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Fermentable dietary carbohydrates as triggers of functional gut symptoms in patients with inflammatory bowel disease

Submission date
20/01/2014

Recruitment status
No longer recruiting

Registration date
04/03/2014

Overall study status
Completed

Last Edited
22/05/2017

Condition category
Digestive System

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

Plain English summary of protocol

Background and study aims
Inflammatory bowel disease (IBD) is a chronic relapsing remitting disease characterised by inflammation of the gut. Between 35% and 57% of patients with IBD in remission also report a range of gut symptoms similar to those experienced in functional bowel disorders, including irritable bowel syndrome (IBS), such as abdominal pain, bloating and diarrhoea. These symptoms are not associated with underlying inflammation of the disease, but may result in reduced quality of life. There is growing evidence for the use of a diet low in fermentable carbohydrates (the low FODMAP diet) for the management of functional gut symptoms (FGS) in patients with IBS. There is early evidence for the use of this diet in patients with IBD who have FGS during inactive disease; however, there are no studies published in this area. The aim of this study is to find out whether IBD patients are sensitive to individual fermentable dietary carbohydrates (FODMAPs). Patients receive drinks containing common dietary carbohydrates and symptom response is compared with a placebo (dummy) challenge.

Who can participate?
Male and female adult IBD patients who have experienced a sustained improvement in their symptoms whilst following the low FODMAP diet, recruited from outpatient clinics at Guys and St Thomas NHS Foundation Trust, London, UK.

What does the study involve?
At an initial visit before the start of the study demographic and disease characteristics and details regarding FGS are collected. Measurements include disease activity scores, bowel habits diary, diet history, and stool and blood markers of inflammation. Participants continue on the low FODMAP diet throughout the study. Participants are then randomly allocated to a sequence of four carbohydrate test drinks. Participants take one measure of powdered carbohydrate mixed into water with breakfast or in the morning within a specified time frame. The drinks are consumed once daily for three days and a daily gut symptom and stool diary is kept to monitor symptoms. In addition, a daily adherence diary is kept. After the three test days participants are instructed on following a four-day washout phase in which they continue the diet with no test drinks. This phase is to ensure that symptoms have returned to as they were before the start of

the intervention before starting the next test. This is repeated for each of the four test drinks. Once a participant has completed all four tests, they attend a final visit for an end of study blood and stool sample to recheck inflammation. Any adverse events are also recorded.

What are the possible benefits and risks of participating?
The main benefit of participating in the study is that patients learn which carbohydrates they are most sensitive to, enabling appropriate dietary changes to be made to help them manage their symptoms effectively. The low FODMAP diet is well tolerated, is not known to have any negative effects and is routinely used in clinical practice. Risk to patient safety is not expected. The main burden to participants is continuing a strict low FODMAP diet for the duration of the study, completing gut symptom and stool diaries, providing two blood and stool samples, and consuming the test drinks. The test drinks may induce symptoms that cause abdominal discomfort and/or a change in bowel habit, but the quantities of carbohydrates used in the test drinks are similar to those consumed in their previous normal diet and symptoms are not expected to be greater than those experienced by patients before starting the diet. There are no safety concerns of consuming these dietary carbohydrates. Taking blood samples is a routine procedure used frequently in clinical practice. Participants may experience mild pain or discomfort during the procedure and may notice a small bruise or mild soreness for a few days afterwards. The procedure is performed by an experienced and trained phlebotomist.

Where is the study run from?
King's College London and Guys and St Thomas NHS Foundation Trust gastroenterology outpatient clinics (UK).

When is the study starting and how long is it expected to run for?
March 2014 to January 2017

Who is funding the study?
King's College London (UK)

Who is the main contact?
1. Prof. Kevin Whelan
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Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
N/A

Study information

Scientific Title
Fermentable dietary carbohydrates as triggers of functional gut symptoms in patients with inflammatory bowel disease: a randomised controlled crossover trial

Study objectives
It is hypothesised that, in patients with inactive inflammatory bowel disease who have reported an improvement in functional gut symptoms (FGS) following a low fermentable carbohydrate diet, rechallenge with individual fermentable dietary carbohydrates (FODMAPs) will induce FGS compared with a placebo, glucose.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee London - Camberwell St Giles, 16/01/2014, ref: 13/LO/1878

Study design
Double-blinded placebo-controlled crossover rechallenge trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Inflammatory bowel disease (Crohn's disease and ulcerative colitis)

Interventions
Interventions as of 06/02/2017:
Eligible participants are allocated to undergo four dietary carbohydrate Fermentable Oligo-Di-Monosaccharides and Polyols (FODMAP) challenges in a random order. Each challenge lasts for 3 days, followed by at least 4 days washout. Participants record gastrointestinal symptoms and stool frequency and consistency during each challenge and on the final day of the washout period. Participants and researchers are blinded to the order of challenges. An online random number generator is used to produce the randomisation sequences.

1. Test: Fermentable carbohydrate drink containing 12 grams of fructans
2. Test: Fermentable carbohydrate drink containing 6 grams of galactooligosaccharides
3. Test: Fermentable carbohydrate drink containing 6 grams of sorbitol
4. Control: Fermentable carbohydrate drink containing 12 grams of glucose

Interventions as of 23/04/2014:
Each participant will complete all four dietary carbohydrate Fermentable Oligo-Di-Monosaccharides and Polyols (FODMAP) challenges in a random order:

1. Test: Fermentable carbohydrate drink containing 12 grams of fructans
2. Test: Fermentable carbohydrate drink containing 6 grams of galactooligosaccharides
3. Test: Fermentable carbohydrate drink containing 6 grams of sorbitol
4. Control: Fermentable carbohydrate drink containing 12 grams of glucose

Original interventions:
Each participant will complete all four dietary carbohydrate Fermentable Oligo-Di-Monosaccharides and Polyols (FODMAP) challenges in a random order:

1. Test: Fermentable carbohydrate drink containing 12 grams of fructans
2. Test: Fermentable carbohydrate drink containing 6 grams of galactooligosaccharides
3. Test: Fermentable carbohydrate drink containing 2 grams of sorbitol
4. Control: Fermentable carbohydrate drink containing 12 grams of glucose

Intervention Type
Other

Phase
Not Applicable

Primary outcome(s)
To find out whether FGS are adequately controlled following rechallenge with individual FODMAPs compared with a placebo, glucose. This will be measured by a Global Symptom Question Do you currently have satisfactory relief of your gut symptoms? with a 'yes' or 'no' response. This will be measured at baseline, for 3 days during each test and on day 4 of the washout phase to ensure symptoms have returned to baseline.

Key secondary outcome(s))
1. Ratings and mean scores for individual symptoms during each test phase, measured by the Gastrointestinal Symptom Rating Scale at baseline, for 3 days during each test and on day 4 of the washout phase.
2. Faecal calprotectin and serum CRP levels, measures of inflammation, measured at baseline and at the end of the trial

Completion date
27/01/2017

Eligibility

Key inclusion criteria
1. Men and women aged 18 years or over
2. Individuals able to give informed consent

3. Diagnosis of IBD confirmed by standard clinical, histological and radiological criteria
4. Diagnosis of IBD for duration of at least 6 months. IBD in remission as defined by physician global assessment, patient report and two markers of absence of inflammation: C-reactive protein (CRP) <10mg/l and faecal calprotectin <250µg/g.
5. Stable medications (see exclusion criteria), no recent surgery (see exclusion criteria) and stable symptoms for at least 2 months
6. Diagnosis of functional bowel disorder as defined by Rome III criteria (IBS or functional bloating or functional diarrhoea or functional abdominal pain syndrome) with marked and sustained improvement of these symptoms on the low fermentable carbohydrate diet
7. A willingness to participate

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Patients with active IBD
2. Recent use of the following treatments: antibiotics or prebiotics in the preceding 4 weeks, non steroidal anti-inflammatory drugs (NSAIDs) during the preceding week.
3. Currently taking steroids
4. Recent changes in dose to the following treatments: azathioprine, 6-mercaptopurine, methotrexate or alpha tumor necrosis factor (alpha-TNF) agents during the preceding 12 weeks, oral 5-aminosalicylic acid (5-ASA) or steroids during the preceding 4 weeks
5. Previous panproctocolectomy, pure perianal disease or short bowel syndrome
6. Stenotic disease
7. Sepsis or fever
8. Diabetes or coeliac disease (by serology and/or duodenal biopsy)
9. Other concomitant serious comorbidity e.g. significant hepatic, renal, endocrine, respiratory, neurological or cardiovascular disease
10. Pregnancy or lactation
11. Taking any medications with the potential to influence gastrointestinal symptoms unless taking a long term stable dose that is unlikely to change or stop during the trial

Date of first enrolment
14/04/2014

Date of final enrolment
16/09/2015

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Guy’s and St Thomas’ NHS Foundation Trust
Great Maze Pond
London
United Kingdom
SE1 9RT

Study participating centre
Barts Health NHS Trust
The Royal London Hospital
Whitechapel road
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Sponsor information

Organisation
King's College London (UK)

ROR
https://ror.org/0220mzb33

Funder(s)

Funder type
University/education

Funder Name
King’s College London

Alternative Name(s)

King's, Collegium Regium apud Londinenses, Collegium Regale Londinense, Collegium Regale Londiniense, KCL

Funding Body Type
Government organisation

Funding Body Subtype
Universities (academic only)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The current data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	04/12/2017		Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	version V3	24/02/2015	06/02/2017	No	Yes
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes