ISRCTN99660610 https://doi.org/10.1186/ISRCTN99660610

Assessment of different doses of tomato intake on blood pressure and endothelial function in patients at high vascular risk: nutrigenomics effect on different phenotypes of risk

Submission date
27/05/2013

Recruitment status
No longer recruiting

Registration date
02/08/2013

Overall study status
Completed

Last Edited
09/08/2013

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
Eating habits play a key role in the development and treatment of cardiovascular (heart) diseases. Research suggests that consumption of fruits, vegetables as well as other antioxidant-rich food (wine, cacao, virgin olive oil) is associated with lower incidences of heart diseases. Tomato is the most consumed vegetable in Spain and contains many nutrients. Regular consumption of tomatoes and their by-products are always associated with a reduced risk of several cancers and lower incidence of heart disease. However, there is no direct evidence for the preventive effects of tomato against heart disease. The aim of this study is to find out the effects of different amounts of tomato on the cardiovascular system, and to define the effective amount of tomato juice that reduces blood pressure and improves blood circulation, considering the great variability of the effects in patients at high risk for heart diseases.

Who can participate?
Healthy men and women with no history of heart disease can participate in the acute study. Patients with high blood pressure aged between 55 and 80 years without known heart disease but at risk of heart disease (e.g. smokers, diabetics, etc) can participate in the chronic study.

What does the study involve?
Participants will be randomly allocated into one of five different groups. For the acute study, participants will drink tomato juice either with or without refined olive oil. For the chronic study, they will drink one of two different quantities of tomato juice or mineral water every day for 28 days. Participants will not consume any other tomatoes or tomato products during the study.

What are the possible benefits and risks of participating?
Participants may receive an effective amount of tomato juice that will reduce the risk of heart disease. The effect of tomato on blood pressure and other risk factors for heart disease will be found. There are no risks involved in participating in this study.

Where is the study run from?
Participants will be recruited in the Hospital Clinic of Barcelona, Spain. The analysis will be performed at the laboratories of the Hospital Clinic of Barcelona (Spain), the University of Barcelona (Spain) and the University of Valencia (Spain).

When is the study starting and how long is it expected to run for?
The study started in January 2011 and is expected to finish in December 2014.

Who is funding the project?
Ministry of Science and Innovation (Ministerio de Ciencia e Innovación, MICINN) (Spain).

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
AGL2010-22319-C03

Study information

Scientific Title
Effect of bioactive compounds of tomato on classical and novel cardiovascular risk factors: an open randomized crossover controlled trial

Acronym

TEMTOM-1

Study objectives
1. The daily consumption of tomato will produce a decrease of blood pressure measurements and an improvement of endothelial function in patients at high vascular risk.
2. The daily consumption of tomato will produce an improvement in insulin resistance and lipid profile, as well as a reduction in oxidative stress and inflammatory biomarkers related to atherosclerosis.
3. The intensity of the observed clinical responses will be dose-dependent; that is, it will depend on the dose administered.
4. Consumption of tomato at different doses will produce a differential expression (over-expression or inhibition) of certain genes related to cardiovascular risk.
5. The identification of genetic variants in differently expressed genes will reveal those variants associated with endothelial function markers, blood pressure and other cardiovascular risk phenotypes contributing to explain the inter-individual response to dietary intervention with tomato products.
6. The effects of tomato consumption and patterns related with cardiovascular phenotypes (blood pressure, plasma lipids, glycaemia, endothelial function markers) in a population at high vascular risk will be modulated by some genetic polymorphisms.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Institutional Review Board of the Hospital Clinic Committee 28/01/2010, Ref: 2010/5580
2. University of Barcelona (UB) Committee 08/07/2010, Ref: IRB00003099

Study design
1. Acute, open, randomized, crossover and controlled study in healthy volunteers
2. Chronic, open, randomized, crossover and controlled feeding trial in hypertensive patients

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
GP practice

Study type(s)
Screening

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Arteriosclerosis and its risk factors

Interventions

Written material on the study protocol and the diet that should be followed by the subjects is administered at admission.

Acute study. Study of bioavailability and pharmacokinetics of tomato juices in healthy humans.
Intervention 1: 750 g of tomato juice with refined olive oil/70 kg of body weight
Intervention 2: 750 g of tomato juice without oil (water matrix)/70 kg of body weight

The total duration of intervention for the acute study is two days.

Chronic study.
Intervention 1: 200 ml of mineral water per day for 28 days.
Intervention 2: 200 ml of tomato juice per day for 28 days.
Intervention 3: 400 ml of tomato juice per day for 28 days.

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
Acute study.
a. Analysis of the antioxidants (vitamin C, carotenoids and phenolic compounds) in the tomato juices (with and without oil) administered to participants;
b. Analysis of the antioxidant capacity (TEAC, ORAC, TRAP and FRAD), total phenolic concentration (Folin-Ciocalteu method) in plasma and urine samples;
c. Analysis of polyphenols and their metabolites in plasma and urine samples of the participants by LC-MS/MS;
d. Analysis of carotenoids and vitamins metabolites in plasma samples of the participants;
e. Pharmacokinetic studies.

Chronic study.
a. Determination of the antioxidant content (vitamins C and, E, carotenoids and polyphenols of the juices used in the study, and its stability throughout the trial.
b. Measurement of blood pressure, endothelial function, body weight, waist perimeter, glucose, insulin, HOMA index, lipid profile, and markers of oxidative stress,
c. Study serum and cellular inflammatory biomarkers related to atherosclerosis, as well as study of adhesion of monocytes to an endothelial cell line.
d. Analysis of carotenoids, vitamins, and polyphenols and their metabolites in plasma and urine samples.
e. Genetic studies: genotyping of pre-selected SNPs and analysis of the association between SNPs and their corresponding phenotypes; gene expression analysis; analysis of whole genome expression; bioinformatic analysis of the gene expression results and validation of differentially expressed genes.

Determinations reported in points b to e will be performed before and after each intervention.

Evaluation of different doses of tomato juice on endothelial function and hypertension in high cardiovascular risk volunteers will be assessed in an open, controlled, randomized and cross-over feeding clinical trial following three interventions: (0 ml tomato juice (water)/day-control; 200 ml /day; 400 ml/day) for four weeks. Before and after each intervention the following measures will

be taken: blood pressure, body weight, waist perimeter, glucose, insulin, HOMA index, lipid profile, markers of oxidative stress, serum and cellular inflammatory biomarkers related to atherosclerosis, as well as study of adhesion of monocytes on an endothelial line; analysis of polyphenols in plasma and urine and lycopene in plasma; genotyping of the pre-selected single nucleotide polymorphisms (SNPs); preliminary analysis of the association between the selected SNPs and the corresponding phenotypes; gene expression analysis with the high-density array.

Secondary outcome measures
Acute study and chronic study.
a. In all participants a complete medical record before will be carried out entering to the study and data on dietary habits, alcohol consumption, smoking and physical activity will be recorded before and after each intervention (only in chronic study).
b. Determination of carotenoids and polyphenols in plasma and urine before and after each intervention, that will also be used as an objective measurement of intervention compliance.
c. In addition, in all volunteers all adverse events will be recorded and the following parameters will be measured: number of red and white cells, hematocrit, mean corpuscular volume, serum glucose, creatinine, electrolytes, uric acid, transaminases, lactate dehydrogenase, alkaline phosphatase, gammaglutamyl transpeptidase, bilirubin, creatinkinase and aldolase.

Overall study start date
01/01/2011

Completion date
31/12/2014

Eligibility

Key inclusion criteria
Acute study.
Healthy volunteers, body mass index between 18.5 and 24 Kg/m2, and no history of cardiovascular disease or haemostatic abnormalities.

Chronic study.
Hypertensive patients, male and female, between 55 and 80 years without documented cardiovascular disease (ischemic heart disease -angina pectoris or recent myocardial infarction or old-, stroke, or peripheral vascular disease), but who had two or more of the following cardiovascular risk factors:
1. Smoking,
2. Diabetes mellitus,
3. LDL-cholesterol > 160 mg/dl.
4. HDL-cholesterol < 40 mg/dl.
5. Overweight or obesity (Body mass index > 25 kg/m2).
6. Family history of premature ischemic heart disease.

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit

18 Years

Sex
Both

Target number of participants
12 healthy volunteers. 60 patients with high cardiovascular risk.

Key exclusion criteria
Acute study.
Previous history of cardiovascular disease (ischemic heart disease - angina or recent or old myocardial infarction, cerebral vascular accident, or peripheral vascular disease), homeostatic disorders, any several chronic diseases, hypertension or dislipemia, smokers, alcoholism or other addiction, or allergy or intolerance to tomatoes .

Chronic study.
Healthy adults (males and females). Participants with previous history of cardiovascular disease, any severe chronic illness, alcoholism or other addiction, or allergy or intolerance to tomatoes.

Date of first enrolment
01/01/2011

Date of final enrolment
31/12/2014

Locations

Countries of recruitment
Spain

Study participating centre
Food Science Department, Pharmacy Faculty, University of Barcelona
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Sponsor information

Organisation
Spanish Ministry of Science and Innovation (Ministerio de Ciencia e Innovación, MICINN) (Spain)

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Government

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Funder(s)

Funder type
Government

Funder Name
Spanish Ministry of Science and Innovation (Ministerio de Ciencia e Innovación, MICINN) (Spain) (AGL2010-22319-C03)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration