Arginine-stimulated indication of early outcome after islet transplantation

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Primary Objective: We aim to create a prediction model to predict islet graft function at 3 months post-transplantation, using early islet graft function assessed in the first week after islet transplantation.Secondary Objective(s): - To determine...

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

Summary

ID

NL-OMON51657

Source
ToetsingOnline

Brief title
ALADDIN

Condition

- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
diabetes, diabetes mellitus

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Afdelingsfonds eilandjes (eigen middelen)

Intervention

Keyword: arginine, c-peptide, endocrine function, islet transplantation

Outcome measures

Primary outcome

The primary outcome is the correlation between peak C-peptide after arginine bolus at day 3 post-transplantation and AUC C-peptide after mixed meal tolerance test at 3 months post-transplantation.

Secondary outcome

o Stimulation index during in vitro arginine stimulated insulin secretion test

o Fasting C-peptide

o Fasting glucose

o Stimulated C-peptide (during AST and/or MMTT)

o AUC C-peptide (during arginine stimulus and/or MMTT)

o Concentration of circulating-free insulin deoxyribonucleic acid (DNA)

o Insulin concentration in islet product

o Complete blood count with differential (e.g. platelets, peripheral mononuclear blood cells (PBMCs))

o T-cell immunophenotype

o Plasma-circulating microRNA

o Complement factors and markers

o Inflammatory cytokines

o Coagulation factors and markers

o Concentration of secreted peptides by pancreatic islets (e.g. insulin, proinsulin)

o Insulin requirements (IU/kg)

o HbA1c

o Number of severe hypoglycaemic events (SHE)

o Flash/continuous glucose monitoring parameters: time in range (% TIR; 3.9 -

10.0 mmol/l); time above range (% TAR; >= 10.0 mmol/l); time below range (% TBR;

<3.9 mmol/l); time in hypo (% TIH; < 3.0 mmol/l); coefficient of glucose

variation (CV); time active use; number of scans per day (n)

o β-cell graft function as assessed by Igls 2.0 criteria

o Treatment success/failure as assessed by Igls 2.0 criteria

Study description

Background summary

Transplantation of pancreatic islets is a treatment for diabetes mellitus. For patients with severe type 1 diabetes, allogeneic islet transplantation is sometimes possible, with pancreatic islets from a donor pancreas. For patients with a benign disease of the pancreas, necessitating a pancreatectomy, autologous islet transplantation is sometimes possible. After the transplantation, the glucose concentration is tightly regulated to prevent damage to the islets by hyperglycaemia.

Monitoring islet graft function is essential to predict clinical requirements. Currently, the earliest moment to assess islet graft function is 3 months post transplantation with a 2 hour mixed meal tolerance test. An alternative assessment can be done with an arginine stimulation test. This amino acid stimulated the beta cells in the pancreatic islets to secrete insulin. With this test, a rise in glucose concentration is not required, as in the mixed meal tolerance test. This makes it possible to assess islet graft function at an early timepoint after transplantation.

We hypothesize that an arginine stimulation test in the first week after islet transplantation has a predictive value for islet graft function after 3 months.

Study objective

Primary Objective: We aim to create a prediction model to predict islet graft function at 3 months post-transplantation, using early islet graft function assessed in the first week after islet transplantation.

Secondary Objective(s):
- To determine the relationship between markers of β-cell death and C-peptide concentrations.
- To determine the correlation between fasting C-peptide and stimulated C-peptide.
- To determine the relationship between in vitro insulin secretory function and in vivo insulin secretory function of the islet graft.
- To determine the relationship between early islet graft function and long-term islet graft success as assessed by Igls score.
- To determine the relationship between pre-transplant islet function and post-transplant islet graft function in autologous islet transplant recipients.
- To assess immunological markers in the early post-transplant phase in relation to long-term islet graft function
- To assess the concentration of insulin in the islet preparations

Study design

This is an observational study with invasive measurements.

Study burden and risks

This study can only be performed in these subjects because of the specific treatment. The arginine stimulation tests have been performed many time worldwide and we think this is a minor burden. We will draw blood on 9 days for this study. The subjects will already be in the hospital for regular care in at least 6 of the 9 days. In total, we will draw a maximum of 502.5 ml blood in the autologous islet recipients and 466.5 ml blood in the allogeneic islet recipients. Although more than half of this amount is drawn in the first week post transplantation, the rest is drawn outside this window. Because the drawing of blood is spread over the study period, it is our opinion that the burden for the subjects is acceptable.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (16-17 years)
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Aged 16 years or older
Currently on the waiting list for allogeneic or eligible for autologous islet transplantation
Willing to use a flash glucose monitoring (FGM) system in the two weeks prior to transplantation (if not yet using a flash or continuous monitoring system (CGM))

Exclusion criteria

Pregnancy
Patients with known hypersensitivity to arginine

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	15-03-2023
Enrollment:	30
Type:	Actual

Ethics review

Approved WMO

Date:	25-01-2023
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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
CCMO	NL79536.058.22