ISRCTN77500181 https://doi.org/10.1186/ISRCTN77500181

Virgin olive oil and high-density lipoprotein functionality: a model for tailoring functional food

Submission date
06/03/2012

Recruitment status
No longer recruiting

Registration date
09/05/2012

Overall study status
Completed

Last Edited
25/04/2016

Condition category
Nutritional, Metabolic, Endocrine

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

Plain English summary of protocol

Background and study aims
The aim of this study is to find out whether consuming olive oil enriched with olive oil phenolic compounds (OOPC) and olive oil enriched with OOPC plus flavonoids from thyme increases quality and quantity of high density lipoprotein (HDL) compared with consuming normal virgin olive oil.

Who can participate?
Male and female hypercholesterolemic (>200mg/dL) patients aged 20-80 years.

What does the study involve?
Participants will receive 25 ml per day of one of the three types of olive oil in three separate periods of 3 weeks, preceded each one by a 2-week wash-out period.

What are the possible benefits and risks of participating?
The benefit for the participants will be the possibility of reducing their cardiovascular disease risk. No harmful effects have been found to be associated with olive oil consumption.

Where is the study run from?
Institut Hospital del Mar dInvestigacions Mèdiques (IMIM) , Barcelona, Spain

When is the study starting and how long is it expected to run for?
April to September 2012

Who is funding the study?
Spanish Ministry of Economy and Competitiveness

Who is the main contact?
Dr María-Isabel Covas
mcovas@imim.es
mfito@imim.es

Contact information

Type(s)
Scientific

Contact name
Dr Maria Isabel Covas

Contact details
Doctor Aiguader, 88
Barcelona
Spain
08003
+34 (0)933 160 720
mcovas@imim.es

Additional identifiers

Protocol serial number
AGL2009-13517-C03-01

Study information

Scientific Title
Virgin Olive oil and HDL Functionality (VOHF): a model for tailoring functional food: the VOHF project

Acronym
VOHF

Study objectives
A flavoured functional olive oil enriched not only with its own phenolics but also with complementary ones (regarding structure/function) from thyme could provide additional health benefits and consumers acceptation.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Clinical Research Ethical Committee of the "Institut Municipal dAssistència Sanitària (IMAS)", 09 /09/2009, ref: 2009/3347/I

Primary study design
Interventional

Study design
Randomized controlled double-blind cross-over single-centre clinical supplementation trial

Study type(s)

Quality of life

Health condition(s) or problem(s) studied
Hypercholesterolemic patients

Interventions
Current interventions as of 23/04/2014:
Randomized, controlled, double-blind, cross-over, single-centre clinical supplementation trial, in which 33 subjects (19 men and 14 women) will be randomised to one of 3 orders of administration of 25 ml/day of raw:

1. Virgin olive oil (Control)
2. Functional Olive Oil 1 enriched with its own phenolic compounds (FOO1)
3. Functional Olive OIl 2 enriched with its olive oil phenolic compounds plus those of thyme (FOO2)

This will be in 3 periods of 3 weeks

Previous interventions:
Randomized, double-blind, cross-over, single-centre clinical supplementation trial, in which 30 subjects (15 men and 15 women) will be randomised to one of 3 orders of administration of:

1. 25 mL/day of raw refined virgin olive oil (Control)
2. Functional Olive Oil 1 enriched with its own phenolic compounds (FOO1)
3. Functional Olive OIl 2 enriched with its olive oil phenolic compounds plus those of thyme (FOO2)

This will be in 3 periods of 3 weeks

Intervention Type
Supplement

Primary outcome(s)
1. HDL functionality:
The following parameters will be measured at baseline and before and after each intervention:
1.1. Markers of compliance: Measurement of tyrosol and hydroxytyrosol in spot morning urine will be performed by GC/mass spectrometry
1.2. Parameters of HDL functionality: Isolation of HDL will be done by sequential centrifugation.
2. The following parameters will be measured in isolated HDL:
2.1. Fatty acid content, vitamin E, and total phenolic content in HDL by HPLC-DAD
2.2. Apolipoproteins (Apo)A1, ApoA2, and ApoA4 by ELISA
2.3. Cholesterol esther transfer protein (CETP) and lecitine cholesterol acyl transferase (LCAT) by fluorometry
2.4. Paraoxonase (Organophosphatase activity) PON1) and PAF-AH activities by spectrometry with automated mode
2.5. 3 chlorotyrosine and 3-nitro-tyrosine by GC/MS
2.6. Bilayer fluidity of HDL will be measured by confocal microscopy. Cholesterol efflux from cells will be measured in culture of macrophages.
3. OMICS
Gene expression assay will be performed as previously described. Several candidate genes implicated in the increase of the HDL cholesterol and in the improvement of the HDL

functionality in humans will be tested. Candidate genes: ABCA1: ATP-binding cassette, sub-family A (ABC1), member 1; ABCG1: ATP-binding cassette, sub-family G (WHITE), member 1; and ABCG4: ATP-binding cassette, sub-family G (WHITE), member 4 ApoA1: apolipoprotein A- I; and ApoE: apolipoprotein E; LPL: lipoprotein lipase; PAF-AH1B3: platelet-activating factor acetylhydrolase, isoform Ib, gamma subunit 29kDa; PPARalpha: peroxisome proliferator - activated receptor alpha; PPARgamma: peroxisome proliferator-activated receptor gamma; and PBPPAR: PPAR binding protein; RARA: retinoic acid receptor, alpha. Proteomic analyses, by separation with 2-DE (two-dimensional gel electrophoresis) and PMF (protein mass fingerprinting) with MALDI-TOF-MS (matrix -assisted laser desorption/ionization time of flight mass spectrometry ,will be performed in plasma samples.

Key secondary outcome(s)
Oxidative damage
The following parameters will be measured at baseline and before and after each intervention:
1. Plasma lipids will be performed by enzymatic methods in a automated mode. In vivo circulating oxidized LDL and 3 chlorotyrosine derivates in urine will be determined by ELISA
2. Protein carbonyl content (PCC) by spectrometry
3. 8-isoprostane (8-epi PGF2á)
4. 8-hydroxydeoxyguanosine (8-OHdG) by enzyme-linked immunosorbent assay (ELISA)

Added 23/04/2014:
5. Endothelial function
6. Intestinal microorganism study

Completion date
07/09/2012

Eligibility

Key inclusion criteria
Current inclusion criteria as of 23/04/2014:
1. Hypercholesterolemic patients (>200 mg/dL)
2. Aged 20-80 years

Previous inclusion criteria:
1. Hyperlipidemic patients
2. Patients with low (<40 mg/dL) HDL cholesterol
3. Aged 20-60 years

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
Current exclusion criteria as of 25/04/2014:
1. Smokers
2. Athletes with PA >3000 kcal/day
3. BMI >35 kg/m2
4. Diabetes, multiple allergies, intestinal diseases
5. Any condition that limits the mobility of the subject making study visits impossible
6. Life threatening illness such as cancer or severe disease with a lowered expected 3 year survival
7. Any other disease or condition that would worsen the adherence to the measurements or treatment

Previous exclusion criteria:
1. Intake of antioxidant supplement or acetylsalicylic acid or any other drug with established antioxidative properties
2. Athletes with PA >3000 kcal/week in leisure-time
3. Obesity (BMI > 30 kg/m2)
4. Diabetes, multiple allergies, intestinal diseases
5. Any condition that limits the mobility of the subject making study visits impossible
6. Life threatening illness such as cancer or severe disease with a lowered expected 3 year survival
7. Any other disease or condition that would worsen the adherence to the measurements or treatment

Date of first enrolment
02/04/2012

Date of final enrolment
07/09/2012

Locations

Countries of recruitment
Spain

Study participating centre
Doctor Aiguader, 88
Barcelona
Spain
08003

Sponsor information

Organisation
Spanish Ministry of Economy and Competitiveness (Spain)

Funder(s)

Funder type
Government

Funder Name
Spanish Ministry Science and Technology (Spain) ref: AGL2009-13517-C03-01

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	10/06/2015		Yes	No