Modified Exclusive Enteral Nutrition with the Crohn's Disease Exclusion Diet for Induction and Maintenance of Remission and Re-biosis

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To prove that sustained clinical remission can be maintained at week 14 with a new dietary strategy that involves only 2 weeks of EEN with Modulen and 22 weeks of an exclusion diet involving selected table foods. We hypothesize that use of EEN for...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Gastrointestinal infections
Study type	Interventional

Summary

ID

NL-OMON49852

Source
ToetsingOnline

Brief title
DIETOMICS

Condition

- Gastrointestinal infections

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: Wetenschappelijke Adviesraad Emma Kinderziekenhuis voor coordinatie van het onderzoek

Intervention

Keyword: Crohn's disease, diet, microbiome, remission

Outcome measures

Primary outcome

ITT, sustained Corticosteroid-free remission at week 14 (defined as Pediatric

Crohn Disease Activity Index- PCDAI *10 without exposure to systemic steroids).

Secondary outcome

1. ITT steroid-free clinical remission at week 8

2. Microbiome composition difference between groups at week 14

3. Reduction of at least 50% from baseline in fecal calprotectin at week 24 for

patients who did not change their treatment

4. Steroid and biologic free remission at week 24.

5. Need for additional treatment to achieve remission by week 14

6. Transmural healing as assessed by MRE in dietary responsive disease at week

52

7. The proportion of patients who respond with the susceptible genes compare to

those without the susceptible genes

8. Microbiome composition difference between dietary responders to healthy

controls at week 24

Study description

Background summary

Exclusive enteral nutrition (EEN) is an established but difficult to perform method for induction of remission and is not practical or effective for maintenance of remission. It entails drinking a liquid medical formula for 8 weeks as the sole intake of food. Refusal to use or to adhere to this therapy is not uncommon and leads to use of other non- dietary strategies in children including steroids and immunosuppression. Partial enteral nutrition (PEN) appears to have some benefit in maintenance of remission in adults but paediatric data are conflicting. There is no prospective pediatric controlled trial to provide evidence. The Crohn*s Disease Exclusion Diet (CDED) with partial enteral nutrition has been shown to be effective for induction of remission in children with mild to moderate disease. We have developed a maintenance strategy based on the CDED that appears to maintain remission while allowing increased access to table foods over time.

Study objective

To prove that sustained clinical remission can be maintained at week 14 with a new dietary strategy that involves only 2 weeks of EEN with Modulen and 22 weeks of an exclusion diet involving selected table foods.
We hypothesize that use of EEN for only 2 weeks followed by partial enteral nutrition with the CDED diet with PEN will be superior in sustaining Corticosteroid-free remission by week 14 compare to 8 weeks of EEN followed by PEN and free diet, and that this remission will be maintained through week 24 while the diet is maintained. From a translational viewpoint, we intend to compare the effects of dietary therapy on the microbiome, including microbial function and mucosa associated bacteria, between patients using standard EEN and free diet and those on modified EEN and CDED with PEN. We will also compare changes in microbiome to healthy controls, siblings and parents. We further hypothesize that the CDED will promote butyrate producing species while EEN will reduce these species.

Study design

This is a multicenter, open-label, randomized controlled trial. The study will be performed in 5 countries in and outside the EU. The study duration is 52 weeks. Children in group 1 will follow a diet during 24 weeks. Children in group 2 will receive standard of care treatment during 8 weeks (with gradual reduction of EN to week 12)

Intervention

Group 1 will receive a short course (14 days) of EEN followed by partial enteral nutrition, providing 50% of their needs from Modulen along with CDED for 6 weeks (total 8 weeks); this will be followed by CDED phase 2 with 25% of the patients* dietary needs from Modulen for an additional 6 weeks (weeks 9-14). Starting at week 15, patients will continue to CDED phase 3 (maintenance

phase) with 25% of dietary needs from Modulen.

Group 2 will receive Standard EEN for 8 weeks using Modulen, followed by free diet with gradual reduction of Modulen to 25% PEN by week 12.

Study burden and risks

The burden in this study consists of a long-term dietary adjustment, which can be a burden. We attempt to reduce this burden to the minimal amount by providing clea instructions and sample recipes. In addition, participants must answer a number of questionnaires during the study, something that takes up their time. Urine collection and MRE at week 52 is something that would not be performed during standard care. If the child's own doctor decides on a colonoscopy, we will ask for ileal washes and additional biopsies. This is optional. All these (additional) actions take time and may be a burden but do not pose a substantial risk to the participant of the study. Also, following the diet itself does not entail any additional risks.

The resutls on which this study is based are promising and there is a good chance that this dietary adjustment will allow children to remain complaint-free (in remission) for longer and.or postpone additional treatments with steroids and biologicals. In current practice, the CDED (according to Levine et al, Gastroenterology 2019) is well tolerated, allowing induction of remission. Motivated parents even continue the diet after end of the "schedule" because of the positive effects and the "minimal" effort they have to make by excluding certain table foods. In addition, standard treatment (EEN) for induction of remission is foten poorly tolerated and/or refused by children.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

For Patients
1. Established diagnosis of Crohn's disease.
2. Patients with mild to severe active Crohn's disease (15*PCDAI*47.5)
3. Ages 8-18
4. Duration of disease * 36 months
5. Active inflammation (CRP*0.6 mg/dL or ESR*20 or Calprotectin*200 mcg/gr during screening
6. Patients with B1, P0 uncomplicated disease at enrollment
7. Patients with disease defined as L1, L4, L3 or L2 limited to cecum, ascending or transverse colon or L2 with left sided disease with terminal ileum or small bowel involvement in the past by the Paris classification (patients with macroscopic disease)
8. Signed informed consent

Inclusion criteria comments:
1. Patients with stable medication (IMM/5ASA) use or no medication use for the past 8 weeks may be enrolled.
2. Patients with few aphthous ulcers in the rectosigmoid only can be enrolled as L2

Exclusion criteria

For patients
1. Patients with very mild disease (PCDAI 12.5-15) or very severe disease

(PCDAI >47.5)
2. Pregnancy
3. Patients who have disease confined to the colon involving the descending colon, rectum or sigmoid colon and no prior history of small bowel involvement
4. Patients who have active extra intestinal disease (such as arthritis, uveitis, pyoderma gangresom, erythema nodosum, etc.)
5. Patients with complicated disease (B2, B3)
6. Patients with recent onset use of an immunomodulator <8 weeks, or dose change in past 8 weeks.
7. Patients with past or current use of biologics, or patients who currently use systemic steroids or used steroids over the last 8 weeks
8. Patients who have active perianal disease (active fistula or abscess)
9. Patients who have positive stool cultures with relevant pathogens, or positive tests for parasites or C. difficile. Stool tests are mandatory only if diarrhea is present.
10. Patients with fever > 38.3
11. Documented milk protein allergy

Exclusion criteria comments:
1. Aphthous stomatitis is not an exclusion criterion. Isolated aphthous ulcers of the rectosigmoid need not be excluded as left sided L2 only
2. Patient may receive a stable dose immunomodulator or start thiopurines at or after week 4 or Methotrexate at week 6, since the effect of thiopurine starts after 8 weeks and that does not affect the primary endpoint remission at week 8.
3. Patients are allowed use of Omeprazole if ulcers or erosions are present in the stomach or duodenum.
4. Patients may receive antibiotics for intercurrent infections for up to 10 days with the exception of quinolones, metronidazole, rifaximin or oral vancomycin; antibiotics used must be registered in the CRF.
5. Patients with skin tags or fissures can be enrolled.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	35
Type:	Anticipated

Ethics review

Approved WMO Date:	09-09-2020
Application type:	First submission
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
ClinicalTrials.gov	NCT02843100
CCMO	NL73108.018.20