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Fermentable carbohydrate and gut hormone release

Submission date	Recruitment status	[_] Prospectively registered
16/10/2017	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[X] Statistical analysis plan
19/10/2017	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
20/06/2024	Digestive System	

Plain English summary of protocol

Background and study aims
In England, 60% of the adult population is overweight or obese. There is an urgent need to understand how dietary components effect appetite regulation. Previous research has demonstrated that increased dietary intake of fermentable carbohydrate promotes weight loss. Fermentable carbohydrates are not digested in the small intestine (the ileum) and therefore enter the large intestine (the colon) where they are fermented by the resident bacteria producing short chain fatty acids (SCFAs). SCFAs have been shown to stimulate the release of appetite suppressing hormones called PYY and GLP-1 from the colon. Understanding how the gut senses ingested food to reduce food intake, will permit the design of foods that make people feel full. The aim of this study is to look at the effects of different types of carbohydrates on gut contents and the effects this has on how hungry people feel. This may be important in terms of controlling body weight and therefore preventing obesity.

Who can participate?
Adults aged 18 and to 65 who have a BMI of 18-30 kg/m2.

What does the study involve?
This study involves three separate 4-day inpatient assessments. For each 4-Day study visit, participants stay at the Clinical Research Facility at Hammersmith Hospital for three nights. During each study visit participants are provided with a diet containing different types and amounts of carbohydrate rich foods (sugars, starchy foods, fruits and vegetables). They receive the different carbohydrate diets in a random order. The amounts of dietary fat and protein will be the same at each of the 3 study visits. On Day 1 of the study visit, participants have a tube placed through their nose by a trained medical professional under fluoroscopy. Fluoroscopy is a type of medical imaging that shows a continuous X-ray image on a monitor, much like an X-ray movie. The end of this tube lies within the small intestine (ileum) allowing us to collect and measure the contents of the gut.
On the morning of Day 3, participants are provided with a test meal at approximately 09:00. Before the breakfast and for 8 hours afterwards samples will be collected from the tube to measure the gut contents. On the morning of day 4, a small plastic cannula tube is inserted into a vein in one arm. A vein is the type of blood vessel commonly used for taking blood samples. The cannula tube is used to take blood samples to measure the levels of hormones which control

hunger in the body. During each study visit approximately 100 ml of blood (5 tablespoons of blood) is collected. At approximately 09:00 a test meal is provided and gut content samples and blood samples are collected throughout an 8 hour study period. After each sample is collected participants are asked to fill in a chart describing how hungry they feel. At approximately 17:00 on Day 4, the nasal tube and cannula tube are removed and participants are free to go home. In addition, participants are also asked to collect a stool sample on each day of the 4-Day study visit.

What are the possible benefits and risks of participating?
Taking part in the study will provide no direct benefit for participants. If any of the screening questionnaires or blood tests reveal any medical problems (e.g. diabetes, kidney or liver problems), the participant's GP will be informed so that they can coordinate further care, arrange any further tests, and refer the participant on to Hospital Doctors if necessary. Insertion of the cannula on each of the study visits may cause minor discomfort or superficial bruising. Serious risks associated with the insertion of the tubes are very rare and almost negligible. These risks include bleeding, perforation or damage to the base of the skull. Minor discomfort of the back of the throat does occur in the majority of patients and may result transiently in a sore mouth, thirst, swallowing difficulties or hoarseness. The fluoroscopy procedure will expose participants to a small dose of radiation. The mean effective dose from each nasogastric tube procedure is equivalent to 2.8 months of natural background radiation (the same amount as you would be exposed to walking around outside) and would increase the risk of inducing cancer by 0.0025% (or 1 in 40,000). The minimum number of fluoroscopy procedures that will be conducted is 3. The maximum number of fluoroscopy procedures that will be conducted is 6.

Where is the study run from?
Imperial College London (UK)

When is the study starting and how long is it expected to run for?
June 2014 to June 2019

Who is funding the study?
Biotechnology & Biological Sciences Research Council (UK)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
33144

Study information

Scientific Title
Understanding the interplay between fermentable carbohydrates and gut hormone release

Study objectives
The aim of this study is to determine the effects of diets containing different amounts of fermentable carbohydrates on ileum contents and to determine the subsequent impact on appetite responses and PYY and GLP-1 release from the colon.

Ethics approval required
Old ethics approval format

Ethics approval(s)
London-Bloomsbury REC, 08/03/2017, ref: 17/LO/0354

Study design
Randomised; Interventional; Design type: Prevention, Dietary

Primary study design
Interventional

Secondary study design
Randomised controlled trial

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
Obesity

Interventions
This is a randomised crossover study during which healthy volunteers are clinical research facility inpatients for four days on three separate occasions. On day one of the study, a naso-enteric tube is inserted through the nose, with a small balloon at the terminal end which is inflated and used to carry the tube through the small intestine by peristalsis. Once the tube reaches the terminal ileum, the balloon is deflated and the tube is restrained from additional movement for the rest of the 4-day study visit.

During the three separate study visits, volunteers will be provided with different diets differing in carbohydrate quality. All the diets have similar macronutrient content (55% energy from carbohydrate, 30% energy from fat, 15% energy from protein). In a randomised order, volunteers receive:
1. DIET 1: Highly refined and processed carbohydrate: Foods will be low in fibre and intact cell structures.
2. DIET 2: High fibre with high intake cellular structure: Will contain foods with resistant cell structures such as beans, nuts, minimally processed wholegrain wheat cereal and vegetables.
3. DIET 3: High fibre with disrupted cellular structure: The same as DIET 2, but the food is processed in order to disrupt the cell structure.

Volunteers are fed one of the diets over the 4-day study period. The diet starts on Day 1 and end on Day 4. The collection of ileal samples start on day 3. On day 4, ileal samples are collected as on day 3 and are matched with blood sampling and visual analogue scales (VAS) to assess appetite responses. Volunteers will also be asked to collect a stool sample on each day of the 4-day study period.

Intervention Type
Other

Primary outcome measure
1. Metabolic profiling of ileal samples is measured using 1H NMR spectroscopy, ultra-performance LC-MS and GC-MS on Day 3 and Day 4 at baseline and 60, 120, 180, 240, 300, 360, 420 and 480 min following breakfast
2. Microbiological profiling of ileal samples is measured using 16S sequencing on Day 3 and Day 4 at baseline and 60, 120, 180, 240, 300, 360, 420 and 480 min following breakfast

Secondary outcome measures
Current secondary outcome measures as of 13/09/2018:
1. Metabolic and hormonal profiling of blood samples is measured using radioimmunoassay, 1H NMR spectroscopy, ultra-performance LC-MS and GC-MS on Day 4 at baseline and 60, 120, 180, 240, 300, 360, 420 and 480 min following breakfast
2. Microbiological profiling of faecal samples is measured using 16S sequencing on each day of the 4-day study visit
3. Subjective appetite is measured using visual analogue scales on Day 4 at baseline and 60, 120,

180, 240, 300, 360, 420 and 480 min following breakfast
4. Nausea is measured using visual analogue scales on Day 4 at baseline and 60, 120, 180, 240, 300, 360, 420 and 480 min following breakfast
5. Metabolic profiling of faecal samples is measured using 1H NMR spectroscopy on each day of the intervention
6. Detection of plant structures, cell structures and starch granules in ileal samples is measured by microscopy on Day 3 and Day 4 of the intervention

Previous secondary outcome measures:
1. Metabolic and hormonal profiling of blood samples is measured using radioimmunoassay, 1H NMR spectroscopy, ultra-performance LC-MS and GC-MS on Day 4 at baseline and 60, 120, 180, 240, 300, 360, 420 and 480 min following breakfast
2. Microbiological profiling of faecal samples is measured using 16S sequencing on each day of the 4-day study visit
3. Subjective appetite is measured using visual analogue scales on Day 4 at baseline and 60, 120, 180, 240, 300, 360, 420 and 480 min following breakfast
4. Nausea is measured using visual analogue scales on Day 4 at baseline and 60, 120, 180, 240, 300, 360, 420 and 480 min following breakfast

Overall study start date
01/06/2014

Completion date
01/06/2019

Eligibility

Key inclusion criteria
1. Male or female
2. Age between 18-65 years (inclusive)
3. Body mass index (BMI) of 18-30 kg/m2
4. Willingness and ability to give written informed consent and willingness and ability to understand, to participate and to comply with the study requirements

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
65 Years

Sex
Both

Target number of participants

Planned Sample Size: 15; UK Sample Size: 15

Total final enrolment
16

Key exclusion criteria
1. Abnormal ECG
2. Screening blood results outside of normal reference values
3. Weight change of > = 5kg in the preceding 2 months
4. Current smokers
5. History of substance abuse and/or excess alcohol intake
6. Pregnancy
7. Diabetes
8. Cardiovascular disease
9. Cancer
10. Gastrointestinal disease e.g. inflammatory bowel disease or irritable bowel syndrome
11. Kidney disease
12. Liver disease
13. Pancreatitis
14. Started new medication within the last 3 months likely to interfere with energy metabolism, appetite regulation and hormonal balance, including: anti-inflammatory drugs or steroids, antibiotics, androgens, phenytoin, erythromycin or thyroid hormones
15. Participation in a research study in the 12 week period prior to entering this study
16. Any blood donation within the 12 week period prior to entering this study

Date of first enrolment
23/08/2017

Date of final enrolment
01/04/2019

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Imperial College London
London
United Kingdom
W12 0NN

Sponsor information

Organisation
Imperial College of Science, Technology and Medicine

Sponsor details
Joint Research Compliance Office
London
England
United Kingdom
W12 0NN

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Government

Funder Name
Biotechnology and Biological Sciences Research Council

Alternative Name(s)
UKRI - Biotechnology And Biological Sciences Research Council, BBSRC UK, BBSRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer reviewed journal within 12 months of the overall trial end date

Intention to publish date
01/10/2023

Individual participant data (IPD) sharing plan

The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication.

IPD sharing plan summary

Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	05/03/2019	09/06/2020	Yes	No
HRA research summary			28/06/2023	No	No
Statistical Analysis Plan			10/08/2023	No	No
Results article		24/10/2015	16/08/2023	Yes	No
Results article		17/11/2015	16/08/2023	Yes	No
Results article		19/06/2024	20/06/2024	Yes	No