reflecting islet distribution.
- Correlate the distribution of uptake in the liver (PET) with structural hepatic abnormalities, such as hepatic steatosis (MRI/MRS)
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Study design

Proof-of-concept study in which we will compare the uptake of 68Ga-NODAGA-exendin-4 in the liver of 10 patients with intrahepatic islet transplantation with the uptake in the liver of 5 healthy volunteers and correlate the distrubution of uptake with graft performance and structural hepatic abnormalities (as determined with MRI).

Study burden and risks

All individuals will undergo physical examination and blood sampling for laboratory parameters (first visit). In addition, all patients with islet grafts will undergo a mixed meal tolerance test. At the second visit 68Ga-NODAGA-exendin-4 will be administered intravenously and dynamic scanning with breath gating will be performed for 60 minutes at a single bed-position.

After this a static scan of 20 minutes will be made. After injection of the radiopharmaceutical, blood samples will be drawn from an intravenous catheter for determination of blood glucose levels. Also, blood pressure will be measured. Injection of the radiopharmaceutical may theoretically result in nausea and headache as has been reported for (much higher doses) of Byetta® in therapy studies. In addition, single cases of low blood pressure and low blood glucose levels have been described after accidental heavy overdosing of Byetta®. Therefore, participants will be closely monitored. However, in another study (CPOP-EX), we did not observe any side or adverse effects after 111In-DTPA-[K40]-Exendin 4 injection for all 20 patients included. After the PET/CT a MRI will be performed to visualize hepatic abnormalities (MRS spectra will be obtained to identify hepatic steatosis) and this will take about 45 minutes.
The expected radiation exposure is 5.5 mSv and is therefore considered minimal to little. However, if the technology would indeed allow visualization of the transplanted islets, the impact on optimizing islet transplantation and thereby diabetes treatment and potential cure of the disease would be very high.

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

Patients:
- > 18 years old
- T1D patient undergone islet transplantation
- Clinically proven functional islet graft (stimulated C-peptide > 0.8 nmol/L)
- Signed informed consent
Inclusion criteria T1D patients without an islet transplant
- > 18 years old
- Signed informed consent;on the waiting list for islet transplantation

Exclusion criteria

- Treatment with synthetic Exendin (Exenatide, Byetta®) or Dipeptidyl-Peptidase IV inhibitors within the last 3 months
- Breast feeding
- Pregnancy or the wish to become pregnant within 6 months
- Affected kidney function * Calculated creatinine clearance below 30ml/min
- Liver disease defined as aspartate aminotransferase or alanine aminotransferase level of more than three times the upper limit of normal range (45 U/L).
- Age < 18 years
- No signed informed consent
- Exclusion criteria for MR:
* Metallic fragments, clips or devices in brain, eyes, spinal canal
* Implantable defibrillator or pacemaker (wires)
* Mandibular magnetic implants
* Neurostimulator, bladder stimulator, non-removable insulin pump
* Metal tissue-expander in chest
* Cochlear implant
* Ossicular replacement prosthesis

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):	06-06-2016
Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	68Ga-NODAGA-exendin-4
Generic name:	n.v.t.

Ethics review

Approved WMO Date:	13-08-2015
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	22-09-2015
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	22-10-2015
Application type:	Amendment

Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	16-12-2015
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	09-11-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	06-04-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	18-04-2019
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	EUCTR2015-000821-35-NL
CCMO	NL52630.091.15

Study results

Date completed:	27-05-2021
Actual enrolment:	13