Characterization of Inflammatory Cell Subpopulations of the Gut Associated Lymphoid Tissue and Peripheral Lymph Nodes in Inflammatory Bowel Disease

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

Summary

ID

NL-OMON51080

Source
ToetsingOnline

Brief title
Immunotyping Lymph Nodes in IBD

Condition

- Gastrointestinal inflammatory conditions

Synonym
Inflammatory bowel disease-Crohn's 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: IBD, Immunogenicity, Immunotyping, Lymph nodes

Outcome measures

Primary outcome

Our first aim is to determine the involvement of GALT (Peyer*s patches, mesenteric lymph nodes) and peripheral lymph nodes in the immune deregulation that is observed in IBD.

We have defined primary study parameters as:

1) Frequencies and phenotype of immune cell populations in GALT in active and inactive IBD

2) Differences in immune cell populations (frequency, phenotype, cytokine production, genetic, epigenetic and transcriptional alterations) and stromal cells in GALT compared to peripheral lymph nodes

Secondary outcome

As secondary study parameters for our first aim we have defined:

1) Frequency and gene expression profiles of immunoglobulin producing B-cells and plasma cells in active and inactive disease

2) Differences in immune cell populations (frequency, phenotype, cytokine production, genetic, epigenetic and transcriptional alterations) and stromal cells in in peripheral lymph nodes in IBD patients and healthy controls

Our second aim is to understand the pathophysiological mechanisms in inguinal

lymph nodes of IBD patients in the development of immunogenicity to therapeutic antibodies.

For this aim the study parameter will be:

3) Differences in immune cell populations, amongst other germinal center B cells and T follicular helper cell responses, in peripheral lymph nodes of patients with active and inactive IBD, with and without anti-drug antibodies (ADAs).

Study description

Background summary

One of the biggest barriers to progress towards better treatments in inflammatory bowel disease (IBD) is 1) our lack of understanding of the disease etiology and 2) our lack of understanding the mechanisms involved in response or lack/loss of response to treatments, such as the development of anti-drug antibodies. The gut associated lymphoid tissue (GALT) as well as peripheral lymph nodes (LN) are lymphoid structures that play an important role in and antibody formation and are involved in shaping intestinal and peripheral immunity. It is however unknown whether and how these lymphoid structures are involved in IBD etiology and whether they are involved in anti-drug antibody formation. We hypothesize that 1) GALT and peripheral LN are involved in IBD pathophysiology, and 2) GALT and peripheral LN are involved in anti-drug antibody formation, and thereby loss of response to therapy.

Study objective

1) Our first aim is to determine the involvement of GALT (Peyer*s patches, mesenteric lymph nodes) and peripheral lymph nodes in the immune deregulation that is observed in IBD

2) Our second aim is to understand the pathophysiological mechanisms in peripheral lymph nodes of IBD patients in the development of immunogenicity to therapeutic antibodies.

To achieve these aims we will:
Analyze immunological alteration in mesenteric lymph nodes, Peyers patches and/or inguinal lymph nodes (including phenotype and function of B- and T

cells, cytokine production, genetic, epigenetic and transcriptional alterations of immune and stromal cells) of IBD patients, and correlate these alterations with diagnosis, disease stage, treatment response.

Study design

We will perform a cross sectional study for immune cell characterization and gene expression analysis in the GALT and inguinal lymph node compartments and lymphoid organs, to elucidate the mechanisms involved in the pathogenesis of IBD, as well as, in the development of immunogenicity against biological treatments. Patients with UC and CD will be recruited from the outpatient IBD clinic at Amsterdam University Medical Centers. Demographic data and clinical data regarding classification of diagnosis, medication use and disease activity, will be collected. Patients will be included starting March 2020 with an inclusion period of 2-3 years.
Since these are pioneering studies in the field of IBD, we will also study inguinal lymph node biopsy sampling in healthy controls, in order to detect differences that are specific for IBD patients.

To get access to GALT tissues and mesenteric lymph nodes, IBD patients undergoing surgery because of extensive inflammation or stenotic disease will be included in our study. For this procedure we will collaborate with the gastrointestinal surgery department of the gastroenterology unit. In addition, we will obtain peripheral (inguinal) lymph node biopsy samples under ultrasonographic guidance both from IBD patients undergoing surgery as well as those without surgical treatment.

Study burden and risks

IBD is a chronic destructive incurable disease, characterized by a medical need for novel drugs and therapeutic protocols. Furthermore, the application of personalized medicine approaches on current treatments is necessary, to achieve a more favourable outcome for the patients, as well as, to improve their quality of life. Our research will contribute significantly in this goal and the long-term benefits of the patients definitely outweight the risks of the individuals involved. Moreover, as it is previously described, the sampling procedures (blood and lymph node), are accompanied by insignificant adverse events, and are safe for the subjects. Potential hematomas due to the needle biopsy or blood withdrawal, are easily addressed with no impact for the health condition of the individuals.

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 inflammatory bowel disease patients:
- Age 18-80 years
- Additional for aim 1 of METC research protocol: Patients with Crohn's disease undergoing ileocecal resection because of (inflammatory or fibrotic) stenosis or extensive inflammation or therapy refractory disease

Inclusion criteria healthy controls

- Negative for inflammatory bowel pathologies.
- Age 18-80 years.

Exclusion criteria

Exclusion criteria for inflammatory bowel disease (IBD) patients:

- Patients, who are not able to provide informed consent.
- History of malignancy
- Viral or bacterial infection within the past 4 weeks
- Patients using anticoagulant therapy
- Present or previous use of systemic corticosteroids less than 28 days before enrolment

- Present or previous use of general immunosuppressive agents (e.g. Azathioprine, Methotrexate, Mycophenolate Mofetil)
Exclusion criteria healthy controls:
- Presence of bowel complaints or other intestinal inflammatory conditions (e.g. diverticulitis)
- Individuals using anticoagulant therapy
- Present or previous use of systemic glucocorticoids less than 28 days before enrolment
- Present or previous use of experimental drugs
- Present or previous treatment with any cell depleting therapies, including investigational agents
- Presence of any disease for which study subjects need chronic or intermittent immunosuppressive therapy (e.g. prednisolone).
- History of chronic viral infection
- Recent (<1 week) bacterial or viral infection
- History of autoimmune disease
- History of malignancy
- Individuals, who are not able to provide informed consent

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL
Recruitment status: Recruiting

Start date (anticipated):	30-09-2021
Enrollment:	64
Type:	Actual

Ethics review

Approved WMO Date:	18-05-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-10-2022
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	NL76643.018.21