Effect of Fecal Transplantation on Satiety, Sarcopenia, Inflammation and Chemotherapy Toxicity in patients with Metastasized Oesophageal and Gastric Cancer.

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Primary objective:Effect of fecal transplantation (from healthy obese donors) on faecel microbiota composition in relation to satiety (questionnaires, biomarkers) and metabolism (REE) in patients with metastasized or locally advanced oesophageal or...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Appetite and general nutritional disorders
Study type	Interventional

Summary

ID

NL-OMON43382

Source
ToetsingOnline

Brief title
TRANSIT-study

Condition

- Appetite and general nutritional disorders
- Muscle disorders

Synonym
Anorexia en sarcopenia

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Anorexia, Fecal transplantation, Gut microbiota, Satiety

Outcome measures

Primary outcome

Faecal gut microbiota composition (morning stool samples)

Satiety, measured by: 1. Visual Analog Scale (VAS) 2. Plasma markers for satiety (tryptophan, ghrelin, leptin, neuropeptide Y and orexin levels) 3. Energy expenditure, measured by indirect calorimetry.

Secondary outcome

- Sarcopenia (muscle mass measured by CT-based analysis and grip strength)

- Body composition (measured by Bio Impedance Analysis)

- Faecal energy excretion (caloric bomb method) and short chain fatty acid and bile acid concentration (2x24h collected faeces) and urine excretion of 5-HIAA (24 h collected urine).

- Systemic inflammation and gut barrier function (CRP, plasma interleukins/LPS binding protein levels and fecal calprotectin) in relation to energy metabolism as measured by resting energy expenditure (REE).

- Chemotherapy toxicity, graded with the Common Terminology Criteria for Adverse Events (CTCAE)11

- Treatment response measured by CT-scan at baseline and after the first 3 cycles of chemotherapy (week 12).

- Overall survival (defined as the number of days of survival after PA

diagnosis).

Study description

Background summary

Sarcopenia, the loss of skeletal muscle mass and strength, is associated with increased risk of chemotherapy toxicity and poor overall survival in patients with cancer. The two most important causes giving rise to sarcopenia are poor nutritional status and chronic inflammation. In fact, poor nutritional status is frequently associated with loss of appetite, due to early satiety. Moreover, the chronic inflammatory state often seen in patients with cancer is thought to be driven by a gut barrier dysfunction (GBD), characterized by breakdown and leakage of the gut epithelial barrier. These changes in intestinal mucosal barrier are due to transient disruptions in the microbial composition, a phenomenon known as dysbiosis. Based on our previous experience, we postulate that faecal microbiota transplantation (FMT) from obese donors in patients with cancer can improve satiety (appetite) and subsequently nutritional status. Secondly, FMT might restore the gut barrier function and hence reduce systemic inflammatory tone.

Study objective

Primary objective:
Effect of fecal transplantation (from healthy obese donors) on faecel microbiota composition in relation to satiety (questionnaires, biomarkers) and metabolism (REE) in patients with metastasized or locally advanced oesophageal or gastric cancer receiving standard first-line palliative chemotherapy (capecitabine and a platinum-containing therapy).

Secondary objectives:
Effect of fecal transplantation on:
1. Sarcopenia (measured by CT-scan).
2. Body composition (BIA)
3. Systemic inflammation and gut barrier function (CRP, plasma interleukins/LPS binding protein levels and fecal calprotectin) in relation to energy metabolism as measured by resting energy expenditure (REE).
4. Chemotherapy toxicity, graded with the Common Terminology Criteria for Adverse Events (CTCAE)11
5. Treatment response measured by CT-scan at baseline and after the first 3 cycles of chemotherapy (week 12).
6. Overall survival (defined as the number of days of survival after PA

diagnosis).

Study design

Double blinded randomized controlled single centre trial.

Patients will be randomized to the following 2 treatment arms:
1. Allogenic (obese donor) fecal transplantation (n=8)
2. Autologous (own) fecal transplantation (n=8)

Intervention

Patients will be treated with infusion of either allogenic or autologous microbial transplantation by duodenoal tube after bowel lavage. Bowel lavage is performed by drinking 3-4 liter Klean Prep de evening prior to the fecal transplantation. De duodenal tube is placed using the Cortraksystem and abdominal X is performed afterward to check position of the tube in the duodenum. Meanwhile, fllogenic or autologous feces mixed in 500 cc saline (filtered, <2 hours after processing) and will be infused in the duodenum through positioned duodenal tube.

Study burden and risks

Total study duration is 12 weeks, during which subjects will visit the AMC 2 times extra (total duration 4 hours) and in total 200 (20ml screening and 60 ml blood at 0,4 and 12 weeks). At 0 and 4 weeks, a REE and BIA will be performed. Also, at baselinge (T=0) faecaltransfusion will be performed. In the last 5 years we have performed over 300 fecal transplantations at the AMC in several patientgroeps without seeing any short or long term complications (FANFARE MEC 2013_278, FATLOSE-1 MEC, 07/114; FATLOSE-2 MEC 11/023; FEBALIGO MEC 2013_090). Although in theory there is always the risk of transferring (unknown) infectious diseases (just like with bloodtransfusions), however using a thorough donor screening protocol can minimize this risk.
The total dose equivalent of the participating patients (aged 18-40 years) will be 0.7mSv for the abdominal X-ray during coretrack resulting in 0.7 mSv for the whole study (which is less than the currently allowed 10.0 mSv WHO category IIb). A 3-monthly response evaluation measured by CT-scan is a standard procedure for this population receiving chemotherapy. Therefore, no additional imaging for this study is required. Since we feel that this intervention can help us to improve metabolic dysregulation in patients with metastasized or locally advanced oesophageal and/or gastric cancer, we believe that the burden of this study is in line with the potential therapeutic insight that will be gained.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Recipients:
- Male or female with metastasized or locally advanced oesophageal and/or gastric cancer receiving standard first-line palliative chemotherapy (capecitabine and platinum-containing therapy)
- Age >18 years old
- Meeting the criteria for sarcopenia, using computed tomography (CT)-scan: the L3 muscle area surfaces will be normalized for patient height to calculate the L3 muscle index and expressed in cm2/m2. The cutoff values used for sarcopenia are 52.4 cm2/m2 for men and 38.5 cm2/m2 for women, based on the method of Prado et al1
- Meeting the International Classification of Functioning, Disability and Health (ICF), WHO 1, 2 or 3.
- Stable medication use, all subjects use PPI.

- Subjects should be able and willing to give informed consent;Donors:
- Obese otherwise healthy caucasian male or female
- BMI >25 kg/m2

Exclusion criteria

Recipients:
- XTC, amphetamine or cocaine abuse
- Alcohol abuse (>3/day)
- Cholecystectomy
- HIV infection with a CD4 count < 240
- Patients with diabetes mellitus (there are several studies indicating that a high level of NLR may reflect ongoing vascular inflammation and play an important role in the pathophysiology of DM and even prediabetes). ;Donors:
- Presence of chronic low grade inflammation or criteria of metabolic syndrome
- Use of any medication including PPI and antibiotics
- Presence of type 2 diabetes or hypertension
- Diarrhoea
- Cholecystectomy
- HIV, HAV, HBV, HCV, active CMV, active EBV, IBD
- Unsafe sex practice (questionnaire)
- Presence of faecal bacterial pathogens (salmonella, Shigella, Campylobacter, Yersinia), virus (Rotavirus, Noroviru, enterovirus, parechovirus, sapovirus, adenovirus, astrovirus) or parasites
- Positive C. difficile stool test

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	23-08-2016
Enrollment:	16
Type:	Actual

Ethics review

Approved WMO Date:	29-03-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-11-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL56559.018.16