Combination Therapy with Drug and Diet for Induction of Remission in Mild to Moderate Active Pediatric Ulcerative colitis: A Single Blinded, International Randomized Controlled Trial

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In the current study we will attempt to evaluate if the diet, termed the UC Diet (UCD), can improve outcomes when administered with a 5ASA regimen to pediatric patients with mild-moderate UC, through a single blinded multinational RCT.

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

Summary

ID

NL-OMON54904

Source
ToetsingOnline

Brief title
INDUCT

Condition

- Gastrointestinal inflammatory conditions

Synonym
chronic bowel inflammation, Inflammatory bowel disease

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: beurs voor studiecoordinator in Israel + divisie/persoonlijk onderzoeksgeld

Intervention

Keyword: combination therapy, diet, pediatric ulcerative colitis, remission

Outcome measures

Primary outcome

Remission defined as PUCAI<10 at week 6

Secondary outcome

Clinical Secondary End Points:

- Response defined as a drop of PUCAI at least 10 points or remission

(intention to treat) week 6 .

- Mean/median change in Calprotectin at week 6

- Sustained steroid & biologic free remission week 12

- Need for topical therapy by week 12

- Change in UCDEIS at week 12 (optional)

- Tolerance to diet defined by withdrawal from the study because of

difficulties with the diet.

Translational Secondary End Points:

- Changes to the microbiome: diet vs. no diet

- Change in microbiome: remission vs. failures

- Short chain fatty acids in stool by group week 6

Study description

Background summary

Recent evidence suggests that environmental factors and diet in particular may play an important role in IBD pathogenesis, with the strongest evidence to date for Crohn*s disease. Understanding of these processes facilitated development of effective dietary therapies for patients with CD. To date, there is no proven dietary intervention that may help patients with ulcerative colitis (UC). On the microbiota side, UC is characterized by decreased production of short chain fatty acids (SCFA) and increased Proteobacteria and sulfide-reducing bacteria (SRBs). From the host*s perspective, a decrease in goblet cells and mucin production coupled with a permeable mucous layer is demonstrated in UC. Each of these observations can be linked to factors found in Western diet that may promote and accelerate intestinal inflammation. As an example, soy and casein have been shown to exacerbated dextran-sodium sulfate (DSS) colitis in mice and dairy fat was shown to induce colitis in a rodent model as well.

The PIBD research center at WMC has developed a diet (UC Diet, or UCD) based on restriction and addition of dietary components that may affect the host mucous layer or microbiome, based on these observations. This diet is rich in fruits and vegetables but reduces exposure to certain animal-based sources of protein and fat while favoring other animal sources of protein and healthy oils.

In two ongoing pilot trials to evaluate efficacy in patients with mild to moderate UC who have failed induction on 5ASA therapy or relapsed on 5ASA (5ASA failures), this led to a clinical response in 17/19 (88%) and a steroid-free clinical remission in 9/19 (47%) of treatment courses in children and 3/6 (50%) in adults (2 with complete mucosal or near complete healing after 8 weeks). These results imply that diet could play a more important role in induction of remission than currently appreciated.
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Study objective

In the current study we will attempt to evaluate if the diet, termed the UC Diet (UCD), can improve outcomes when administered with a 5ASA regimen to pediatric patients with mild-moderate UC, through a single blinded multinational RCT.

Study design

This will be a 12 week, single blinded RCT in children and adolescents with mild to moderate UC comparing 5ASA (recommended dosing 60-75 mg/kg/day; minimum

2.5 maximum 4 grams/day) with fiber restriction for 6 weeks followed by free diet (Group 1) to 5ASA with UCD for 6 weeks, followed by the step down UCD for the next 6 weeks.

Intervention

Current clinical practice is to reduce exposure (now withhold fiber) to fiber during active bleeding and diarrhea and to gradually increase access to grains fruit and vegetables once patients improve. This practice has no evidence behind it and was based on common sense. We will compare two dietary strategies, insoluble fiber reduction via current practice in each site to the UC Diet. The UC diet will restrict certain sources of animal protein, animal fat, and emulsifiers and food additives during the 12week period, while allowing access to fruit, vegetables, and certain grains. It is not a vegan or vegetarian diet as it contains portions of chicken and eggs. It will be structured with mandatory foods, foods that are restricted to certain days or certain quantities, and other foods that are unlimited, to provide better food related quality of life. Both groups will receive a calcium supplement and vitamin D supplement for 6 weeks. Dietitians will assess dietary intake of calories and food groups at week 0 and 6 and will assess compliance by local analysis of food diaries. Intolerance to diet will be defined as patients stopping the diet because of difficulty with the diet (not because of inadequate response).

Study burden and risks

The burden in this study consists of a dietary adjustment. This burden is limited by providing clear instructions (on what can be consumed or not) about the diet and example recipes. Participants must also answer a number of questionnaires during the study and spend more time than if they did not participate. On the other hand, the results on which this study is based are positive and it seems that it could have a beneficial effect on the remission of the participant. In addition, participating involves no further risks.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

1. Informed consent
2. Established diagnosis of UC by the Paris classification and Revised Porto Criteria.
3. Age: 10 - 19 years (inclusive)
4. Mild to moderate active disease, 10 <= PUCAI <=45
5. Extent E2-E4 by the Paris classification
6. Weight >30 kg (ensures that patients who received 5ASA <=2 grams are eligible)
7. Stable medication (IMM/ 5ASA) use or no change in medication use for the past 6 weeks. Patients who have received topical 5ASA therapy for <10 days and are active may be included if topical therapy is stopped at enrolment.
8. Patients not receiving 5ASA or using 5ASA<50mg/kg/day

Exclusion criteria

1. Any proven current infection such as positive stool culture, parasite or C. difficile.
2. Steroids (oral or intravenous) use in the past 3 months.
3. Patients who continue topical 5ASA or steroids after enrolment
4. Use of biologics in present or in past 6 months
5. Use of antibiotics for more than one week in the past 60 days
6. PUCAI >45
7. Acute severe UC in the previous 12 months.

8. Current extra intestinal manifestation of UC.
9. PSC or Liver disease
10. Pregnancy.
11. Vegans or patients unwilling or unable to consume eggs
12. IBD unclassified

Exclusion criteria Comments:
1. Stool culture, parasite or C. difficile will only be measured if the patient has diarrhea.
2. Patients who have received treatment enemas for 3 weeks or less then 3 days and are active, can be included but must stop the enemas on the day of enrolment

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-04-2021
Enrollment:	10
Type:	Actual

Ethics review

Approved WMO

Date:	13-05-2020
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO Date:	23-06-2020
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

No registrations found.

In other registers

Register	ID
CCMO	NL72407.018.19