Nano-MRI to visualize pancreatic inflammation in individuals with recent-onset type 1 diabetes

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Ethical review	Approved WMO
Status	Will not start
Health condition type	Autoimmune disorders
Study type	Interventional

Summary

ID

NL-OMON48407

Source
ToetsingOnline

Brief title
Nano-PRIDE

Condition

- Autoimmune disorders

Synonym
Diabetes Mellitus type 1, Type 1 diabetes

Research involving
Human

Sponsors and support

Primary sponsor: Nucleaire geneeskunde en radiologie
Source(s) of monetary or material Support: JDRF

Intervention

Keyword: FDG PET, Nano-MRI, pancreas inflammation, type 1 diabetes

Outcome measures

Primary outcome

The main study parameter is the difference in iron particle accumulation in macrophages between individuals with T1D and control individuals as a measure for pancreatic macrophage infiltration.

Secondary outcome

o Comparison of pancreatic perfusion between individuals with T1D and controls

o Comparison of nano-MRI with [18F]FDG PET/CT for cross-validation of the potential of nano-MRI to determine pancreatic inflammation

o Correlation of pancreatic macrophage infiltration to (residual) beta cell function

Study description

Background summary

In this project we propose to use Ferrotran-enhanced MR imaging (nano-MRI) using ultra-small superparamagnetic nano-iron oxide particles (Ferrotran: ferumoxtran-10 Lyophilisate) as a contrast agent to visualize both endocrine and exocrine pancreatic inflammation in early-onset type 1 diabetes (T1D). Reliable visualization and quantification of inflammation in the pancreatic islets and the exocrine pancreas will provide important information on the inflammatory processes involved in the early development of T1D. Furthermore, it could represent an early marker for monitoring of disease progression and response monitoring of anti-inflammatory therapies.

Study objective

The primary objective is to compare pancreatic macrophage infiltration between individuals with T1D and controls by imaging intracellular iron particle

accumulation in macrophages by late-phase MR imaging. To achieve this we will first develop an optimized nano-MRI protocol in 5 healthy volunteers.

Study design

We aim to perform an observational clinical trial in which we will include 10 individuals with recent-onset T1D and 10 healthy control subjects. We will assess pancreatic perfusion by MR imaging after infusion of Ferrotran in the angiographic phase before and after stimulation of the pancreatic beta cells with glucose. Also, we will assess uptake of the iron particles in infiltrating macrophages by performing MR imaging in the lymphotrophic phase. Furthermore, we aim to cross-validate this technique by comparing the results to quantitative dynamic [18F]FDG PET/CT imaging, an established method to visualize inflammation.

Intervention

Intravenous injection of Ferrotran and 18F-FDG

Study burden and risks

All individuals will undergo blood sampling for specific laboratory parameters. In addition, all participants in the second phase of the trial will undergo an oral glucose tolerance test (first visit). At the second visit, Ferrotran Lyophilisate will be administered intravenously. Subsequently (for participants in the second phase of the trial), [18F]FDG will be administered intravenously and dynamic PET scanning will be performed for 1 hour starting at the time of injection of the tracer. At the third visit, 2 MR acquisitions (lymphotrophic and angiotrophic phase) will be performed. Subsequently, 0.33 g/kg glucose will be administered intravenously over 1 minute. After this, 1 additional MR acquisition of the angiotrophic phase will be performed.

There are some risks associated with administration of Ferrotran Lyophilisate. Ferrotran Lyophilisate was administered to 1,663 adult subjects in phase I to III studies. About 18.2% of subjects experienced at least one adverse reaction. These reactions were not dose-dependent but partially related to the infusion speed * by fast intravenous infusion the risk of side effects was higher. The most frequently reported adverse reactions were back pain, headache and hypersensitivity symptoms. Most adverse reactions were mild to moderate, short (75% occurred within and lasted less than one hour after the start of the infusion), and had a favorable outcome. Some delayed adverse reactions (up to several days after the start of the infusion) have been reported.
Serious potentially allergic reactions have been uncommonly (0.4%) observed during clinical studies of Ferrotran Lyophilisate. These types of reactions, which included anaphylactic shock, may very rarely be life- threatening or fatal. They can occur irrespectively of the dose of Ferrotran Lyophilisate

administered.

Participants do not personally benefit from participation in the study.

The study could have a large impact on research into the pathophysiology of T1D. Currently, diagnosis of T1D as well as monitoring of disease progression is based on plasma markers like glucose and C-peptide combined with the presence of auto-antigens. Plasma markers are late markers, which usually lead to diagnosis when significant beta cell loss has already occurred. Also, auto-antibodies are persistent and do not reflect the inflammatory status at a specific time. This is limiting for research into new therapeutic options and the possibility of disease prevention.
By visualizing pancreatic inflammation with nano-MRI, individuals with T1D could be diagnosed early in the disease process, before significant beta cell loss has occurred. This will facilitate screening individuals in high-risk populations. Furthermore, the development of the disease can be followed closely, enabling reliable staging of the disease and monitoring of therapeutic interventions. In addition to disease staging and monitoring, nano-MRI will provide crucial information on the genesis, early development and progression of T1D. Nano-MRI could give new insights into the specific inflammatory processes, that play a role in the development of T1D. Also, in combination with beta cell imaging, which is performed at the Radboudumc in Nijmegen using [68Ga]exendin PET/CT, the extent to which pancreatic inflammation correlated with beta cell destruction could be determined. This increase in knowledge will be of great value for research into future therapeutic options and possible prevention of the disease.

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

- Inclusion criteria (Individuals with type 1 diabetes):
* Within 6 months of diagnosis with type 1 diabetes
* Auto-antibody positive, - Inclusion criteria (Control individuals):
* No evidence of impaired glucose tolerance (HbA1c < 42 mmol/mol (6%), fasting glucose < 6.1 mmol/L), - Inclusion criteria (general):
* Age > 18 years
Signed informed consent

Exclusion criteria

- Contra-indication to MRI scanning, iron infusion or hypersensitivity to the active substance or any of the excipients (like mentioned in the SPC).
- Known drug allergies or history of severe asthma, eczema or other ectopic allergies.
- Inability to lie still for at least 30 minutes or comply with imaging
- Hemochromatosis or liver disease defined as ALAT or ASAT level of more than three times the upper limit of normal range
- Renal dysfunction defined as MDRD < 40 ml/min/1.73m^2
- Current pregnancy or the wish to become pregnant within 2 months
- Breast feeding
- Incapability to provide informed consent
- Pancreatitis
- Evidence of other inflammatory disease(s)

Study design

Design

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

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	25
Type:	Anticipated

Ethics review

Approved WMO Date:	07-08-2019
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	29-01-2020
Application type:	First submission
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	EUCTR2019-001869-32-NL
CCMO	NL69987.091.19