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Gut microbiota in patients with Crohn's disease and their relatives

Submission date	Recruitment status	[_] Prospectively registered
18/06/2010	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
18/06/2010	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
27/08/2014	Digestive System	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
6446

Study information

Scientific Title
Gut microbiota in patients with Crohn's disease and their relatives: a case-control study of the gut microbiota and related immunological and biochemical markers of gut inflammation in patients with quiescent Chrohn's disease and the effect of a prebiotic diet

Study objectives
The inflammation associated with Crohn's disease is driven by the intestinal bacteria. Patients with Crohn's disease have been shown to have an altered pattern of gut bacteria in comparison to healthy people. It is not known whether this alteration occurs early in the disease and may be a cause of Crohn's disease or is a reaction to the damage that Crohn's disease causes to the gut. A proportion of relatives of patients with Crohn's disease have some evidence of mild forms of inflammation similar to their affected relatives (leaky gut and a rise in faecal calprotectin which is a marker of inflammation) but it is not known whether they also have altered bacteria.

The aim of study one is to determine whether an altered pattern of bacteria is present in relatives of patients with Crohn's disease. The aim of study two is to find out whether following a prebiotic diet high in fructo-oligosaccharides (FOS) can increase the levels of anti-inflammatory bacteria and can reverse these mild inflammatory changes.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Bromley Local Research Ethics Committee, 26/02/2008, ref: 07/H0805/46

Study design
Multicentre non-randomised observational prevention and treatment case-controlled study

Primary study design
Observational

Secondary study design
Case-control study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Topic: Oral and Gastrointestinal; Subtopic: Oral and Gastrointestinal (all Subtopics); Disease: Gastrointestinal

Interventions
Study one:
Patients, siblings and controls are compared with the following parameters:
1. Gut permeability
2. Faecal calprotectin
3. Luminal and mucosal gastrointestinal microbiota
4. Genetic predisposition to Crohn's disease
5. Peripheral lymphocyte sub-populations and expression of homing markers
6. Intestinal permeability

Study two:
Patients with Crohn's disease and their unaffected siblings who have a faecal calprotectin above the reference range are invited to undergo a 3-week dietary intervention with a supplement of fructo-oligosaccharides (FOS).

Duration of study 1: 5 hours
Duration of study 2: 3 weeks
Follow-up length: 3 weeks
Study entry: registration only

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
1. Study one: significant difference in gut microbiota between relatives of patients with Crohn's disease and healthy controls, measured at baseline
2. Study two: significant fall in faecal calprotectin in patients and their relatives following a FOS-enriched diet, measured at 3 weeks.

Secondary outcome measures
1. Study one: significant differences in faecal calprotectin, gut permeability, gut-homing lymphocytes in patients' relatives in comparison to patients with Crohn's disease and healthy controls. The influence of genotype on these measures will also be characterised. Measured at baseline.
2. Study two: alterations in gut microbiota, gut-homing lymphocytes and gut permeability after consuming a FOS-enriched diet for 3 weeks in patients and their relatives, measured at 3 weeks

Overall study start date
02/01/2008

Completion date
01/08/2011

Eligibility

Key inclusion criteria

Inclusion criteria:
1. Aged 16 years or older, either sex
2. Diagnosis of Crohn's disease for at least 3 months defined by histology or radiology
3. Quiescent (inactive) disease as defined by a Crohn's Disease Activity Index (CDAI) below 150
4. Normal C-reactive protein (CRP) as defined by local laboratory
5. On stable Crohn's disease therapy with a total steroid dose not exceeding 10 mg prednisolone or equivalent
6. Relatives of patients:
6.1. Will be aged between 16 and 35 years
6.2. Will be a first degree relative of a patient as described above. Relatives older than 35 will not be recruited to maximise the chance of including some individuals who will develop Crohn's disease in the future.
7. Healthy controls will comprise age-matched patients with functional constipation or those undergoing polyp surveillance who are scheduled to undergo flexible sigmoidoscopy. A second group of controls who will not undergo sigmoidoscopy will comprise healthy volunteers.

Concomitant medication:
Patients currently taking maintenance oral 5 aminosalicylic acid (5ASA) therapy must have been on a stable dose for 4 weeks prior to study entry, and will be maintained at the same dose for the duration of the study. No rectally administered medications (steroid or 5ASA) are allowed for the two weeks preceding entry to the study. Patients on a stable dose of oral (not exceeding 10 mg) prednisolone or equivalent for 4 weeks prior to baseline are permitted to enter the study. Patients taking azathioprine or 6 mercaptopurine must have commenced the drug at least 16 weeks prior to entry to the study and been maintained on a stable dose for at least 4 weeks prior to entry. No antibiotics, probiotics or prebiotics will be used during the study or for the preceding month. Non-steroidal anti-inflammatory drugs (NSAIDs) will not be permitted for 1 week before entry to the study. The requirement for a normal CRP is to ensure inactive disease.

For participants in study two, no changes in medication will be permitted during the study period. Participants requiring changes to their drug regime will be withdrawn from the study and continue with their usual medical care.

Participant type(s)
Healthy volunteer

Age group
Adult

Sex
Both

Target number of participants
Planned sample size: 72; UK sample size: 72

Key exclusion criteria
The principal exclusion criteria are standard for this type of trial in Crohn's disease.

All participants:
1. Current infection with an enteric pathogen
2. Use of antibiotics within the last month
3. Consumption of any probiotic or prebiotic within the last month

4. Change in dose of oral steroids within the last 4 weeks
5. Dose of steroids exceeding 10 mg prednisolone per day or equivalent
6. Change in dose of oral 5 ASA products within the last 4 weeks
7. Commencement of azathioprine or methotrexate within the last 4 months or change in dose of these drugs within the last 4 weeks
8. Infusion of infliximab within the last 3 months
9. Use of any alternative biological therapy within the last 3 months
10. Use of rectal 5 ASA or steroids within the last 2 weeks
11. Imminent need for surgery
12. Participant requiring hospitalisation
13. Pregnancy or lactation
14. Short bowel syndrome and previous proctocolectomy or purely anal Crohn's disease
15. Significant hepatic, renal, endocrine, respiratory, neurological or cardiovascular disease as determined by the principal investigator
16. A history of cancer with a disease-free state of less than 2 years

Patients:
17. Evidence of active Crohn's disease as defined by a CDAI of greater than 150

Relatives:
18. Previously been diagnosed with inflammatory bowel disease

Controls:
19. Previously been diagnosed with inflammatory bowel disease
20. First or second degree relative with inflammatory bowel disease

Date of first enrolment
02/01/2008

Date of final enrolment
01/08/2011

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Barts and The London NHS Trust
London
United Kingdom
E1 1BB

Sponsor information

Organisation
Barts and The London NHS Trust (UK)

Sponsor details
Queen Mary's Innovation Centre
5 Walden Street
London
England
United Kingdom
E1 2EF

Sponsor type
Hospital/treatment centre

Website
http://www.bartsandthelondon.nhs.uk/

ROR
https://ror.org/00b31g692

Funder(s)

Funder type
Research organisation

Funder Name
Digestive Diseases Foundation (CORE) (UK)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/10/2014		Yes	No