Transplantation of faeces in ulcerative colitis; restoring nature*s homeostasis

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Primary objective: to study the effect of faecal transplantation in a phase II randomised placebo controlled design on simple clinical colitis activity index (SCCAI) and endoscopic Mayo score. Secondary objective: to study intra individual changes...

Ethical review	-
Status	Recruiting
Health condition type	Gastrointestinal inflammatory conditions
Study type	Interventional

Summary

ID

NL-OMON36482

Source
ToetsingOnline

Brief title
TURN trial

Condition

- Gastrointestinal inflammatory conditions
- Autoimmune disorders

Synonym
inflammatory bowel disease, ulcerative colitis

Research involving
Human

Sponsors and support

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

Intervention

Keyword: donor faeces, faeces transplantatie, IBD, ulcerative colitis

Outcome measures

Primary outcome

* Complete clinical remission (SCCAI <2).

* Reduction of Mayo endoscopic inflammation score (decrement >1)

Secondary outcome

* Adverse events (AE) at t=3, t=6 and t=12 weeks

* SCCAI score reduction at t=6 weeks (pairwise SSCAI reduction of > 1.5 points

will be regarded as a relevant reduction (10))

* Frequency of bowel movements (starting to report at t= -2 weeks)

* Reduction of Mayo endoscopic score at t=6 wk

* Time to recurrence (recurrence is defined as a SCCAI of *4 and Mayo score *1

(10))

* Intra individual changes in presence of microbial DNA in faecal samples at

t=0, t=6, and t=12 weeks after faecal transplantation.

* Intra individual changes in presence of microbial DNA in mucosal biopsies at

t=0, t=6, and t=12 weeks after faecal transplantation.

Study description

Background summary

Ulcerative colitis (UC) is a chronic inflammatory bowel disease (IBD) of the colon. Complaints such as abdominal pain, cramps and bloody diarrhoea usually start in early adulthood and lead to life-long substantial morbidity. Despite decades of research the etiology and pathogenesis of this disease are still

poorly understood. Hence, there is no medical treatment available that meets the desired criteria of high efficacy versus low adverse effects. The current prevailing hypothesis regarding the cause of UC states that the pathogenesis involves an inappropriate and ongoing activation of the mucosal immune system driven by the intestinal microbiota in a genetically predisposed individual.
Four non-mutually exclusive hypotheses have been proposed regarding the role of the microbiota in IBD: (i) a dysbalance between protective and harmful bacteria (dysbiosis hypothesis); (ii) impaired intestinal barrier hypothesis; (iii) excessive immune response against normal microbiota; (iv) unidentified persistent pathogen hypothesis.
There are several clinical observations that support the dysbiosis hypothesis. (i) germ-free mice will not develop experimentally induced colitis; (ii) there are several papers on the beneficial effects of probiotics in mild to moderate colitis (iii) there are several case reports of patients achieving remission after faecal transplantation. However, systematic investigation into the effect of correcting the dysbiosis in UC has never been performed. The most radical way to restore the presumably disturbed natural homeostasis in UC is to perform faecal transplantation from a healthy donor.
By designing a specific treatment protocol using faecal transplantation a unique opportunity is created to investigate the potential beneficial effects of restoring microbial homeostasis

Study objective

Primary objective: to study the effect of faecal transplantation in a phase II randomised placebo controlled design on simple clinical colitis activity index (SCCAI) and endoscopic Mayo score. Secondary objective: to study intra individual changes in microbiota composition of faeces and mucosal biopsies at t=0, t=6, and t=12 weeks after faecal transplantation.

Study design

This is a double-blind randomized placebo controlled clinical proof-of-concept study as well as a reversed translational part.

Intervention

Patients will be treated with faecal transplantation, processed for duodenal-tube infusion. Faeces will be collected from a donor as well as the patient him/herself, in which their own faeces will be used as a placebo

Study burden and risks

It seems plausible that patients have benefit from donor faeces of strictly selected healthy donors. Sigmoidoscopies have a very small risk of complications; the same holds for cortrak duodenal tube positioning. According

to our experience with human faecal transplantation in therapy resistant Clostridium difficile associated colitis as well as from the pilot trial studying the effects of faecal transplantation on obesity no serious side effects were observed.

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

*Age *18
*Ability to give informed consent
*Established left sided ulcerative colitis according to the Lennard-Jones criteria
*SCCAI (Simple Clinical Colitis Activity Index) of 4 - 11
*Endoscopic Mayo score of >1
*Stable dose of thiopurines, 5-ASA, or corticosteroids in preceding 8 weeks

*Women need to use reliable contraceptives during participation in the study

Exclusion criteria

* condition leading to profound immunosuppression
o For example: HIV, infectious diseases leading to imunosuppression, bone marrow malignancies
o Use of systemic chemotherapy
* Anti-TNF treatment in preceding 2 months
* Ciclosporine treatment in preceding 4 weeks
* Prednisolone dose * 10 mg
* Life expectancy < 12 months
* Use of antibiotics in preceding 6 weeks
* Use of probiotic treatment in preceding 6 weeks
* Positive stool cultures for common enteric pathogens (Salmonella, Shigella, Yersinia, Campylobacter, enteropathogenic e coli)
* History of surgery:
o hemicolectomie (defined as: surgery resulting in a resection of > * of the colon)
o presence of a pouch due to surgery
o Presence of stoma
* Known intra-abdominal fistula
* Pregnancy or women who give brestfeeding
* Vasopressive medication, icu stay
* Signs of ileus, diminished passage
* Allergy to macrogol or substituents, eg peanuts, shellfish

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Double blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL
Recruitment status: Recruiting

Start date (anticipated):	24-06-2011
Enrollment:	40
Type:	Actual

Ethics review

Not available

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	NL35247.018.11