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Relationship between hormones that decrease blood glucose and the resident bacterial content of the intestine

Submission date	Recruitment status	[_] Prospectively registered
25/09/2020	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
01/10/2020	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
06/12/2021	Digestive System	

Plain English summary of protocol

Background and study aims
The gut microbiome is made up of trillions of bacteria, fungi and other microbes. The gut microbiome plays a very important role in health by helping control digestion and benefiting the immune system and many other aspects of health. In obese people, the diversity of the gut microbiome is reduced. Also, there are changes in chemical messenger substances (hormones) that communicate between the gut and fat cells in the body.
In this study, we plan to investigate the effect of weight loss in moderately obese patients on intestinal hormones, gut microbial composition, and the effect on the fat tissue.

Who can participate?
Subjects with a body mass index (BMI) between 30 and 40 kg/m² with no known previous diseases, as well as a group of healthy control participants of a similar age range with BMI between 18 and 25 kg/m²

What does the study involve?
Patients with obesity will be recruited and subjected to a reduced-calorie diet for six months, after which the initial assessments will be repeated to verify the effect of effective weight reduction on fat tissue.

What are the possible benefits and risks of participating?
The benefits of participating in the study may be related to improvement associated with weight loss. Although it may be that no benefits are obtained.

Where is the study run from?
Joan XXIII University Hospital in Tarragona (Spain).

When is the study starting and how long is it expected to run for?
June 2015 to June 2017

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

Who is the main contact?
Prof. Joan J. Vendrell, jvo@comt.es

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Protocol serial number
PI14/00228

Study information

Scientific Title
Incretin mediation on microbiome, metainflammation and adipose tissue plasticity. Functional study in an obese cohort after a dietary intervention

Acronym
IncMic

Study objectives
The activity of glucagon-like peptides (GLPs) and gastric inhibitory polypeptide (GIP) on adipose tissue can influence the adipogenic, proliferative and functional capacity of human adipose-derived mesenchymal cells (hADSCs). Thus, differences in the dynamics of the GLPs/GLPRs and GIP/GIPR axis may influence the pattern of insulin resistance and metal inflammation associated with obesity and type 2 diabetes.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 03/11/2014, Hospital Universitari Joan XXIII ethics committee (Avda Mallafre Guasch, 4, 43005 Tarragona, Spain; +34 977759394; no email provided), ref: 83/2014

Study design
Interventional non randomized

Primary study design
Interventional

Study type(s)
Other

Health condition(s) or problem(s) studied
Relationship between hormones that decrease blood glucose and the resident bacterial content of the intestine

Interventions
Equal numbers of non-morbidly obese and age-matched healthy controls will be recruited.

All participants will be prescribed a six-month low-calorie Mediterranean type Diet (20 Kcal/Kg baseline body weight), with 4 daily meals for 6 months (50% carbohydrates, 25- 30% lipids, and 20 to 25% protein) and will be encouraged to increase their physical activity. Monthly visits by a dietitian with a health status review and diet reminder recommendations will be scheduled.

Assessment will be carried out as follows:

Collection of clinical and anthropometric variables (age, sex, weight, height, BMI, BP).Analytical determination of complete blood count, glycemia, HbA1c, insulin, C peptide, total cholesterol, HDL and LDL and triglycerides, creatinine, MDRD, basic biochemistry. HOMA index (glucose [mmol/l] x insulin [mIU/l] / 22.5). Serum and plasma samples that will be frozen at -80C and stored in the HUJ23 Biobank for the subsequent determination of low-grade inflammation markers (ultrasensitive C-reactive protein (PCRus), interleukin-6 (IL-6) and adiponectin. Stool collection. Biopsy of subcutaneous adipose tissue in obesity group.

Plasma concentrations of active GLP-1 (7-36 and 7-37) plasma levels of GLP-2 and Glucagon Standard food test (Meal test): Administration of 200ml of EDANEC (Abott Laboratories; 101kcal /100ml, of which 54% are carbohydrates, 16% proteins and 30% lipids). Extraction at 0, 15, 30, 60 and 120min. Determination of plasma concentrations of glucose, insulin, GLP-1, GLP-2.

Lipid overload test (Lipid test): Administration of a preparation (Patent No P201030776) that contains a total of 50g of fat (100ml) of which 30% is saturated, 49% monounsaturated and 21% polyunsaturated. unsaturated. Blood will be drawn at 0, 60, 120 and 180 min for the determination of plasma concentrations of GLP-1, GLP-2 and triglycerides.
The two tests will be carried out on two different days (at least 3 days apart) and after a fasting period of 12 hours.

Intestinal permeability study: Administration of a solution with 10g of Lactulose and 5g of Mannitol in 100ml of water. Urine collection for 5h. The permeability index (lactulose/mannitol ratio) will be analyzed by HPLC.

Microbiota study: Extraction of both microbial and host genomic DNA using the PowerFecal DNA Isolation Kit (MOBIO) system. Mesenchymal ADSCs from patients with different degrees of obesity will be obtained before and after weight loss.

Intervention Type
Behavioural

Primary outcome(s)
Measured at every visit at baseline and every month until the end of the study:
1. Bodyweight (kg)
2. Height (m)
3. Waist circumference (cm)
4. Blood pressure (mmHg)

At baseline and 6 month follow up:
5. Meal Tolerance Test (MTT) (blood will be taken before meal ingestion (time 0 min) and at 15, 30, 60, and 120 min after meal ingestion)
5.1. GLP-1 and GLP-2 assessed using ELISA methods
5.2. Glucose, cholesterol, and triglycerides determined using standard enzymatic methods
5.3. Plasma insulin analyzed by immunoassay
6. A study of the intestinal microbiome-related with the incretin response will be determined using shotgun sequencing of stool DNA for whole metagenome analysis

Key secondary outcome(s))
There are no secondary outcome measures

Completion date
30/06/2017

Eligibility

Key inclusion criteria
1.1. Obese group: Non-morbid obese subjects with a body mass index (BMI) range ≥30 to ≤40 kg /m²
1.2. Control group:
2. Aged >18 and <65 years
3. Absence of acute or chronic systemic disease (other than obesity)
4. Absence of any pharmacological treatment and weight stability at least during the 3 previous months before entry in the study
5. Informed consent signed
6. BMI range ≥18 to ≤25 kg/m²

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
36

Key exclusion criteria
Both groups:
1. Active smokers
2. Alcohol intake >40gr/day
3. Presence of other cardiovascular risk factors except obesity (arterial hypertension, dyslipidemia, diabetes mellitus or history of disease cardiovascular disease)
4. Moderate-severe chronic liver disease or chronic renal failure
5. Chronic inflammatory diseases
6. Surgery or recent hospital admission (<3 months)
7. Glucocorticoid treatment in the last 6 months
8. Neoplasia in the previous 5 years
9. Pregnancy or lactation

Date of first enrolment
01/06/2016

Date of final enrolment
30/01/2017

Locations

Countries of recruitment
Spain

Study participating centre
Hospital Universitari Joan XXIII
Mallafre Guasch, 4
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43005

Sponsor information

Organisation
Institut d'Investigació Sanitària Pere Virgili

ROR
https://ror.org/01av3a615

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
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		06/11/2021	06/12/2021	Yes	No