ISRCTN76272133 https://doi.org/10.1186/ISRCTN76272133

Effects of fish oil on blood vessel function

Submission date
27/03/2013

Recruitment status
No longer recruiting

Registration date
17/04/2013

Overall study status
Completed

Last Edited
28/10/2014

Condition category
Circulatory System

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

Plain English summary of protocol

Background and study aims
The ability of blood vessels to respond to stress and injury is an important factor in the regulation of blood flow and blood pressure. Poor blood vessel function, leading to stiffness of the arteries, is associated with cardiovascular risk, and may be improved by dietary modification. Although total fat intake does not appear to have a significant impact on vascular function, long-chain n-3 polyunsaturated fatty acids (PUFA), which are found in fish oil and oily fish, have been demonstrated to modestly reduce blood pressure and improve blood vessel function, which could at least partly contribute to the cardioprotective effects of these fatty acids. The mechanisms underlying vascular protection by n-3 PUFA are not known, and there have been no studies to date which examine the ability of n-3 PUFA to modulate the repair and maintenance of vessel walls by effects on endothelial progenitor cells. There have also been no studies to date which report effects of n-3 PUFA on endothelial microparticles, which have been proposed as surrogate markers for vessel wall injury.
Circulating levels of endothelial progenitor cells (EPC) have recently been highlighted as a potential biomarker of blood vessel health. EPC originate in the bone marrow, are seen in small numbers in healthy individuals, and are related to repair and maintenance of the integrity of existing vessel walls. A number of known cardiovascular disease (CVD) risk factors have been shown to influence EPC number, including smoking, hyper tension, hypercholesterolaemia, diabetes and obesity. A number of studies have now demonstrated the independent prognostic value of EPCs, demonstrating an inverse association between cardiovascular event rate and EPC in patients with coronary artery disease. Importantly, several studies have demonstrated that EPC levels can be modified. For example, cessation of smoking, treatment of hypercholesterolaemia and weight loss can restore the EPC pool. However, there are no studies to date which have examined the effects of dietary fat on EPC numbers or function.
Endothelial microparticles (EMP) are small vesicles that are released from endothelial cells (which line blood vessels) and can be found circulating in blood. Increased numbers have been identified in individuals with certain disease states, including hypertension and venous thromboembolism. Importantly, several studies have shown that raised levels of EMPs are correlated with poor vascular function and obesity. The potential value of measuring EPC and EMP numbers as novel markers of vascular function and CVD risk is becoming recognised. Use of these novel vascular function markers in relation to other more classical measures of vascular reactivity and their response to dietary modification requires further investigation.
There is currently no information on the effects of n-3 PUFA on EMPs.
There is increasing recognition that an individual's genetic background can influence the

response to diet. Several studies have reported a link between polymorphisms (common mutations) in the eNOS gene, which is responsible for the production of nitric oxide, and blood vessel function. This is because nitric oxide causes blood vessels to dilate, but a variant of the eNOS gene means that some individuals are less able to produce nitric oxide and tend to exhibit greater stiffness of the arteries. Dietary interventions targetting these high risk individuals are therefore of interest. Since n-3 PUFA increase vascular reactivity, it is possible that individuals carrying the so-called Asp298 polymorphism in the eNOS gene might derive particular benefit from supplementation with fish oil, since they have naturally lower production of nitric oxide. This has not been investigated to date.
This study aims to investigate, for the first time, the influence of eNOS genotype on the vascular response to fish oil, incorporating in vivo measures of vascular reactivity, as well as novel markers of vascular injury and repair.

Who can participate?
Total of 90 subject aged between 21 and 65 years old, at mild/moderate risk of cardiovascular disease.

What does the study involve?
The participants are prospectively genotyped for the eNOS polymorphism. 45 subjects with the 'GG' genotype and 45 subjects with the 'GT/TT' genotype will be recruited. These subjects will be randomly allocated to one of two groups: group 1 will receive fish oil (6g per day) and group 2 will receive corn oil (dummy treatment; 6g per day) for 8 weeks, before a 'washout' period of 8 weeks with no treatment. Then group 1 will receive the dummy treatment while group 2 will receive the fish oil. We will measure blood vessel function, blood levels of nitric oxide, and markers of blood vessel damage and repair.

What are the possible benefits and risks of participating?
We do not expect any side effects or risks of the treatment, apart from a slight after-taste from the fish oil capsules. Possible benefits include an improvement in blood vessel function and/or blood pressure during the study.

Where is the study run from?
The study is run from the Hugh Sinclair Unit of Human Nutrition at the University of Reading (UK).

When is the study starting and how long is it expected to run for?
The study started in October 2010 and will be completed in September 2013.

Who is funding the study?
Nutricia Research Foundation (Netherlands).

Who is the main contact?
Professor Parveen Yaqoob
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Contact information

Type(s)
Scientific

Contact name

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
UoR 09/69

Study information

Scientific Title
Influence of eNOS genotype on the vascular response to fish oil

Acronym
FIVAS

Study objectives
Fish oil will improve vascular function by reducing endothelial damage and promoting endothelial repair. The effects will be influenced by the eNOS genotype of the individual.

Ethics approval required
Old ethics approval format

Ethics approval(s)
25th March 2010, reference 09/69; University of Reading Research Ethics Committee.

Study design
Randomised double blind placebo controlled crossover

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Not Specified

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
Cardiovascular disease

Interventions
Fish oil capsules vs placebo

Intervention Type
Other

Phase
Not Specified

Primary outcome measure
Vascular reactivity (using EndoPAT), numbers of endothelial progenitor cells and endothelial and platelet micro particles.

All outcome measures to be assessed at baseline and after 8 weeks intervention on each arm of the crossover study (i.e. Week 0, week 8, week 16 and week 24). Outcomes as follows:

Arterial function assessed by EndoPAT
Nitric oxide by nitric oxide analyzer
Endothelial progenitor cells and microparticles by flow cytometry
Circulating markers of inflammation and vascular function by ELISA
Fatty acid composition of plasma by gas chromatography

Secondary outcome measures
Blood lipids, glucose, insulin, inflammatory markers, nitric oxide, dietary intake.

All outcome measures to be assessed at baseline and after 8 weeks intervention on each arm of the crossover study (i.e. Week 0, week 8, week 16 and week 24.

Overall study start date
01/10/2010

Completion date
30/09/2013

Eligibility

Key inclusion criteria

Age 21-65 years old

Criteria for selection of an at-risk population (1 or more of the following):
1. Total cholesterol : > 5.2 mmol/l but < 7.25 mmol/l
2. HDL cholesterol : < 1.5 mmol/l (male), < 2 mmol/l (female)
3. Systolic blood pressure > 130 mmHg but < 160 mmHg
4. Dystolic blood pressure > 80 mmHg but < 100 mmHg
5. Body mass index between 24.5-35 kg/m2 or waist >102 cm male or > 84 cm female
6. Family history of cardiovascular disease

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
90

Key exclusion criteria
Diabetes; previous stroke, myocardial infarction or angina, renal; bowel or liver disease; hormonal abnormalities; medication for high blood pressure, high blood fats, inflammatory conditions or depression; consuming large amounts of oily fish; taking dietary supplements; breastfeeding; excessive alcohol consumption.

Date of first enrolment
01/10/2010

Date of final enrolment
30/09/2013

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Department of Food & Nutritional Sciences
Reading
United Kingdom
RG6 6AP

Sponsor information

Organisation
Nutricia Research Foundation (Netherlands)

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Sponsor type
Charity

ROR
https://ror.org/00vt3ry76

Funder(s)

Funder type
Charity

Funder Name
Nutricia Research Foundation (2012-E3) (Netherlands)

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
Netherlands

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

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/11/2014		Yes	No