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ANGIO-EX study: to determine whether the blood circulating protein angiopoietin like-2 (angptl2) is associated with a poor vessel health in young and old healthy volunteers, patients with a coronary artery heart disease and in obese subjects

Submission date
18/02/2013

Recruitment status
No longer recruiting

Registration date
27/02/2013

Overall study status
Completed

Last Edited
20/12/2016

Condition category
Circulatory System

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

Plain English summary of protocol

Background and study aims
Aging is associated with an increased risk of developing atherosclerotic plaques - fat deposits inside the arteries. When these plaques completely block an artery of the heart (coronary artery), it causes a heart attack. These patients have coronary heart disease (CHD). Risk factors for CHD such as obesity and an unhealthy lifestyle accelerate this process of plaque formation and thus lead to atherosclerosis and CHD. Angiopoietin like-2 (angptl2) is a protein that is released into the blood by the cells lining the arteries (vascular endothelium). The levels of angptl2 in the blood are much higher in patients with CHD than in healthy and physically active people, and it has been shown that angptl2 levels are increased in overweight people. Therefore, the aim of this study is to investigate the changes in blood levels of angptl2 in patients with CHD and obese people after a beneficial lifestyle intervention, and to see if this is associated with a change in the regulation of the production of angptl2. The study findings should help identifying people who have a greater risk of developing a plaque.

Who can participate?
Healthy volunteers aged 18 to 39 and aged 50 to 70, and patients with CHD and obese people aged 50 to 70.

What does the study involve?
There are two distinct phases in the study. Phase 1 runs over a period of 3 weeks. During the first week, healthy volunteers and obese people get a complete medical history and physical examination, provide a fasting blood sample and undergo an exercise test. In the two following weeks, each participant is randomly allocated to perform one of two exercise tests. These tests are performed at one week intervals. Blood samples are collected before, and 20 minutes, 24

and 72 hours after the end of the exercise test. Phase 2 runs over 3 to 9 months and involves two groups of patients with CHD or obesity. Participants get a complete medical history and physical examination as above, provide a fasting blood sample and undergo an exercise test. Participants then receive nutritional counselling and exercise two to three times a week. CHD patients follow a 3-month program; obese patients follow a 9-month weight loss program. At the end of each program, participants undergo the same evaluation as at the start of the study including medical history and physical examination, blood samples and an exercise test. The blood concentration of angptl2 is compared between young and old healthy volunteers; between old healthy volunteers and age-matched obese people; and between old healthy volunteers and age-matched CHD patients.

What are the possible benefits and risks of participating?
The CHD and obese patients may benefit from participating in the diet and exercise program. No side effects are expected from this study.

Where is the study run from?
Montreal Heart Institute (Canada)

When is the study starting and how long is it expected to run for?
January 2012 to December 2015

Who is funding the study?
The Foundation of the Montreal Heart Institute (Canada)

Who is the main contact?
Prof. Eric Thorin
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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
ANGIO-EX 11-1328

Study information

Scientific Title
A randomized trial to determine whether circulating levels of angptl2 correlates with the improvement in cardiopulmonary fitness associated with a exercise training-based secondary prevention in coronary artery disease patients and obese subjects compared to age-matched healthy, physically active volunteers

Acronym
ANGIO-EX

Study objectives
The clinical benefits of exercise is associated with a reduction in circulating levels of angptl2 and a modification of the leukocyte epigenome signature towards that of age-matched healthy physically active subjects

Ethics approval required
Old ethics approval format

Ethics approval(s)
Montreal Heart Institute, Comité dÉthique de la Recherche et du Développement des Nouvelles Technologies, 24/11/2011, ref: 11-1328

Study design
Four-year open randomised parallel-group single-site trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Diagnostic

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
Aging and age-related cardiovascular diseases

Interventions
Phase 1 will consist of measuring angptl2 in the blood extracted from two groups of healthy and physically trained volunteers (men and women) and a group of obese subject (men and women). At enrolment, participants provide written informed consent form and undergo a complete medical history and physical examination including measurement of anthropometric variables and body composition with bioelectrical impedance analysis (Tanita BC 418, Japan). A fasting blood profile (total cholesterol, HDL, LDL, triglycerides, free fatty acids, glycaemia, insulin, HbA1c, CRP) will be measured in the clinical biochemistry laboratory of the MHI, while angptl2 is measured by ELISA in the laboratory of Professor Thorin. Blood will be drawn between 8 and 9 a. m.

On a separate, non-fasting day, obese and healthy study participants will perform a maximal cardiopulmonary exercise test on a bicycle ergometer using an incremental protocol with gas exchange analysis. This test represents the gold standard assessment of maximal aerobic exercise capacity (VO2max).

One week later, on a separate non-fasting day, volunteers will perform one of the two-planned isocaloric exercises test, a maximal intensity continuous exercise (MICE) or the high intensity interval exercise (HIIE) test. These tests will be performed at one-week interval. Blood will be collected before, and 20 min, 24 and 72 hours after the end of the exercise test in non-fasting condition (2 h after breakfast). MICE is a continuous cycling at 60% of VO2max.

Electrocardiogram is continuously recorded and monitored for cardiac arrhythmias, and systolic arterial pressure is determined at 2 min intervals for abnormal blood pressure response during the 28-min test. The HIIE is 35-min long and consists of a standardized 5-min warm-up bout at 50% of mean arterial pressure followed by a set of three 10-second bouts at 100% of VO2max interspersed by 1 min of active recovery at 50% of mean arterial pressure. A 5-min passive recovery phase separated the warm-up from the HIIE session.

In phase-2 of this clinical study, we will follow two groups of 20 patients (men and women) either with documented CHD or obesity. All study participants in phase-2 will be newly referred Montreal Heart Institute prevention centre members and naive to our prevention programs. Again, at enrolment, participants will provide written informed consent followed by a complete medical history and physical examination as noted above. Fasting blood profile will be measured as above. The VO2max will be acquired on a separate, non-fasting day.

Subjects will then be incorporated into the prevention program consisting of individualized nutritional counselling, optimized HIIE and resistance training two to three times a week. CHD patients will follow a 3-month protocol; obese patients will follow a 9-month weight loss protocol. At the end of each program, subjects will undergo the same evaluation as at baseline including medical history and physical examination, fasting blood profile and maximum cardiopulmonary evaluation.

All phase 2 patients enrolled will be on optimal medical therapy for a minimum of 4 weeks prior to inclusion.

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
Measure of circulating levels of angptl2

Secondary outcome measures
To demonstrate modifications in biomarkers including leukocyte epigenetic changes after a secondary prevention program

Overall study start date
15/01/2012

Completion date
20/12/2015

Eligibility

Key inclusion criteria
In phase 1, two groups (n=20 each) of healthy and physically trained volunteer members (men and women) of aged 18 to 39 years and 50 to 70 years.
Obese subjects (n=20) aged 50 to 70 years, men and women.
Healthy subjects are defined as men and women without cardiac, pulmonary or muscular diseases.
Obese patients are recruited at a BMI >30 kg/m2, without cardiac, pulmonary and muscular disease.

In phase 2 of the study, newly referred patients with CHD (n=20) aged 50 to 70 years, and obese subjects (n=20) aged 50 to 70 years, men and women.

Inclusion criteria for CHD patients are:
1. Documented prior acute coronary syndrome
2. Documented coronary revascularization or documented myocardial ischemia or necrosis on myocardial scintigraphy.

Obese patients are recruited at a BMI >30 kg/m2, without cardiac, pulmonary and muscular disease.

Participant type(s)
Mixed

Age group
Mixed

Sex
Both

Target number of participants
80

Key exclusion criteria
Active smokers (≥1 cigarette per day) are excluded.

Exclusion criteria for healthy subjects:
1. Dyslipidemia (total cholesterol > 5.20 mM
2. HDL < 1.04 mM
3. LDL > 2.60 mM
4. Triglycerides > 1.7 mM or use of lipid-lowering therapy)
5. Hypertension (SBP >140 or DBP >90 mmHg or use of antihypertensive medications)
6. Treated or untreated diabetes mellitus
7. Impaired fasting glucose (>5.6 mM)
8. Overweight or obesity (BMI>25 kg/m2)
9. Abdominal obesity (waist circumference >90 cm in men, 80 cm in women)
10. Documented CHD (prior acute coronary syndrome, prior coronary revascularization, presence of myocardial ischemia or necrosis on myocardial scintigraphy), and for any other contraindication to exercise testing/training.

Exclusion criteria for CHD patients are:
1. Recent acute coronary event (within one month of inclusion)
2. History of exercise-induced or severe arrhythmias, unstable angina, pacemaker or defibrillator, presence of a pulmonary or skeletal muscle disease limiting maximal exercise testing/training
3. Body mass index (BMI) >28 kg/m2.

Exclusion criteria for obese subjects is the presence of a pulmonary or skeletal muscle disease limiting maximal exercise testing/training.

Date of first enrolment
15/01/2012

Date of final enrolment
20/12/2015

Locations

Countries of recruitment
Canada

Study participating centre
Montreal Heart Institute
Montreal
Canada
H1T 1C8

Sponsor information

Organisation
Montreal Heart Institute (Canada)

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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/03vs03g62

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Foundation of the Montreal Heart Institute (Canada)

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	01/10/2015		Yes	No
Results article	results	21/04/2016		Yes	No
Results article	results	13/10/2016		Yes	No