Effect of donor Intestinal Microbiota Infusion on Thyroid function in patients with autoimmune HypOThyreoidism

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To investigate whether microbial transplantation from either allogenic (healthy) or autologous (own) donor, administered every 8 weeks during 6 months through a small intestinal tube, has beneficial effects on residual thyroid function at baseline,...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Thyroid gland disorders
Study type	Interventional

Summary

ID

NL-OMON48031

Source
ToetsingOnline

Brief title
IMITHOT-trial

Condition

- Thyroid gland disorders

Synonym
hypothyrodism, thyroid disease

Research involving
Human

Sponsors and support

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

Intervention

Keyword: fecal transplantation, gutmicrobiota, hypothyreoidism

Outcome measures

Primary outcome

The primary endpoint is effect on residual thyroid function as determined by plasma thyroid markers (TSH/FT4 and antiTPO) as well as determined by rTSH test (0.9mg intramuscular injection) at baseline, 6, 12 and 24 months.

Secondary outcome

Secondary endpoints are reduction in autoimmunity makers including FACS on peripheral blood lymfocyte subsets (change Th17 (CD4+IL-17+) and T-regs (CD4+CD25+ FoxP3+) and in FNAC thyroid (for Imaging Mass Spectrometry) at baseline and after 6 and 24 months. Moreover, intestinal transit time (Sitzmark capsules) will be determined at these three timepoints. Also, quality of life questionnaires (ThyPro, a disease specific QoL scale) and dietary intake lists online (via mijn.voedingscentrum.nl/nl/eetmeter) are measured at 0, 6, 12 and 24 months. Finally, oral and fecal intestinal microbiota and plasma metabolite are determined at 0, 6, 12 and 24 months.

Study description

Background summary

Autoimmune hypothyroidism is a frequently seen disease (400.000 patients in the Netherlands) which is associated with dysfunction of thyroid hormone production, for which the aetiologie is not well known. Treatment comprises of supplementation of thyroid hormone, a treatment that is not affecting the underlying autoimmune process. Autoimmune hypothyroidism is associated with increase morbidity (increased fatigue, lower quality of life). Recent data have

shown that Autoimmune hypothyroidism is associated with altered gutmicrobiota composition. Since we have shown over the last 10 years at AMC in about 500 patients that donor fecal transplantation is safe and has effects on human metabolism, we therefore aim to study the effect of allogenic versus autologous fecal transplantation in subjects with subclinical autoimmune hypothyroidism.

Study objective

To investigate whether microbial transplantation from either allogenic (healthy) or autologous (own) donor, administered every 8 weeks during 6 months through a small intestinal tube, has beneficial effects on residual thyroid function at baseline, 6 , 12 and 24 months after intervention in recently diagnosed patients (n=34) with subclinical autoimmune hypothyroidism.

Study design

Double blind randomized controlled single center trial.

Intervention

fecal transplantation from either allogenic healthy donors or own (autologous) will be given three times (baseline, 8 and 16 weeks) via a small intestinal tube

Study burden and risks

At this moment, there is no treatment available that stops autoimmune destruction of the thyroid gland that results in hypothyreoïdie. Based on the fact the this is a frequently seen disease (400.000 patients in the Netherlands) associated with high morbidity (reduced quality of life and chronic fatigue) new treatment modalities are warranted. Since recent data has shown that these patients have altered gutmicrobiota and bowel function in conjunction with fact that we have shown at AMC that fecal transplantation with donor or own feces is safe and has no side effects in more than 500 patients, we feel that this treatment should be tested in this patient group. In total patients visit AMC for 40 hours during 2 years and In total 240 ml blood is drawn. Also three FNACs of thyroid gland and intestinal transit time tests as well as four Thyrogen thyroid function tests are done. As treatment with intramuscular injection of rTSH (Thyrogen) as well as ultrasound guided FNAC (fine needle aspiration) to obtain thyroid tissue is regularly done in routine patient care, we feel that the potential risks of this study do outweigh the potential benefit (new bacterial strains and/or metabolites that can stop autoimmune destruction and thyroid dysfunction).

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 patients with subclinical autoimmune hypothyroidism aged 18-70 years,
TSH > 10 mU/L
BMI 18-30 kg/m2,
male/females,
no concomitant medication,
antiTPO positive and increased TSH (above 5.0mE/L) with FT4 within normal reference value
;feces donoren:
Healthy male/female volunteers
aged 18-70 years,
BMI 18-28 kg/m2,
no medication use,

no family history of autoimmune diseases

Exclusion criteria

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).;fecal donors:
1. (chronic) diarrhoea
2. family history of autoimmune diseases (type 1 diabetes, Hashimoto hypothyreoidism, Graves hyperthyreoidism, rheumatoid arthritis, inflammatory bowel diseases eg. Crohn*s disease, Colitus ulcerosa or coeliakie)
3. HIV, HAV, HBV, HCV, active CMV, active EBV
4. Unsafe sex practice (questionnaire)
5. presence of fecal bacterial pathogens (salmonella, Shigella, Campylobacter, Yersinia) or parasites
6. positive C. difficile stool test
7. any medication use including PPI and antibiotics
8. smoking

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:	Recruiting
Start date (anticipated):	22-10-2019
Enrollment:	51
Type:	Actual

Ethics review

Approved WMO Date:	04-06-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-08-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-05-2020
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

ID: 23348
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL69382.018.19
OMON	NL-OMON23348