The influence of alterations in the intestinal microbiome on the clinical course of inflammatory bowel disease

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Primary Objective: * What is the influence of alterations in the intestinal microbiome composition on the course of disease in patients with IBD?Secondary Objective(s): * Is the intestinal microbiome composition associated to fatigue scores?* Is the...

Ethical review	Approved WMO
Status	Pending
Health condition type	Gastrointestinal inflammatory conditions
Study type	Observational invasive

Summary

ID

NL-OMON45843

Source
ToetsingOnline

Brief title
Intestinal microbiome and disease activity in Inflammatory Bowel Disease

Condition

- Gastrointestinal inflammatory conditions

Synonym
IBD, Inflammatory bowel disease

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Disease course, Inflammatory Bowel Disease (IBD), Microbiome

Outcome measures

Primary outcome

The main study parameter is the composition of the patients* intestinal microbiome defined by the proportion and diversity of fecal bacterial species and phyla.

Secondary outcome

* Blood parameters including CRP, leukocytes and inflammatory cytokines

* Fatigue scores measured by FACIT-F and MFI

* Anxiety, depression scores measured by PROMIS NIH questionnaires

* Relapse (defined as FCP>250 µg/g, elevated CRP levels, and HBI*4 or SCCAI*2)

* Quality of life measured by SIBDQ

* Dietary habits measured by a series of 24-hour recalls and a food additive questionnaire

* Medication adherence measured by MAS-8

Study description

Background summary

Inflammatory bowel disease (IBD), which includes Crohn*s disease (CD) and ulcerative colitis (UC), is a complex chronic inflammatory disorder of the gastrointestinal tract. The course of the disease is characterized by periods of remission and recurrent active inflammation (1). Its management includes the use of immunosuppressive medication to alleviate symptoms and induce clinical remission, but in some cases surgery is necessary (1). Though the pathogenesis of IBD is not entirely understood, it is thought to involve complex interactions between the immune system, the microbiome and environmental

factors in genetically susceptible individuals.

The intestinal microbiome is a complex entity including up to 1000 microbial species and several million genes. Through a bi-directional relationship between the intestinal microbiome and the host, the immune system and metabolic processes can be affected (4). The composition of the microbiome is considered to be involved in the pathogenesis of chronic diseases, including IBD. Microbial dysbiosis, an alteration of the intestinal microbiome composition, has been repeatedly observed in patients with IBD. Compared to a healthy population, these patients have a fecal microbiome characterized by a less diverse array of bacteria (5). In addition, studies have consistently reported a decrease in members of the Firmicutes phylum and an increase in members of the Bacteroidetes phylum in IBD cases, representing a shift towards a more pro-inflammatory microbiome.

Although dysbiosis has been described in many studies, little is known about the changes in the composition of the intestinal microbiome and their influence on the course of disease. Some studies have reported a difference in the intestinal microbiome composition of patients in active and inactive phases... However, the cross-sectional design of those studies provides no information on the long-term status of bacterial diversity in relation to disease. To date, only one prospective study has been performed in which no overall patterns in microbial changes related to the presence of an exacerbation of disease were found. Nevertheless, their small study population may have biased the results, highlighting the need for prospective data on a larger number of patients.

As a result, this study aims to provide insight into the relationship between the intestinal microbiome and disease activity in a cohort of IBD patients. Data collection at various time points would give a better picture of the disease course and the impact changes in the composition of the microbiome upon it. In addition, information on important factors associated with disease such as quality of life, fatigue levels and medication side effects would broaden the knowledge of the influence of the microbiome on IBD. Ultimately, this study aims to find markers of disease activity to provide insight into novel approaches for disease management.

Study objective

Primary Objective:
* What is the influence of alterations in the intestinal microbiome composition on the course of disease in patients with IBD?

Secondary Objective(s):
* Is the intestinal microbiome composition associated to fatigue scores?
* Is the composition of the intestinal microbiome associated with the concentration of serum circulating cytokines?
* Is the composition of the intestinal microbiome correlated to disease

activity and response to pharmaceutical treatment?
* Do lifestyle factors (i.e.: dietary habits) influence the composition the intestinal microbiome composition?

Study design

This study consists of a longitudinal prospective non-interventional design where a cohort of IBD patients will be followed for a period of two years. As part of their routine check-up at the Erasmus MC, participants will come to the outpatient clinic every six months, for a total of five visits within a period of two years. During those visits, they will be asked to fill out various questionnaires measuring a series of variables (see table below). In addition, they will be invited to provide a fecal sample to assess fecal calprotectin levels and for microbiome analysis. Blood samples will also be collected as part of patients* routine visit at the outpatient clinic.

Three months after their visit at the outpatient clinic, participants will receive a phone call (4 phone calls within two years). This call will be used to inquire about the patient*s disease status and to remind them to fill out questionnaires and send a fecal sample to the hospital via mail.

During moments of disease relapse (defined as fecal calprotectin (FCP)>250 µg/g, elevated C-reactive protein (CRP) levels, HBI*4 or SCCAI*2) patients will be asked to provide an extra fecal sample and fill in additional questionnaires (HBI, SCCAI, FACIT-F and MFI).

Study burden and risks

The extent of the burden associated with this study is minimal. In addition to their habitual check-up at the outpatient clinic of the department of Gastroenterology at Erasmus MC, patients who decide to join the study will be asked to provide fecal samples and fill out a series of questionnaires every three months. In addition, patients with an exacerbation of disease will be asked to provide an extra fecal sample and fill out a few questionnaires at the time of disease onset. Furthermore, the risks associated with this study are minimal, as no investigational medicinal product will be used.

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

Aged > 18
Confirmed CD or UC or IBD-unspecified based on diagnostic criteria using clinical symptoms, endoscopic, biochemical and/or histological results

Exclusion criteria

Use of pre-, pro- and/or antibiotics within 8 weeks prior to start of the study
Presence of active malignancy or dysplasia
Pregnant and/or breastfeeding women
Presence of active rotavirus or clostridium infection at start of study
Patients with a pouch or stoma

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-04-2019
Enrollment:	250
Type:	Anticipated

Ethics review

Approved WMO

Date:	28-09-2018
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL66161.078.18