Exploring the role of faecal mesalazine (5-ASA) concentrations in therapeutic drug monitoring in ulcerative colitis: a pilot study.

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

Summary

ID

NL-OMON48827

Source
ToetsingOnline

Brief title
TDM-5-ASA

Condition

- Gastrointestinal inflammatory conditions

Synonym
'inflammatory bowel disease', 'ulcerative colitis'

Research involving
Human

Sponsors and support

Primary sponsor: Maag, darm, leverziekten

Source(s) of monetary or material Support: Bedrijven;zie G2.,Ferring

Intervention

Keyword: Colitis, Mesalazine, Therapeutic drug monitoring, Ulcerative

Outcome measures

Primary outcome

Included patients will be divided in two groups: active disease and clinical remission. Patients will start collected urine and faeces (for 1 and 3 days, respectively) 5 days before endoscopy. During endoscopy mucosal biopsies will be collected. The 5-ASA and N-Ac-5-ASA concentration will be determined using quantitative HPLC analysis.

The main study parameters/endpoints include: 5-ASA concentration in faeces, expressed in mgs in patients with active and quiescent disease.

Secondary outcome

- faecal excretion of 5-ASA in 24-hours faeces expressed in % of ingested dose

- faecal excretion of 5-ASA in 24-hours faeces expressed correlation to dry weight

- faecal N-Ac-5-ASA concentration in 24-hours faeces expressed in % and mg and in relation to dry weight

- mucosal 5-ASA and N-Ac-5-ASA concentration in colonic biopsies expressed in ng/mg

- 5-ASA and N-Ac-5-ASA concentration in 24 hours urine expressed in % and mg

- composition of gut microbiome

All in patients with active and quiescent disease ulcerative colitis

Study description

Background summary

Oral 5-aminosalicylic acid (5-ASA) is an effective and widely used treatment for ulcerative colitis (UC). The mechanism of action is unknown, but thought to be topical rather than systemic. The concentration of 5-ASA (and the inactive metabolite N-Ac-5-ASA) can be measured in plasma and urine but this reflects the systemic uptake and not the exposure of the drug to the mucosa. Limited data suggest that the concentration of 5-ASA in the rectal or colonic mucosa is higher in patients in clinical remission as compared to patients with active UC. Surprisingly, almost no data on faecal excretion of 5-ASA or N-Ac-5-ASA in UC patients and healthy volunteers are available. We propose to study faecal excretion of 5-ASA and its putative association with remission and active UC. Potentially, this marker could be used for therapeutic drug monitoring of 5-ASA therapy in UC patients in the clinical setting. Through therapeutic drug monitoring, the dose and frequency of 5-ASA will be optimized for the individual patient. On top of that, we will determine the gut microbiome in UC patients and their rol in drug metabolism, like 5-ASA.

Study objective

The primary objective of this study is to explore if faecal 5-ASA levels are correlated with flares or with response to 5-ASA therapy in patients with UC. The secondary objectives of this study are to determine if faecal N-Ac-5-ASA concentration, mucosal 5-ASA (and N-Ac-5-ASA) concentration and urine 5-ASA (and N-Ac-5-ASA) concentration are correlated with response to 5-ASA therapy in patients with UC. In addition, we aim to study the inter- and intra-individual variation of faecal 5-ASA (and N-Ac-5-ASA) levels, and the gut microbiome (mucosa, faeces) of the UC patient

Study design

Observational cohort study.

Study burden and risks

Collection of faeces over three consecutive days and urine for 24 hours. All patients will receive usual clinical care. Patients not using Pentasa 3 gram per day but another 5-ASA formulation 2.0-4.8 gram per day will switch their 5-ASA formulation to Pentasa 3 gram per day for two weeks: this cause not any risk for the patient but could be any burden for the patient. During endoscopy, four extra biopsies will be taken. The additional risk of bleeding and perforation, associated with taking these biopsies, is very small (1:1000) and

these complications can almost always be managed endoscopically.

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

In order to participate in this study, a subject must meet all of the following criteria:
- Patients >18 year old with established ulcerative colitis in care in the UMC Utrecht
- Indication for an endoscopy (diagnostic endoscopy during a flare or regular surveillance endoscopy during clinical remission; colonoscopy or sigmoidoscopy)
- Using an oral 5-ASA formulation (except a prodrug) per day for at least two weeks in a dose of 2.0 until 3,0 gram/day during active disease (thus endoscopy for flare) or 2.0 until 4.8 gram/day during remission (endoscopy for surveillance)

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
- Previous intestinal surgery (with the exception of appendectomy)
- Need for surgical interventions
- Active use of laxatives (bisacodyl, poly ethyleen glycol / Pegol) or anti-diarrheal mediation (opioids, codeine, loperamide)
- Combination use with other 5-ASA formulations (enema, suppository)
- Pregnancy
- Stool frequency less than 1 time a day (slow intestinal transit time)
- Uncontrolled or sever liver, renal, cardiac or pulmonary disease:
o Liver: Child-Pugh score > 7
o Renal: GFR < 60 ml/min for more than 3 months
o Pulmonal: COPD GOLD stage 3-4, need of oxygen supply at home, or uncontrolled asthma
o Cardiac: heart failure NYHA class 3-4 or myocardial infarct in the past 12 months

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-05-2018
Enrollment:	28
Type:	Actual

Ethics review

Approved WMO

Date:	22-01-2018

Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	21-02-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	14-06-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	22-05-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	NL62046.041.17