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Effects of intravascular contrast media on platelet function in patients undergoing coronary angiography

Submission date	Recruitment status	[_] Prospectively registered
19/06/2013	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
05/08/2013	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
20/01/2016	Circulatory System	

Plain English summary of protocol

Background and study aims
Thousands of patients each year require a test called a coronary angiogram. This test uses X-rays and dye (contrast) to provide cardiologists with detailed pictures of the heart arteries. There are several types of X-ray dyes used but all have the ability to cause harm and there is a small risk associated with an angiogram procedure. The two most commonly used dyes are Omnipaque and Vispaque. These is no agreement as to which is best and many centres (such as Raigmore) use both. Heart attacks and strokes are more likely if patients have sticky blood. The purpose of this study is to find out the effects of these two dyes on the stickiness of blood. This may help doctors in the future decide which is the best dye in which patients.

Who can participate?
Patients who are undergoing a coronary angiogram can participate.

What does the study involve?
This study involves giving blood samples. This will require two blood samples taken at the start and the end of the procedure from an artery and a vein (a total of four blood samples). As you will have a small tube in both the artery and the vein as a normal part of your procedure, this will not involve any additional needles. After you have given these blood samples, the blood will be taken to the laboratory. You will not undergo any further procedures as part of this study and participation in this study will in no way change the treatment you receive.

What are the possible benefits and risks of participating?
There are no benefits to you taking part in this study. However, the information we get might help improve the future studies and treatment of heart patients. This study involves only the taking of an extra blood sample and no additional needles or procedures and therefore we would not expect any risk to the study participants.

Where is the study run from?
The study is being run by the NHS (UK) and University of the Highlands and Islands (UK).

When is the study starting and how long is it expected to run for?
March 2011 to March 2013.

Who is funding the study?
Funding for this study is from NHS Highland endowments, UK.

Who is the main contact?
Prof. Stephen Leslie
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Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
1

Study information

Scientific Title
A pilot study into the effects of intravascular contrast media on platelet function in patients undergoing coronary angiography

Study objectives
That iodixanol, but not iohexol, influences the release of tissue plasminogen activator (tPA) and plasminogen activator inhibitor-1 (PAI-1) to favour increased fibrinolysis in patients undergoing elective coronary angiography.

Ethics approval required
Old ethics approval format

Ethics approval(s)
North of Scotland Research Ethics Committee

Study design

Randomised controlled trial

Primary study design
Interventional

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Coronary artery disease

Interventions
Randomised controlled trial of two contrast agents, iodixanol vs iohexol.
The specific aims of this study are two-fold:
1. to obtain pilot flow cytometry data to establish whether platelets from patients undergoing angiography or interventional cardiology procedures are activated and to confirm whether any difference in activation is evident with ionic vs non-ionic CM.
2. to test the hypothesis that inactivation of NO by oxidative stress is a factor in the pro-thrombotic state associated with CM through induction of acute endothelial dysfunction.

Methods
1. In vitro assessment of the interaction of CM with nitric oxide: role of oxidative stress
The possibility of chemical inhibition of NO, which is ordinarily generated by the endothelium and platelets, will be assessed by testing the quenching effect of CM on NO from a donor drug (DETA/NO). The oxygen-centred radical generating capacity of ionic and non-ionic CM will be assessed using electron paramagnetic resonance (EPR) spectrometry. Briefly, this involves treating samples with a spin trap that is specific for oxygen-centred radicals and measuring the formation of the stable spin-adduct that is generated in the presence of oxygen-centred radicals with time. In the event that one or more of the CM are found to generate significant radicals, inclusion of simple antioxidants (e.g. vitamin C) in the medium will be assessed in vitro.
2. Ex vivo analysis of platelet function and thrombotic risk
To our knowledge, flow cytometry has not yet been applied to the question of thrombotic risk associated with CM. This technique allows assessment of platelet activation ex vivo (e.g. through measurement of surface P-selectin exposure) in the immediate aftermath of CM infusion and is as close as we can yet get to an in vivo measure of platelet activation. The technique also facilitates simultaneous measurement of platelet-leucocyte adhesion, recently identified as a marker for risk of MI.8 We will assess both of these measures in blood from patients undergoing routine angiography. The frequency of procedures at Raigmore Hospital will enable us to have rigorous selection criteria for this study: inclusion criteria will include gender (male) aged 50-70 years old and exclusion criteria will include anti-platelet agents other than aspirin. The study will be of double-blind, randomised design for non-ionic and ionic CM (n=6 for each). Coronary arterial blood will be drawn immediately before, during and 5 min after an infusion of CM and taken for immediate assessment of platelet function and cellular oxidative stress using flow cytometry (P-selectin analysis, platelet-monocyte binding, oxidative stress markers). Plasma samples will also be assessed for tissue plasminogen activator (t-PA) and plasminogen activator inhibitor (PAI-1) to help identify whether there is any effect of ICM on fibrinolytic capacity.

Intervention Type
Other

Phase

Not Applicable

Primary outcome(s)
1. Assessment of platelet function and cellular oxidative stress using flow cytometry (platelet-monocyte binding, oxidative stress markers)
2. Plasma samples will be assessed for tissue plasminogen activator (t-PA) and plasminogen activator inhibitor (PAI-1) to help identify whether there is any effect on fibrinolytic capacity

Key secondary outcome(s)
1. To assess the ability of contrast media to generate oxygen-centred free radicals

Completion date
10/07/2013

Eligibility

Key inclusion criteria
1. Male
2. Aged 50-70
3. Clinical reason for coronary angiography
4. Coronary artery disease defined by coronary angiography
5. No history of diabetes, fasting blood glucose < 6 mmol/l, HbA1c < 6.5%
6. Taking aspirin but not clopidogrel
7. Non-smoker

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
Male

Key exclusion criteria
1. Participation in pharmacological study within last 3 months
2. Taking clopidogrel

Date of first enrolment
10/01/2013

Date of final enrolment
10/07/2013

Locations

Countries of recruitment

United Kingdom

Scotland

Study participating centre
Raigmore Hospital
Inverness
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Sponsor information

Organisation
Centre for Health Science (UK)

ROR
https://ror.org/02s08xt61

Funder(s)

Funder type
Charity

Funder Name
Coronary Thrombosis Trust (CTT 42/10) (UK)

Results and Publications

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	19/01/2016		Yes	No