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Changes in bile acids and microbiota after bariatric surgery

Submission date 06/02/2018	**Recruitment status** No longer recruiting	[X] Prospectively registered [ ] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [ ] Record updated in last year
Registration date 24/02/2018	**Overall study status** Completed	
Last Edited 22/02/2018	**Condition category** Surgery	

Plain English summary of protocol

Background and study aims
Bariatric (weight loss) surgery has proved to be an effective treatment for patients with morbid obesity, but results vary according to the specific type of technique performed. The aim of this study is to find out whether two different techniques (gastric bypass and biliopancreatic diversion) result in different outcomes regarding body weight and associated illnesses (diabetes, dyslipidemia, liver steatosis). Gastric bypass involves making the stomach smaller and bypassing part of the intestines (bowels), so that fewer calories are absorbed. A biliopancreatic diversion is similar, except the stomach is connected further along the small intestine.

Who can participate?
Patients aged 18-65 with morbid obesity on the bariatric surgery waiting list, and non-obese healthy volunteers for comparison

What does the study involve?
Changes in gastrointestinal (digestive system) hormones, biliary acids and gut microbiota (bacteria are studied by collecting blood and stool samples before and one year after bariatric surgery. A liver biopsy (sample) is also taken during surgery.

What are the possible benefits and risks of participating?
Participants will find out about their specific hormone response and changes in gut microbiota, which may allow them to change, for instance, their diet to obtain better outcomes. These tests are simple and do not involve any further risk, and will help to show which bariatric technique is better for patients with obesity and associated illnesses.

Where is the study run from?
Hospital Clínico San Carlos (Spain)

When is the study starting and how long is it expected to run for?
August 2017 to February 2020

Who is funding the study?
Institute of Health Carlos III (Spain)

Who is the main contact?
Dr Miguel A. Rubio

Contact information

Type(s)
Scientific

Contact name
Dr Miguel A. Rubio

ORCID ID
https://orcid.org/0000-0002-0495-6240

Contact details
Endocrinology and Nutrition Department.
Hospital Clínico San Carlos. C/Professor Martín Lagos s/n
Madrid
Spain
28040

Additional identifiers

Protocol serial number
FIS PI-16/01655

Study information

Scientific Title
Role of gastrointestinal hormones and bile acids on microbiota in bariatric surgery with different degrees of malabsorption

Study objectives
Bariatric surgery techniques with different degrees of intestinal malabsorption can modify the metabolism of bile acids (synthesis, absorption and intestinal conjugation/deconjugation), entailing impacts on self-regulation mechanisms and gut microbiota.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Comité Ético de Investigación Clínica del Hospital Clínico San Carlos (San Carlos Hospital Ethics Committee), 22/11/2016, ref: 16/229-E_BC

Study design
Single-centre case-control prospective observational study

Primary study design
Observational

Study type(s)
Other

Health condition(s) or problem(s) studied
Metabolism of bile acids, gastrointestinal hormones and gut microbiota following different bariatric surgery techniques

Interventions
This study will include bariatric surgery candidates with different degrees of intestinal malabsorption (gastric bypass or biliopancreatic derivation), according to the clinical pathway protocol used at our hospital. The trialists will study bile acids and gastrointestinal hormones after a meal test, and microbiota samples, at 2 stages of follow-up: pre-surgery (T1), and 12 months after surgery (T2). They will also collect information from a non-obese sample (control group), comparable in age and gender, for dynamic gastrointestinal and bile acid secretion (meal test), and microbiota studies.

They will analyze fasting and postprandial bile acid levels, the bile acid activation of FXR receptors (FGF19 signaling) and TGR5 receptors (mediated by PYY and GLP1 incretins) and its effect on the patients gut microbiota. The degree of bile acid malabsorption following surgery will be assessed by SeHCAT scanning. As a secondary objective, they will analyze the evolution of the patients with non-alcoholic steatosis (NALF) by liver biopsy during surgery, measuring the serum biomarkers of NALF cytokeratin-18 and α-ketoglutarate.

Intervention Type
Other

Primary outcome(s)
1. Bile acids, measured at baseline and 1 year after bariatric surgery
2. Gastrointestinal hormones (FGF19, incretins GLP1 and PYY incretins), measured at baseline and 1 year after bariatric surgery
3. Gut microbiota profile, measured at baseline and 1 year after bariatric surgery

Key secondary outcome(s))
1. The synthesis capability of bile acids by hepatocytes studied through the serum C4 (7α-hydroxy-4-cholesten-3-one), used as an enzymatic marker of cholesterol-7α-hydroxylase, measured at baseline and 1 year after bariatric surgery
2. Malabsorption of bile acids, determined by the isotopic test SeHCAT at 1 year after bariatric surgery
3. Potential biomarkers of liver damage associated with fatty liver (cytokeratin-18 (CK-18) and its fractions M30/M65 and alpha-ketoglutarate), measured at 1 year after bariatric surgery

Completion date
28/02/2020

Eligibility

Key inclusion criteria
1. Patients on the bariatric surgery waiting list
2. Caucasian men and women aged 18-65
3. BMI ≥ 40 kg/m2 or ≥ 35 kg/m2 with at least one major comorbidities (Type 2 diabetes,

hypertension, hyperlipemia, sleep obstructive apnea)
4. Absence of serious disease (chronic kidney disease, liver disease, neurological disease)
5. Absence of psychiatric pathology
6. Ability to understand the mechanisms involved in the surgery that will be proposed
7. Written informed consent to participate in the study

Inclusion criteria for the control group:
1. Caucasian men and women, aged 18-65 years (matched with patients)
2. BMI 20-29.9 kg/m2
3. No pregnant and lactating women
4. Absence of major comorbidities (Type 2 diabetes, hypertension, hyperlipidemia, sleep obstructive apnea)
5. Absence of serious diseases (chronic kidney or liver disease, inflammatory diseases, neurological diseases, cancer, AIDS)
6. Absence of psychiatric disorders
7. Written informed consent to participate in the study

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
65 years

Sex
All

Key exclusion criteria
1. Systemic disease not associated with obesity (inflammatory bowel disease, inflammatory rheumatic disease)
2. Hepatitis C, known cirrhosis (or discovered during the study)
3. HIV
4. Drug and/or alcohol abuse
5. Eating disorders

Date of first enrolment
01/03/2018

Date of final enrolment
31/07/2018

Locations

Countries of recruitment
Spain

Study participating centre
Hospital Clínico San Carlos
Martín Lagos s/n
Madrid
Spain
28040

Sponsor information

Organisation
Fondo de Investigaciones Sanitarias - Instituto de Salud Carlos III-FEDER (PI-16/01655)

ROR
https://ror.org/00ca2c886

Funder(s)

Funder type
Government

Funder Name
Instituto de Salud Carlos III

Alternative Name(s)
SaludISCIII, InstitutodeSaludCarlosIII, Instituto de Salud Carlos III | Madrid, Spain, Carlos III Institute of Health, Institute of Health Carlos III, Carlos III Health Institute, La misión del Instituto de Salud Carlos III (ISCIII), ISCIII

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Spain

Results and Publications

Individual participant data (IPD) sharing plan

Datasets will be available upon request from Dr Miguel A. Rubio. The data will be archived in a repository and become available when requested, for a period of 10 years. The type of data that will be provided are both the database (with anonymous data) and statistical analyses. Data will be provided once permission is granted, upon request. All the analyses performed will be available at the repository. Consent written forms will be obtained from all participants.

IPD sharing plan summary