Immediate blood mediated immune response in immunocompromised recipients to islet infusion in vitro

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- To determine whether there is a mitigated immediate immune response to islet infusion in immunosuppressed recipients- To determine if complement activation during immediate immune response is affected in immunocompromised recipients

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

Summary

ID

NL-OMON44045

Source
ToetsingOnline

Brief title
IBMIR in vitro

Condition

- Glucose metabolism disorders (incl diabetes mellitus)
- Autoimmune disorders
- Endocrine gland therapeutic procedures

Synonym
Diabetes sugar

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum

Source(s) of monetary or material Support: DCTI;diabetesfonds

Intervention

Keyword: Diabetes, IBMIR, Islet, Transplantation

Outcome measures

Primary outcome

Incremental increase of cytokines (i.e. TNF-alpha) in plasma after whole blood exposure to allogeneic islets

Secondary outcome

Incremental increase of complement membrane attack complex (C5b-9) in plasma after whole blood exposure to allogeneic islets

Incremental increase of islet associated blood markers (Micro-RNA*s, PPP1R1A) in plasma after whole blood exposure to allogeneic islets

Incremental increase of cytokines (i.e. IL-1A and IL1B) in plasma after whole blood exposure to allogeneic islets

Study description

Background summary

Islet transplantation is a highly technological intervention currently utilised in patients with type 1 diabetes and related complications. Directly after infusion of the islets, a substantial portion is destroyed by an immediately occuring blood mediated immune reaction. This reaction occurs through several pathways (including complement, coagulation and cytokinemediated pathways). The current treatment to mitigate this acute inflammation is etanercept (TNF alpha blockade), but this does not appear to be effect in islet-after-kidney patients

Study objective

- To determine whether there is a mitigated immediate immune response to islet infusion in immunosuppressed recipients

- To determine if complement activation during immediate immune response is affected in immunocompromised recipients

Study design

This is an in vitro experiment where fresh blood of three patient groups is used. Around 20 mL of blood will be drawn from the participants, who are: healthy controls, patients > 3 months after islet transplantation, and matched controls with type 1 diabetes mellitus.
The drawing of blood will be timed with availability of isolated islets for research.
The blood sample will then be divided in 15x 1 mL samples in 2 mL heparin-coated reservoirs where either 500 IEQ islets + 100 µL medium or control + 100 µL medium will be added. The samples will then be placed on a rocking plate in a 37C incubator and for every time point a sample will be taken off the plate, put on ice and centrifuged (at 4 gr C, 200G, 15 mins). The supernatant will then be tested for immune response and islet damage markers.
The time points for taking the samples off the rocking plate are:
- 1 control sample before incubation
- T = +5 min, T = +15 min, +30 min, T = +60 min, T = +120 min, T = +240 min, T = +360 min

The supernatant is tested for:
- A pro-inflammatory cytokine panel (i.e. TNF-alpha, IL-1a, IL-1b)
- Complement (i.e. C5b-9)
- Islet damage marker panel (i.e. microRNA kit, PPP1R1A)

Study burden and risks

THe burden consists of two venepunctures, which are conducted at moment agreed by the researcher and the participant, when islets are available for research.
The extent of burden is considered to be low, since the risks of a venepuncture are minimal, the amount of blood drawn is low (20 mL) en the procedure is performed by a skilled professional

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

Group 1: healthy volunteers, i.e. >18 years old and no current medication use except for over the counter drugs
Group 2: patients who are at least 3 months after transplantation
Group 3: patients with type 1 diabetes, matched for duration of diabetes with the patients in group 2

Exclusion criteria

Unable to give consent

Study design

Design

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:	Recruiting
Start date (anticipated):	02-01-2017
Enrollment:	30
Type:	Actual

Ethics review

Approved WMO

Date:	27-06-2016
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	NL55520.058.15