ISRCTN68710020 https://doi.org/10.1186/ISRCTN68710020

Stool transplantation for treatment of insulin resistance in morbidly obese patients

Submission date
17/06/2016

Recruitment status
No longer recruiting

Registration date
11/07/2016

Overall study status
Completed

Last Edited
16/06/2023

Condition category
Nutritional, Metabolic, Endocrine

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

Plain English Summary
Background and study aims
More and more people in Canada and around the world are severely (morbidly) obese (very overweight), and those people are at high risk of not being able to control their blood sugar levels very well (insulin resistance (IR)) and also of developing diabetes. Most morbidly obese people cannot lose weight. Weight loss surgery (bariatric surgery) can help, but it has some risks and is not available to all patients. Therefore, alternative treatments are needed. Gut flora refers to the microorganisms that live in the digestive tract with the relationship between the multitude of bacteria in the gut and their human host beneficial to both parties. An altered composition of the gut bacteria (that is, a change in the type and number of bacteria present) might contribute to obesity and IR. Several animal studies show that giving stool from lean mice or humans to obese mice (stool transplant) can make the obese animals lose weight and improve IR. One human study has confirmed this. This study is looking at whether stool transplant from healthy lean people will improve blood sugar control, weight, and other obesity related problems in morbidly obese patients with IR.

Who can participate?
Morbidly obese patients, age 18 years and older, referred to the Toronto Western Hospital Bariatric Surgery Clinic, Toronto, Canada, for weight loss surgery but decided not to go ahead with it. hHealthy lean volunteers are also recruited as stool donors.

What does the study involve?
Participants are randomly allocated to one of two groups. Those in group 1 receive a stool transplant from a healthy lean donor (treatment group). Those in group 2 receive a stool transplant prepared from the participants own stool (placebo, or control, group) After the stool transplant, participants come back to the hospital after 1 and after 3 months when they are tested for insulin resistance and other blood work, weight, appetite and food intake, quality of life, depression, and anxiety, gut bacteria and bacterial products in stool and blood, and the bacteria found in the mouth. In addition, before the stool transplant, the bacteria attached to the gut wall will be compared to those found in stool. Participants are asked to give blood, stool, and scrape samples from teeth and tongue, and to fill out questionnaires at each visit. The stool transplant is done through a tube that the doctor inserts into the rectum (colonoscopy). During the procedure, a small piece of the gut wall is collected as well. Stool donors are carefully

screened to make sure they do not have any disease they might pass on to the patients who will receive their stool. Each donor gives blood, stool, and urine samples for screening and 3 to 5 stool samples for the study.

What are the possible benefits and risks of participating?
It is not yet known whether the stool transplant works, but if it does, it is possible that blood sugar control will improve. Participants may also lose weight and depression and anxiety may improve.
Stool transplants have been described in the literature in over 1000 patients, mostly for treatment of severe diarrhoea due to a gut infection. From these reports, it is known that about 1/3 of the patients will have minor gastrointestinal problems like bloating, abdominal pain, diarrhoea, constipation, nausea; or fever, but they usually go away within 2 days. More serious problems are rare (less than 1% of patients), including heart and lung problems, strong bleeding, infections, or a hole (perforation) of the bowel.

Where is the study run from?
University Health Network in Toronto, Ontario (Canada)

When is study starting and how long is it expected to run for?
July 2016 to July 2021

Who is funding the study?
Canadian Institutes for Health Research.

Who is the main contact?
1. Professor Johane Allard (scientific)
johane.allard@uhn.on.ca
2. Dr Katherine Schwenger (public)
Katherine.schwenger@uhnresearch.ca

Contact information

Type(s)
Scientific

Contact name
Prof Johane Allard

ORCID ID
http://orcid.org/0000-0002-8956-7059

Contact details
University Health Network, Toronto General Hospital
200 Elizabeth St, 9-NU-973
Toronto, ON
Canada
M5G 2C4
+1 (0)416 340 5159
johane.allard@uhn.on.ca

Type(s)

Public

Contact name
Dr Katherine Schwenger

Contact details
Department of Medicine, Division of Gastroenterology
Toronto General Hospital, University Health Network
200 Elizabeth St
Eaton North, 10th floor Room 243
Toronto, ON
Canada
M5G 2C4
+1 (0)416 340 4413
Katherine.schwenger@uhnresearch.ca

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
NCT02970877

Secondary identifying numbers
16-5475

Study information

Scientific Title
Fecal microbiota transplant from healthy lean donors to morbidly obese individuals: effect on insulin resistance and other obesity-related parameters. A randomized controlled trial.

Acronym
Fecal transplant bariatric

Study hypothesis
Main hypothesis:
Fecal microbiota transplant (FMT) from healthy lean donors to morbidly obese individuals with insulin resistance (IR) (homeostasis model of assessment for IR, HOMA-IR more than 2.73) will improve HOMA-IR

Secondary hypotheses:
1. FMT will also reduce weight, appetite, and food intake
2. FMT will improve quality of life, depression and anxiety scores
3. FMT will change IM as well as fecal and serum metabolome
4. Improvement in clinical parameters (IR, weight, appetite, mood scores) are associated with specific changes in IM or metabolites (eg. short-chain fatty acids)

5. Exploratory: Explore changes in OM and potential associations between OM and IM and their potential relationships with obesity/metabolic parameters
6. Baseline: Comparing luminal (fecal) with mucosa-adherent microbiome and examine their potential relationships with obesity/metabolic parameters

Ethics approval required
Old ethics approval format

Ethics approval(s)
University Health Network Research Ethics Board, 11/01/2017, ref: 16-5475-A

Study design
Single-center Phase II double-blind parallel-group randomized controlled trial

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 contact details to request a participant information sheet

Condition
Morbid obesity and insulin resistance

Interventions
Morbidly obese participants will receive one single dose of fecal filtrate prepared from feces of healthy lean pre-screened donors (allogenic FMT = treatment arm) or prepared from their own feces (autologous FMT = control arm, placebo arm) per colonoscopy.

Patients will be followed for 3 months post FMT.

Patients will be allocated to allogenic or autologous FMT by randomization with a 1:1 chance to be allocated to either group. As diet can influence the IM composition (131, 132), all patients will receive a brief initial counselling on a healthy diet, where they will be provided with basic advice for a healthy diet and appropriate physical activity.

Intervention Type
Biological/Vaccine

Phase
Phase II

Drug/device/biological/vaccine name(s)
Fecal microbiota transplant

Primary outcome measure
Insulin resistance, measured using the homeostasis model of assessment for insulin resistance (HOMA-IR) at baseline and 1 and 3 months after FMT

Secondary outcome measures
1. Weight (in kg) and body mass index (weight kg / height m²) measured with a scale at baseline and 1 and 3 months after FMT
2. Change in body weight (% change) between baseline and 1 and 3 months after FMT
3. Appetite score, assessed with a visual analogue rating scale at baseline, 1, and 3 months after FMT
4. Quality of life, measured using the RAND 36-Item Health Survey 1.0 at baseline and 1 and 3 months after FMT
5. Anxiety and depression scores, measured using the Hamilton Anxiety Rating Scale and the Montgomery-Åsberg Depression Rating Scale, respectively, at baseline and 3 months after FMT

Overall study start date
01/07/2016

Overall study end date
01/07/2021

Eligibility

Participant inclusion criteria
1. Morbidly obese men and women, age 18 years or older, fulfilling the 1991 NIH criteria (BMI >40 kg/m2 or BMI >35–40 kg/m2 with other severe weight loss responsive comorbidities)
2. Referred to the Bariatric Clinic at the Toronto Western Hospital for weight loss surgery, but declining or deferring the surgery
3. Insulin resistant, which is defined as having a HOMA-IR value >2.73

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
48

Total final enrolment
28

Participant exclusion criteria
1. Regular intake of: non-steroidal anti-inflammatory drugs; iron supplements; prebiotics or probiotics from other than food sources, antibiotics, or any experimental drug in the 3 months prior to study entry
2. Type 1 or type 2 diabetes
3. Chronic gastrointestinal diseases
4. Previous gastrointestinal surgery modifying the anatomy
5. Smoking
6. Pregnancy
7. Breastfeeding

Recruitment start date
01/03/2017

Recruitment end date
31/10/2020

Locations

Countries of recruitment
Canada

Study participating centre
University Health Network
200 Elizabeth Street
Toronto, ON
Canada
M5G 2C4

Sponsor information

Organisation
University Health Network

Sponsor details
200 Elizabeth Street
Toronto, ON
Canada
M5G 2C4

Sponsor type
Hospital/treatment centre

Website
http://www.uhn.ca/

ROR
https://ror.org/042xt5161

Funder(s)

Funder type
Government

Funder Name
Canadian Institutes of Health Research

Alternative Name(s)
Instituts de Recherche en Santé du Canada, Canadian Institutes of Health Research (CIHR), CIHR_IRSC, Canadian Institutes of Health Research | Ottawa ON, CIHR, IRSC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Canada

Results and Publications

Publication and dissemination plan
We will present data first in the form of abstracts, posters, and oral presentations, as soon as they become available. Full manuscripts will be submitted for publication in scientific journals. In addition, the progress of the study and the results will be presented to the Bariatric Surgery Clinic Staff and Students in private sessions. We are also planning to disseminate the results through the website of the Canadian Obesity Network (www.obesitynetwork.ca/).

Intention to publish date
01/12/2022

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?

Results article	results	14/10/2022	16/06/2023	Yes	No