ISRCTN15475780 https://doi.org/10.1186/ISRCTN15475780

The effect of a combination of a specific diet and stool therapy (from a healthy individual) in causing improvement in patients with mild to moderate ulcerative colitis

Submission date
12/03/2022

Recruitment status
No longer recruiting

Registration date
16/03/2022

Overall study status
Completed

Last Edited
17/08/2022

Condition category
Digestive System

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Ulcerative colitis is a long-term condition where the colon and rectum become inflamed. The colon is the large intestine (bowel) and the rectum is the end of the bowel where stools are stored. Small ulcers can develop on the colon's lining, and can bleed and produce pus.
Fecal microbiota transplant (FMT), also known as a stool transplant, is the process of transferring fecal bacteria and other microbes from a healthy individual into another individual.

Alteration in the beneficial gut flora (dysbiosis) is proposed as one of the probable causes of ulcerative colitis. The agents used for the treatment of ulcerative colitis try to reduce the inflammation by suppressing the immune response of the body. However, because these agents suppress the immune response of the body, they can increase the chances of infections and cancer. Correction of dysbiosis can also cause symptomatic improvement without causing side-effects associated with agents that suppress the immune response. The beneficial gut flora can be improved with a combination a diet that enhances beneficial flora and fecal microbiota transplantation (FMT) which is the infusion of fecal suspension from a healthy individual (carrying beneficial bacteria) into the gastrointestinal tract of an individual with GI disease. Hence, the present study will evaluate the effect of a combination of specific diet and FMT in causing symptomatic improvement in individuals with ulcerative colitis of mild to moderate disease severity.

Who can participate?
Patients with mild to moderate ulcerative colitis aged between 18 to 65 years can participate in this study.

What does the study involve?
Patients will receive fecal microbiota transplantation (colonoscopic infusion of 250 ml of fecal

infusate from a healthy volunteer, once a week from 0 – 6 weeks) and UC specific diet in the experimental group where as comparator group will receive standard medical therapy as recommended.

What are the possible benefits and risks of participating?
Benefits: By participating in this research patients may benefit from FMT and their disease may improve. If proven to be effective then FMT may be useful as a cheap, effective and safe alternative for all patients with mild to moderate ulcerative colitis.
Risks: The are no risks during clinical assessment, blood or stool sample collection. Patients may only have slight pain during blood sample collection. Patients may have pain during colonoscopy and there is 2-8/10000 (0.02 – 0.08%) risk of hole/ tear in the intestine during colonoscopy which may require urgent surgery.

Where is the study run from?
All India Institute of Medical Sciences (India)

When is the study starting and how long is it expected to run for?
November 2018 to October 2022

Who is funding the study?
This study is funded by The Indian Council of Medical Research (ICMR), Govt. of India.

Who is the main contact?
Dr Vineet Ahuja, Professor, vineet.aiims@gmail.com

Contact information

Type(s)
Principal investigator

Contact name
Prof Vineet Ahuja

ORCID ID
https://orcid.org/0000-0002-1577-0118

Contact details
Room No 3093, Third Floor, Teaching Block
All India Institute of Medical Sciences
New Delhi
India
110029
+91-11-26594615
vineet@aiims.edu

Additional identifiers

Protocol serial number
UC-FMT 2019

Study information

Scientific Title
The effect of microbiome manipulation through diet and Fecal Microbial Transplant (FMT) in inducing and maintaining remission in patients with mild to moderate ulcerative colitis: open label randomized controlled trial

Study objectives
The proposed study will try to overcome the current challenges associated with the treatment of inflammatory bowel disease (IBD)- limitations of immune based therapies: primarily limited efficacy, cost and adverse effects. Both dietary manipulation and fecal microbiota transplantation (FMT) would form a low cost, efficacious and safe alternative for treatment of IBD. By targeting the proposed pathogenesis of IBD, microbial manipulation is also expected to alter the disease course of IBD, thereby improving outcomes in the long-term.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 11/06/2019, Intuitional Ethics Committee, All India Institute Of Medical Sciences (AIIMS, N. Delhi, India; +91-11-26594579; ethicscommitteeaiims@aiims.edu), ref: IEC-51/04. 01.2019, RP-1/2019,OP-30.11.2021

Primary study design
Interventional

Study design
Open label randomized controlled trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Mild to moderate ulcerative colitis

Interventions
Randomization: Patients will be randomized in 1:1 ratio to FMT + diet vs standard therapy arm. The random numbers will be generated by computerized random number (The RAND corp. Inc). The randomization list and numbered packing of the intervention will be prepared by a person not involved in the study. Randomization will be performed using permuted blocks of 4. Randomization will be held centrally to ensure concealment of allocation. After randomization patients' will be allocated to FMT + diet group where they will be receiving FMT at a pre-defined interval along with a defined diet or to standard treatment group (SMT).
Blinding: Neither the patient nor the investigator (doing colonoscopy or giving treatment) can be blinded to the treatment. However, the investigator analyzing the data will be blinded to the treatment details.
Intervention for induction of remission: Patients with active disease will either receive FMT and diet (experimental arm) or standard medical therapy (SMT, comparator arm). Patients in both groups will continue the pre-randomization ongoing treatment.
Experimental arm: Patients will receive colonoscopic infusion of 250 ml of FMT at 0,1,2,3,4,5 and

6 weeks. The first infusion will be delivered in the cecum. Subsequent infusions will be delivered in the left colon. Patients will also be asked to strictly adhere to the specific UC diet.
Control arm: Patients will be given SMT, which would consist of optimizing the dose of 5-ASA and /or addition of topical therapy.
Follow-up: Patients will be followed at 2, 4, 6, and 8 weeks. Clinical disease activity (simple clinical colitis activity index-SCCAI) will be assessed at all visits, and dietary adherence in the experimental arm will be assessed at weeks 2, 4, and 6. Endoscopic assessment will be done at baseline and 8 weeks by 1 investigator which will then be confirmed by another investigator blinded to the study assignment. Endoscopic activity will be assessed using ulcerative colitis endoscopic index of severity (UCEIS). The colonoscopic examination will be carried out till the area of most severe inflammation as per the previous colonoscopy. Blood and stool sample for biochemical and microbiological analysis and fecal calprotectin will be collected at baseline and 8 weeks. The stool samples will be stored at -80°C.
Treatment failure will be considered as increase in SCCAI by 3 points with rectal bleeding score >=1, the requirement for oral steroids, lack of improvement as defined by decline in SCCAI by <=3 points at 4 weeks. At the point of treatment failure in any arm, the patient will be withdrawn from the study and will be administered appropriate treatment as per the disease activity. If during interim analysis, the experimental arm is found inferior to control arm, then the study will be stopped.
Intervention for maintenance of remission: Patients in clinical remission or having clinical response (reduction in SCCAI by >=3 points) at the end of 8 weeks (in either arm) will be followed for the next 40 weeks till 48 weeks.
Experimental arm: Patients will adhere strictly to specific UC diet for next 40 weeks in addition to oral 5-ASA at 2.4 grams/day.
Control arm: Patients will receive oral 5-ASA at a dose of 2.4 grams/day.
Follow-up: Patients will be followed at 12, 24, 36, and 48 weeks. Clinical disease activity (simple clinical colitis activity index-SCCAI) will be assessed at all visits and dietary adherence in the experimental arm will be assessed at weeks 12, 24 and 36. Endoscopic assessment will be done at baseline (8 weeks), 24 and 48 weeks by 1 investigator which will then be confirmed by another investigator blinded to the study assignment. The colonoscopic examination will be carried out till the area of most severe inflammation as per the previous colonoscopy. Blood and stool sample for biochemical and microbiological analysis and fecal calprotectin will be collected at baseline (8 weeks) and 24 and 48 weeks. The stool samples will be stored at -80 .
Treatment failure will be considered as relapse, defined by increase in SCCAI by >=3 points with rectal bleeding score >=1 or requirement for oral steroids. At the point of treatment failure in any arm, the patient will be withdrawn from the study and will be administered appropriate treatment as per the disease activity.

Intervention Type
Other

Primary outcome(s)
1. Deep remission (endoscopic and clinical) at 8 weeks, defined clinically (SCCAI <=2) and endoscopically (UCEIS <=1).
2. Clinical response at 8 weeks, defined as decline in SCCAI by >=3 points

Primary outcome measures for the maintenance phase
1. Deep remission at 48 weeks
2. Maintenance of steroid free clinical remission at 48 weeks, defined as SCCAI <=2 along with no need for steroids over 48 weeks, and tapering of steroids if patients was on steroids at inclusion

Key secondary outcome(s)
1. Clinical remission defined as SCCAI <=2 at 24 weeks and 48 weeks
2. Clinical response defined as decline in SCCAI by >=3 points at 24 weeks and 48 weeks
3. Endoscopic response at 24 weeks, defined by decline in UCEIS by 2 points
4. Maintenance of steroid free clinical response at 48 weeks defined as decline in SCCAI by >=3 points along with no need for steroids over 48 weeks, and tapering of steroids if patients was on steroids at inclusion
5. Adverse events at 12 and 48 weeks

Completion date
15/10/2022

Eligibility

Key inclusion criteria
1. Age between 18 – 65 years
2. Patients with mild to moderate ulcerative colitis as assessed by simple clinical colitis activity index (SCCAI, 3 – 9) of any disease extent along with active disease on endoscopy (ulcerative colitis index of severity, UCEIS >1)
3. Patients on stable doses of 5-ASA (5-amino salicylic acid) for past 4 weeks
4. Patients on stable doses of azathioprine/6-mercaptopurine for past 3 months
5. Patients who received biologics 6 months ago
6. Patients on stable doses of topical therapy for past 2 weeks
7. Patients on oral steroids (equivalent dose of prednisolone <20 mg/day)
8. Patients giving consent for FMT
9. Patients who agree to adhere to the diet schedule

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
65 Years

Sex
All

Total final enrolment
66

Key exclusion criteria

1. Patients with severe disease activity
2. Patients who have received topical 5-ASA or topical steroids in the past 2 weeks
3. Patients with H/O of antibiotic or probiotic exposure in the past 4 weeks
4. Patients requiring hospitalization
5. Patients with H/O bowel surgery
6. Patients with concomitant GI infection
7. Pregnancy
8. Patients with other comorbid illnesses

Date of first enrolment
11/09/2019

Date of final enrolment
15/10/2021

Locations

Countries of recruitment
India

Study participating centre
All India Institute of Medical Sciences
Inflammatory Bowel Disease (IBD) Clinic
Room no.3100
Third floor, teaching block
New Delhi
India
110029

Sponsor information

Organisation
All India Institute of Medical Sciences

ROR
https://ror.org/02dwcqs71

Funder(s)

Funder type
Government

Funder Name
Indian Council of Medical Research

Alternative Name(s)
Indian Council of Medical Research, Government of India, Indian Council of Medical Research (ICMR), New Delhi, ICMROrganisation, , Indian Council of Medical Research, New Delhi, ..., ICMR, ICMRDELHI, ...

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
India

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request
vineet.aiims@gmail.com

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		16/08/2022	17/08/2022	Yes	No
Participant information sheet			15/03/2022	No	Yes