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Effects of acute and one month ingestion of biologically aged Andalusian wines on endothelial function

Submission date
14/12/2012

Recruitment status
No longer recruiting

Registration date
23/04/2013

Overall study status
Completed

Last Edited
30/04/2013

Condition category
Circulatory System

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
In epidemiological studies, moderate consumption of alcohol is consistently associated with a reduction in myocardial infarction as well as several cardiovascular risk factors. However, the effects of the different alcoholic beverages (fermented or distilled) are still debated, as are the subjects who show higher benefits in the cardiovascular system after moderate alcohol consumption. The biologically aged Andalusian wine could give cardioprotective effects because of its singular aging process.
The aim of this study is to understand the risk/benefit ratio of the consumption of 30 g a day (during 3 weeks) of ethanol in the form of gin or Andalusian biologically aged wine in different population subsets regarding several cardiovascular risk factors.

Who can participate?
Males and females between 55 and 80 years old without documented cardiovascular disease (ischaemic heart disease angina or recent or old myocardial infarction or previous or cerebral vascular accident, peripheral vascular disease) and who have diabetes mellitus or three or more of the following factors: current smoking, hypertension, hypercholesterolemia (LDL-cholesterol > 160 mg/dl), HDL-cholesterol < 40 mg/dl, overweight or obese (body mass index > 25 kg/m2) and/or family history of premature coronary heart disease.
Healthy males and females between 20 and 40 years.

What does the study involve?
Participants will not consume alcohol for the first 15 days of the study. Then they will be randomly allocated to one of two groups: a wine intervention or a gin intervention.
Group 1 will be given 0.5g/Kg of aged wine for one day only and then 255ml of wine daily for 21 days.
Group 2 will be given 0.5g/Kg of gin for one day only and then 92ml of gin daily for 21 days.
Then they will have 15 days without alcohol.
Then Group 1 will have the gin intervention and group 2 will have the wine intervention

What are the possible benefits and risks of participating?
It is expected that after the wine intervention the participants will show a decreased cardiovascular risk. There are no risks involved.

Where is the study run from?
Participants will be recruited in the Hospital Clinic of Barcelona and the Reina Sofia Hospital, Cordoba (Spain).

When is the study starting and how long is it expected to run for?
The study started in January 2013 and is expected to finish in December 2014.

Who is funding the study?
The Spanish Foundation for the Wine and Nutrition Research (Fundación para la Investigación del Vino y Nutrición FIVINN).

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
CP040970

Study information

Scientific Title
Effects of acute and one month ingestion of biologically aged Andalusian wines on endothelial function: a randomized crossover trial

Study objectives
The benefit of the main components of aged wine, namely ethanol and polyphenolic content is synergistic, but different between men and women and healthy or at high cardiovascular risk. No adverse events will be observed.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Institutional Review Board of the Hospital Clínic of Barcelona (Spain). May 2011. Reference 2011 /6824

Study design
Randomized crossover clinical trial

Primary study design
Interventional

Study type(s)
Screening

Health condition(s) or problem(s) studied
Arteriosclerosis and endothelial function

Interventions
Run-in period (15d); intervention A - 21d; 15d wash-out and intervention B -21d. Before each intervention, 0.5g OH/Kg will be administered as gin or wine.

Intervention 1: 92 ml/day of gin
Intervention 2: 255 ml/day of aged wine
Acute phase before each intervention: 0.5g/Kg of gin or aged wine

Intervention Type
Other

Phase
Not Applicable

Primary outcome(s)
1. Leukocyte adhesion molecule expression
Lymphocyte and monocyte adhesion molecules on these cells will be marked with monoclonal antibodies (MAb) conjugated with fluorescein-isothiocyanate (FITC) and phycoerythrin (PE) by direct double immunofluorescence. The MAb of the adhesion molecules used will be: anti-CD11a (LFA-1), anti-CD40L, anti-CD11b (Mac-1) (Bender MedSystems Diagnostics, Vienna), anti-Syalil Lewis (anti-CD15s) (Pharmingen, San Diego, CA), anti-CD49d (VLA-4) (Cytogmos) and CD31 (BD, NJ, USA). The monoclonal antibodies used to mark the T-lymphocytes will be anti-CD2 and monocytes, anti-CD14 (Caltag Laboratories, Burlingame, CA).
2. Soluble adhesion molecules
The following serum soluble adhesion molecules will be determined by ELISA kits:
2.1. sICAM-1, sVCAM-1, PECAM, hs-CRP, sE-selectin, and sP-selectin, as well as sMCP-1, TNF-a, IL-6 and IL-1B (Immunotech).
2.2. Nuclear Factor Kappa B by western blot of peripheral blood mononuclear cells.
2.3. Genes and proteins involved in inflammatory response will be determined by real time PCR and Western blot analysis (MCP-1, TF and TFPI, as markers of inflammation and LRP and the LDL receptor as lipoproteic receptors). Moreover, the expression metalloproteases and their activity

will also be analyzed.
3. Oxidative stress
The following plasma molecules will be determined: superoxide dismutase (SOD) with the Superoxide Dismutase Assay SD125 (Randox Laboratories Ltd, UK), catalase (CAT) with the Catalase Assay (Cayman Chemical, Ann Arbor, MI, USA), glutathione reductase (GR) and reduced glutathione (GSH) with the Glutathione Reductase Assay GR2368 (Randox Laboratories Ltd, UK), glutation peroxidase with the RS 504 assay (Randox Laboratories Ltd, UK), el complejo GSH /GSSG (Bioxytech OxisResearch, Foster City, CA, USA), protein carbonyl groups with the Protein Carbonyl Assay (Cayman Chemical, Ann Arbor, MI, USA), lipid peroxides (LPO) with the LPO-CC Assay (Kamiya Biomedical Company, Seattle, USA), malondialdehyde (MDA) and 4-hydroxyalkenals (HAE) with the Bioxytech LPO-586 (Oxys Research, Portland, OR, USA), total antioxidant capacity with the Total Antioxidant Powder (aqueous) Assay (Neogen Corporation, Lexington, KY, USA) and hidroxideoxiguanosina 8-(8-OHdG) with the 8-OHdG Check ELISA Kit (Genox Corporation, Baltimore, USA) in plasma in addition to the concentration of urinary isoprostanes with the Urinary Isoprostane Assay (Neogen Corporation, Lexington, KY, USA).
4. Nitric oxide
The concentration of nitrate / nitrite (NO (x)) in plasma will be determined through purifying the samples with Microcon YM-10 filters (Micon Bioseparations, Millipore, Billerica, MA, USA) and the commercial kit Nitrate / Nitrite Colorimetric Assay Kit (Cayman Chemical, Ann Arbor, MI, USA). In addition, the concentration of nitric oxide synthase (NOS) in plasma will be determined with the commercial kit Bioxytech ® Nitric Oxide Synthase Assay Kit ™ (Oxys Research, Portland, OR, USA).
5. Wine biomarkers and urinary polyphenols
The urinary polyphenol levels will be also determined with the Folin-Ciocalteau assay (Sigma-Aldrich-Fluka, St. Louis, MO, USA). Furthermore, tartaric acid in urine as biomarker of wine intake will be also quantified by LC-MS/MS.

Key secondary outcome(s))

1. Medical record
A complete medical record will be obtained from all participants, which included data on alcohol intake, smoking and dietary habits. Blood pressure and heart rate will be measured with an electronic apparatus Omron HEM-705CP (Netherlands).
2. Nutrition assessment and general analyses
All participants will complete a validated nutritional questionnaire at baseline to determine the total quantity of calories ingested in the previous month as well as the proportion corresponding to carbohydrates, lipids and proteins by using the Food Processor Nutrition & Fitness software (esha RESEARCH, Salem, OR, USA) . Overall nutrition will be determined by percentage of ideal weight, lean body mass and body mass index. Waist Perimeter will be measured. The proteic nutrition will be determined on the basis of the following parameters: hemoglobin, total lymphocyte count, total proteins, albumin, prealbumin, transferrin and retinol-binding protein. Serum and intraerythrocytary folic acid concentrations will be measured, as well as serum vitamin A, B1, B12, C, E, B-carotenes, Zn, Mg and Se concentrations.
Moreover, the following measurements will also be obtained: red blood cell count, hematocrit, mean corpuscular volume, leukocyte count, glucose, creatinine, electrolytes, uric acid, transaminases, lactate dehydrogenase, alkaline phosphatase, gammaglutamyl transpeptidase and bilirrubin.
3. Coagulation tests
The following parameters will also be determined: platelet count, prothrombin time, and plasma fibrinogen.
4. Serum lipoproteins and others
Total cholesterol, triglycerides, cHDL, cLDL, Apo A1, Apo B, lipoprotein (a) and homocysteine will

be determined.
5. Diet and exercise monitoring
All participants will follow an isocaloric diet prepared according to their personal preferences. The diet will be strictly monitored during the study. Diet compliance will be assessed from 7-days diet records administered before each evaluation. This assessment will be administered by trained personnel. The foods ingested will be converted into nutritional values with the aid of the Professional Diet Balancer software (Cardinal Health Systems, Inc., Edina, MN). Physical activity will also be evaluated with the Minnesota Leisure Time Physical Activity questionnaire which has also been validated in Spain. Control of the diet and physical exercise will be carried out before and after each intervention, the same day on which the clinical examinations are performed and blood is withdrawn for immunologic studies.

Completion date
31/12/2015

Eligibility

Key inclusion criteria
1. Males and females between 55 and 80 years old without documented cardiovascular disease (ischaemic heart disease angina or recent or old myocardial infarction or previous or cerebral vascular accident, peripheral vascular disease) and who have diabetes mellitus or three or more of the following factors:
1.1. Current smoking
1.2. Hypertension
1.3. Hypercholesterolemia [LDL-cholesterol > 160 mg/dl, HDL-cholesterol < 40 mg/dl]
1.4. Overweight or obese (body mass index > 25 kg/m2) and/or
1.5. Family history of premature coronary heart disease
2. Healthy males and females between 20 and 40 years
3. The participant should give signed informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
1. Subjects with a previous history of cardiovascular disease (ischaemic heart disease angina or recent or old myocardial infarction, cerebral vascular accident, or peripheral vascular disease)
2. Any severe chronic disease
3. Alcoholism or other toxic abuse

Date of first enrolment
01/01/2013

Date of final enrolment
31/12/2015

Locations

Countries of recruitment
Spain

Study participating centre
Hospital Clínic de Barcelona
Barcelona
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Sponsor information

Organisation
Spanish Foundation for the Wine and Nutrition Research (Fundación para la Investigación del Vino y Nutrición FIVINN) (Spain)

ROR
https://ror.org/002jv8g15

Funder(s)

Funder type
Research organisation

Funder Name
Spanish Foundation for the Wine and Nutrition Research (Fundación para la Investigación del Vino y Nutrición FIVINN) (Spain)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration