ISRCTN10794277 https://doi.org/10.1186/ISRCTN10794277

Beneficial effect of innovative nutraceutical formulation based on grape pomace polyphenolic extract on serum levels of TMAO, a new biomarker of cardiovascular diseases

Submission date
12/09/2018

Recruitment status
No longer recruiting

Registration date
17/09/2018

Overall study status
Completed

Last Edited
06/08/2021

Condition category
Nutritional, Metabolic, Endocrine

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

Plain English summary of protocol

Background and study aim
Cardiovascular diseases (CVD), such as ischemic heart disease (i.e. angina, heart attack) or cerebrovascular diseases (i.e. stroke), are recognised to be the main causes of disability and mortality worldwide. Some risk factors for such diseases cannot be changed i.e. age, sex and family history; however, there are other risk factors that are modifiable, including smoking, alcohol abuse, dietary habits and lifestyle. Monitoring these modifiable risk factors, and associated conditions such as diabetes, obesity, dyslipidaemia and hypertension, is useful and effective in the prevention of CVD.
Research has shown that there is a strong link between the activity of bacteria that live in the intestine (gut microbiota) and CVD risk. Gut microbiota are the main producers of various molecules, which can have positive and negative effects on the body. One of these is TMAO (trimethylamine N-oxide), the presence of which is an indicator of increased risk of CVD. TMAO can promote the development of atherosclerosis, which can then worsen metabolic diseases such as obesity and diabetes. Obesity or prolonged unhealthy dietary habits can change the gut microbiota, leading to a reduction in the presence of beneficial bacteria and an increase in bacteria that produce TMAO. In particular, diets rich in animal-derived protein (meat, eggs and fish) can lead to increased TMAO levels in the blood. Plant-based diets contribute to decreasing TMAO levels through molecules called polyphenols, which are well-known for their antioxidant activity. A polyphenol called resveratrol (RSV), which is found in wine, exerts its effects specifically against increased TMAO levels in the blood. However, polyphenols derived from the diet often have low absorption into the intestine. Therefore, supplements and food additives (nutraceuticals) based on polyphenol may be a way to improve their absorption into the body. This study aims to assess the effects of a new nutraceutical based on grape pomace polyphenols such as RSV on the levels of TMAO in overweight and obese people.

Who can participate?
Overweight and obese women aged 18-83 years old

What does the study involve?
Participants will be randomly allocated to one of two groups - group A or group B. For 4 weeks, all participants will be given a placebo. After this, there will be an 8 week treatment period, where group A will receive 600 mg grape polyphenol extract (GPE) and group B will receive 600 mg GPE and 600 mg pectin. Both groups will be asked to take this daily. Participants will be asked to maintain their usual patterns of physical activity throughout the study period.
Blood samples will be taken at week 0, 4, 8, 12 and 16 and body measurements will be taken at the start and end of the study. Participants will also be asked to record their dietary habits for one week at the start and end of the study.

What are the possible benefits and risks of participating?
Participants taking part in this study should benefit from the effects of polyphenols, including a positive influence on oxidative stress biomarkers. There are no known risks to participants taking part in this study.

Where is the study run from?
1. Samnium Medical Cooperative (Italy)
2. Department of Pharmacy, University of Naples “Federico II” (Italy)

When is the study starting and how long is it expected to run for?
June 2018 to January 2019

Who is funding the study?
1. Samnium Medical Cooperative (Italy)
2. Department of Pharmacy, University of Naples “Federico II” (Italy)

Who is the main contact?
Prof. Gian Carlo Tenore
giancarlo.tenore@unina.it

Contact information

Type(s)
Public

Contact name
Prof Gian Carlo Tenore

ORCID ID
http://orcid.org/0000-0002-0251-9936

Contact details
Via Domenico Montesano 49
Naples
Italy
80131
+39081678607
giancarlo.tenore@unina.it

Type(s)
Public

Contact name
Dr Giuseppe Annunziata

ORCID ID
http://orcid.org/0000-0002-1922-662X

Contact details
Via Domenico Montesano 49
Naples
Italy
80313
+39081678606
giuseppe.annunziata@unina.it

Type(s)
Public

Contact name
Dr Maria Maisto

ORCID ID
http://orcid.org/0000-0002-0340-2254

Contact details
Via Domenico Montesano 49
Naples
Italy
80131
+39081678606
maria.maisto@unina.it

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
18/06/2018 123512

Study information

Scientific Title
Effect of grape pomace extract on TMAO serum levels: a monocentric, double-blind, randomised, placebo-controlled parallel-group study

Acronym

GPE

Study objectives
Grape pomace extract (GPE) is a polyphenol-rich food-derived matrix. Among the GPE polyphenols, resveratrol (RSV) is the most representative. Evidences demonstrated that RSV is a strong antioxidant agent; additionally, a single animal-based study showed the ability of RSV to reduce serum levels of TMAO in mice. Therefore, the aims of this study are:
1. To evaluate the effect of GPE on TMAO serum levels in overweight/obese subjects.
2. To evaluate the effects of GPE on anthropometric and metabolic (plasma glucose, insulin, HOMA-IR, TC, LDL-c, HDL-c, TG) parameters and oxidative stress biomarkers (ox-LDL)

Ethics approval required
Old ethics approval format

Ethics approval(s)
Azienda Ospedaliera Gaetano Rummo Via dell'Angelo, 1 – 82100 Benevento, 18/06/2018, reference number 57993

Study design
Interventional double-blind placebo-controlled randomised parallel trial

Primary study design
Interventional

Secondary study design
Randomised parallel trial

Study setting(s)
Hospital

Study type(s)
Prevention

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet: Gian Carlo Tenore giancarlo.tenore@unina.it

Health condition(s) or problem(s) studied
Overweight/obesity

Interventions
Participants are randomly allocated into two groups - group A and group B.
Participants will be followed by a 2-arm parallel-group design including 4-week run-in periods and 8-week treatment periods. During the run-in periods, participants will be provided with a placebo supplement. During the treatment period, group A will be given 600 mg grape polyphenol extract (GPE) per day, and group B will be given 600 mg GPE and 600 mg pectin per day. All capsules will be identical. There will be a one month follow-up period for both groups. At the start of the study, participants will be subjected to evaluation of anthropometric parameters and nutritional habits, along with an assessment of metabolic parameters and oxidative stress biomarkers. This will then be repeated at the end of the study. Clinic visits and blood sampling will be performed after 12 hours of fasting at weeks 0, 4, 8, 12 and 16.

Intervention Type
Supplement

Primary outcome measure
Trimethylamine N-oxide (TMAO) serum levels, assessed using liquid chromatography/mass spectrometry (LC/MS) analysis of blood samples at weeks 1, 5 and 12 of the study period.

Secondary outcome measures
Unless otherwise stated, the following are assessed at weeks 0, 4, 8, 12 and 16:
1. Clinical history, assessed by interviews and analysis of previous clinical data at the baseline
2. Anthropometric measures, collected by measuring height and weight
3. Nutrient intake and dietary habits, assessed using a seven day food record validated nutritional questionnaire at the baseline and at the end of the study period
4. Blood pressure, assessed using a blood pressure cuff
5. Plasma total cholesterol (TC), measured from blood samples using a Diacron International Free Carpe Diem spectrophotometer (Grosseto, Italy), and commercially available kits from Diacron International
6. HDL-C, measured from blood samples using a Diacron International Free Carpe Diem spectrophotometer (Grosseto, Italy), and commercially available kits from Diacron International
7. LDL-C, measured from blood samples using a Diacron International Free Carpe Diem spectrophotometer (Grosseto, Italy), and commercially available kits from Diacron International
8. Triglyceride levels, measured from blood samples using a Diacron International Free Carpe Diem spectrophotometer (Grosseto, Italy), and commercially available kits from Diacron International
9. Plasma glycaemia, measured from blood samples using a Diacron International Free Carpe Diem spectrophotometer (Grosseto, Italy), and commercially available kits from Diacron International
10. Plasma insulin, measured from blood samples using ELISA
11. ox-LDL, measured from blood samples using a Diacron International Free Carpe Diem spectrophotometer (Grosseto, Italy), and commercially available kits from Diacron International
12. Blood analysis of the following, measured using a Diacron International Free Carpe Diem spectrophotometer (Grosseto, Italy), and commercially available kits from Diacron International:
12.1. Aspartate transaminase (AST)
12.2. Alanine transaminase (ALT)
12.3. Gamma-glutamyltransferase (γ-GTP)
12.4. Alkaline phosphatase (ALP)
12.5. Lactate dehydrogenase (LDH)
12.6. Albumin
12.7. Total bilirubin
12.8. Creatinine

Overall study start date
03/06/2018

Completion date
28/01/2019

Eligibility

Key inclusion criteria

1. Aged 18-83 years of age
2. Of white race
3. Overweight/obese (BMI >25 kg/m²).

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
83 Years

Sex
Both

Target number of participants
118

Total final enrolment
90

Key exclusion criteria
1. Smokers
2. Hepatic disease
3. Renal disease
4. Heart disease
5. Family history of chronic diseases
6. Drug therapy or supplement intake containing grape polyphenols
7. Heavy physical exercise (over 10 hours per week)
8. Pregnant, suspected of being pregnant or hoping to become pregnant
9. Breastfeeding
10. Birch pollen allergy
11. Use of vitamin or mineral supplements 2 weeks prior to entry into the study
12. Donation of blood less than 3 months prior to the study

Date of first enrolment
19/09/2018

Date of final enrolment
27/09/2018

Locations

Countries of recruitment
Italy

Study participating centre
Department of Pharmacy, University of Naples “Federico II” (lead center)
Via Domenico Montesano, 49
Naples
Italy
80131

Study participating centre
Samnium Medical Cooperative (Benevento, Italy)
Viale C. Colombo, 18
Castelvenere (BN)
Italy
82037

Sponsor information

Organisation
Samnium Medical Cooperative (Benevento, Italy)

Sponsor details
Viale C. Colombo, 18
Castelvenere (BN)
Italy
82037

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/02ww5xj89

Funder(s)

Funder type
Not defined

Funder Name
Samnium

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer reviewed journal

Intention to publish date
01/03/2019

Individual participant data (IPD) sharing plan
Data of individual patients will be available upon request of patient permission.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	21/05/2019	06/06/2019	Yes	No
Results article		19/07/2021	06/08/2021	Yes	No