effect of Donor Intestinal Microbiota Infusion on residual betacell function in patients with recently diagnosed Diabetes mellitus type 1 ; the DIMID1-trial

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to investigate whether microbial transplantation from either allogenic (healthy) or autologous (own) donor, administered through a small intestinal tube, has beneficial effects on immune status, betacell function c-peptide secretion upon mixed meal...

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

Summary

ID

NL-OMON41670

Source
ToetsingOnline

Brief title
DIMID1-trial

Condition

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

Synonym
betacell function, gut microbiota, type 1 diabetes mellitus

Research involving
Human

Sponsors and support

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

Intervention

Keyword: betacell function, fecal transplantation, gut microbiota, type 1 diabetes mellitus

Outcome measures

Primary outcome

the primary endpoint is betacell insulin secretion capacity: (beta cell function as assessed by mixed meal test) at 0,2,6,9 and 12 months.

Secondary outcome

Secundary endpoint is changes in Immunologic parameters : FACS on periferal leukocyte subsets (change cytokine/Tr1/nTreg/Th2/Th17 subset population), cellular islet autoimmunity (CD4 and CD8) in relation to mucosa innate en adaptive immunity (CCR4, CXCR3,CXCL10) and antiGAD /c-peptide plasma concentrations at 0,2,4,6,9 en 12 months. Our tertiary endpoint is changes in small intestinal (at baseline and after 6 months) and fecal gutmicrobiota composition at 0,2, 6, 9 and 12 months. Moreover, our fourth endpoint pertains changes in plasma biochemistry (HbA1c levels) and urine (microalbuminuria) at 0, 2, 6, 9 and 12 months. Finally, our fifth endpoint is intestinal integrity: Changes in small intestinal genes (ILLUMINA array en occluding expression) at baseline and at 6 months.

Study description

Background summary

Type 1 diabetes mellitus is an autoimmune disease (associated with progressive betacell destruction and subsequent insulin dependence in the first 2-3 decades of life), which associated with an increased morbidity and mortality risk compared to healthy subjects . In this regard, altered intestinal microbiota composition has been implicated to play an important role in (human) metabolism as well as autoimmune diseases (eg inflammatory bowel diseases like Crohn and Ulcerative Colitis). In this regard, recent mouse and human studies have suggested that bacteria from the small intestine could trigger *-cell destruction, most likely by inducing an altered T-helper cell type 17 (Th17) population in the small-intestinal lamina propria. We thus hypothesize that reshaping the (small) intestinal microbiota could stabilize the betacell destruction of the pancreas, thus (partly) preventing exogenous insulin dependence.

Study objective

to investigate whether microbial transplantation from either allogenic (healthy) or autologous (own) donor, administered through a small intestinal tube, has beneficial effects on immune status, betacell function c-peptide secretion upon mixed meal test or MMT) in recently diagnosed type 1 diabetes mellitus. A parallel objective is to see which small (intestinal biopsies) and large intestinal (fecal samples) microbiota are associated with these clinical changes.

Study design

randomized double blind controlled trial

Intervention

after bowel lavage with macrogol, patients will be treated by small intestinal infusion via a duodenal tube of a microbial solution derived from an allogenic (healthy donor n=17) or autologous (own) fecal sample (n=17) every 8 weeks during 6 months (0, 8, 16 wks).

Study burden and risks

DM1 subjects are five times submitted to mixed meal test (MMT) and two times to agastroduodenoscopy, for which no side-effects are expected. Because strict conditions are applied to healthy fecal donors, the risk of spreaking potential pathogens seems nil. We thus think that the knowlegde of this trial on the pathophysiology of Type 1 diabetes mellitus related progressive betacell destruction and subsequent insulin dependence induced by "bad" commensal bacteria outweights the minor potential risks. Moreover, this study could provide us with novel treatment leads (probiotics) aimed at conserving

betacel/pancreas function in DM1 patients.

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

newly diagnosed (< 6 weeks) patients with type 1 diabetes (n<=34, aged 18-39 years, BMI 20-25 kg/m2, male/females, no concomitant medication use except insulin, plasma C-peptide > 0.2 mmol/l and/or >1.2 ng/mL after MMT), fasting glucose 10-13 mmol/l and positive anti-GAD and/or anti-IA-2 titer concentrations.

Exclusion criteria

Use of concomitant medication including PPI and antibiotics past three months, smoking, (expected) prolonged compromised immunity (due to recent cytotoxic chemotherapy or HIV infection with a CD4 count < 240).

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	08-03-2013
Enrollment:	51
Type:	Actual

Ethics review

Approved WMO Date:	29-01-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-06-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	NL42147.018.12