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Investigating the role of salt inducible kinases in atherosclerosis

Submission date 10/06/2016	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol
Registration date 28/06/2016	**Overall study status** Completed	[_] Statistical analysis plan [X] Results
Last Edited 09/11/2020	**Condition category** Circulatory System	[_] Individual participant data

Plain English summary of protocol

Background and study aims
Cardiovascular disease (CVD) is a medical term used to describe a disease of the heart or blood vessels. This includes heart attacks (myocardial infarction, or MI) and stroke.In the early stages, however, it causes changes in the function of the blood vessels, particularly the arteries (vessels that transport blood being pumped from the heart to other areas of the body) . Some of these changes in function is due to inflammation (swelling) and, in theory, reducing this inflammation could reduce the risk of an MI or stroke. Animal studies have shown that certain substances (called SIKs) promote inflammation in the arteries. This study is investigating whether this is the same for humans by doing tests in both healthy volunteers and people that have cardiovascular disease (for example, have had a heart attack or have narrowing of the leg arteries). SIK levels will also be compared with the results from different measures of artery function. If SIK levels are found to be high in cases of poor artery function then this might be a potential new treatment target to prevent cardiovascular disease.

Who can participate?
Three different groups of people are participating in this study. People with peripheral vascular disease and about to have an amputation (group 1), people who have had a heart attack (group 2) and healthy volunteers (group 3). All participants are adults aged between 18-70.

What does the study involve?
Participants in group 1 are asked to give blood for analysis and their amputated tissue is also analysed. Participants in group 2 are also asked to give blood samples and undergo tests to see how stiff their arteries are (arterial stiffness measurements) and how well blood vessels relax after being dilated (widened with increased blood flow). Participants in group 3 are also asked to give blood samples, flow-mediated dilatation (blood vessels widened with increased blood flow) and pulse-wave analysis (arterial stiffness analysis). All participants are followed up for signs of inflammation, their blood vessel function and SIK levels.

What are the possible benefits and risks of participating?
The researchers do not expect there to be any direct risks or benefits to the patient in taking

part in the study. Routine clinical care will not be affected regardless of participation in the study. For volunteers, there is the small discomfort of having blood samples taken, however steps will be made to make this as easy as possible.

Where is the study run from?
Ninewells Hospital, Dundee (UK)

When is the study starting and how long is it expected to run for?
February 2016 to November 2017

Who is funding the study?
Tenovus (UK)

Who is the main contact?
Dr Faisel Khan
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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
2015CV11

Study information

Scientific Title
Investigating the role of salt inducible kinases in atherosclerosis: a observational cross-sectional study

Study objectives
The key hypothesis is that the SIK-CRTC3 signalling axis will play an important role in development of atherosclerosis. The researchers hypothesise that mechanisms to activate the cAMP response element binding protein (CREB) should protect against cardiovascular disease (CVD), and that inhibition of salt inducible kinase 2 (SIK2) will have beneficial effects on the cardiovascular (CV) system and thus offer a new target for therapy.

Ethics approval required
Old ethics approval format

Ethics approval(s)
East of Scotland Research Ethics Committee 2.

Study design
Observational cross-sectional study

Primary study design
Observational

Secondary study design
Cross sectional study

Study setting(s)
Hospital

Study type(s)
Diagnostic

Participant information sheet

Health condition(s) or problem(s) studied
STEMI, peripheral arterial disease

Interventions
Three groups will be evaluated in this study:

Group 1. 10 patients with peripheral vascular disease (PVD) undergoing elective amputation. These patients will undergo blood sampling and amputated tissue analysis.

Group 2. 40 patients with acute myocardial infarction with ST elevation (STEMI) and requiring primary percutaneous coronary intervention (PPCI). These patients will undergo blood samples, flow mediated dilatation (FMD) and arterial stiffness measurements.

Group 3. 40 healthy subjects, matched to the STEMI group for age and gender. They will undergo blood samples, flow-mediated dilatation and pulse wave analysis.

Intervention Type

Other

Primary outcome measure
Serum levels of inflammatory cytokines taken at the time of operation in PVD group, 48-72 hours after PCI in STEMI group and at the time of assessment in healthy volunteers.

Secondary outcome measures
1. Tissue SIK levels in PVD patients at the time of surgery
2. Arterial stiffness and flow mediated dilatation in STEMI patients at 48-72 hours and in healthy volunteers at the time of assessment

Overall study start date
01/02/2016

Completion date
03/11/2017

Eligibility

Key inclusion criteria
PVD:
1. Age between 18-70 years
2. Admitted for elective amputation for PVD
3. Able to give written informed consent

STEMI:
4. Age between 18-70 years
5. Admitted to CCU for STEMI and undergone PPCI
6. Able to give written informed consent

Healthy volunteers:
7. Age between 18-70 years
8. No current or previous significant medical illness
9. Able to give written informed consent

Participant type(s)
Mixed

Age group
Adult

Lower age limit
18 Years

Upper age limit
70 Years

Sex
Both

Target number of participants
90

Total final enrolment
70

Key exclusion criteria
Healthy volunteers:
1. Positive medical history of:
1.1. Vascular diseases such as peripheral arterial disease, stroke, IHD... etc
1.2. Haematological conditions such as hypercoagulability, deep venous thrombosis... etc
1.3. Hypertension
2. Alcohol excess
3. Unable to give written informed consent

STEMI/PVD:
Unable to give written informed consent

Date of first enrolment
01/08/2016

Date of final enrolment
16/11/2017

Locations

Countries of recruitment
Scotland

United Kingdom

Study participating centre
Ninewells Hospital
Dundee
United Kingdom
DD1 9SY

Sponsor information

Organisation
NHS Tayside/University of Dundee

Sponsor details
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Sponsor type
University/education

ROR
https://ror.org/000ywep40

Funder(s)

Funder type
Charity

Funder Name
Tenovus

Alternative Name(s)
Tenovus Cancer Care

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Publication and dissemination plan
We intend to publish the results at the end of the study in peer-reviewed journals although details are not confirmed as yet.

Intention to publish date
03/11/2018

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results		03/05/2019	17/05/2019	No	No