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An Investigation into the role of Matrix Metalloproteinases (MMPs) in Lower Limb Vascular Restenosis

Submission date 29/09/2006	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 29/09/2006	**Overall study status** Completed	
Last Edited 20/04/2015	**Condition category** Surgery	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N0544170118

Study information

Scientific Title
An Investigation into the role of Matrix Metalloproteinases (MMPs) in Lower Limb Vascular Restenosis

Study objectives
Does blocking enzymes in the wall of the artery - matrix metalloproteinases (MMPs) - prevent the artery from narrowing after angioplasty (balloon treatment) or surgery (bypass graft)?

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Surgery: Cardiovascular

Interventions
Patients under the care of the Cambridge Vascular Unit undergoing femoro-popliteal angioplasty or femoro-popliteal/tibial bypass will be eligible for the study. The indication for intervention will be severe limb ischaemia (rest pain, ulceration, gangrene) or short distance claudication failing to respond to medical and exercise therapy.

Pre-procedural Noninvasive Assessments:
Following informed consent the degree of ischaemia will be measured using ankle brachial pressure index (ABPI) measurements and transcutaneous oxygen measurements (TcPO2). Arterial stiffness and Endothelial Function will also be determined by applying a pressure probe to the carotid and radial arteries in turn with concomitant ECG gating.

Percutaneous Angioplasty:
These procedures are routinely carried out as either day cases or with overnight stay. During the

procedure two 40 ml blood samples will be taken for plasma MMP analysis, plus CRP level, cholesterol, U&Es, elastin breakdown products, elastase activity and genetic analyses. One 40 ml sample will be systemic venous blood taken from the venous access cannula inserted for the procedure. A second 40 ml sample will be taken from the femoral vein in the leg undergoing the procedure. This is blood returning from the treated leg, and is more likely to reflect the local MMP activity potentially related to restenosis. On the same day as the PTA procedure the patients will be commenced on the SDD/placebo medication in a double blind randomised design. One tablet (25 mgs SDD) twice per day. This will be continued for 24 weeks post procedure.

Post Procedure Follow Up:
Colour duplex ultrasound assessment of the angioplasty site will be used to document blood velocities across the lesion and percentage of restenosis. These measurement will take place in the Vascular Laboratory at the following intervals: 1, 6, 12, 24, 36, 52 weeks. At 24 and 52 weeks repeat blood samples will be taken.

Femoro-distal bypass:
The same pre-procedural assessments will be performed as for PTA. These assessments will be co-ordinated with the patients pre-clerking clinic visit, usually 1 week prior to surgery. During surgery 2 tissue samples will be taken. One will be an arterial wall biopsy, to be analysed for arterial tissue MMP status. This will be taken from the proximal anastomosis site as a small ellipse avoiding any stenosis/narrowing of the anastomosis. A second sample will be taken from the venous tissue used for the bypass for MMP analysis.

As soon as patients are taking oral medication post operatively (usually 12-24 hours) the SDD /placebo medication will be commenced. As for PTA this will be for 24 weeks.

Prior to discharge the graft will be scanned to establish baseline graft velocities and any early abnormalities. As with the PTA protocol, further graft monitoring for stenosis, ABPI, and TcPO2 measurements will occur at 6, 12 , 24, 36 and 52 weeks. Surveillance of vein grafts at these intervals is normal clinical practice. Blood samples will be taken at 24 and 52 weeks.

Intervention Type
Mixed

Primary outcome measure
1. MMP activities SDD versus placebo
2. CRP levels
3. Endothelial function and re-stenosis
4. Arterial wall stiffness and re-stenosis.

Secondary outcome measures
Not provided at time of registration

Overall study start date
18/07/2005

Completion date
18/07/2008

Eligibility

Key inclusion criteria
Serum samples collected at the time of vascular intervention (radiologist or surgeon). Follow up samples by vascular research fellow.

Arterial wall and vein biopsies taken at the time of surgery by operating surgeon.

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
35 in each trial arm, ie 270

Key exclusion criteria
1. Patient unable to give informed consent
2. Age < 18 years
3. Pregnancy, planned pregnancy
4. Life expectancy less than 12 months
5. Inability to monitor the angioplasty site or graft with ultrasound for stenosis
6. Unable to take SDD (ie allergic reaction) or currently taking tetracyclines
7. Unable to take adjuvant treatment with antiplatelet/anticoagulant agent and statin

Date of first enrolment
18/07/2005

Date of final enrolment
18/07/2008

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Addenbrooke's NHS Trust
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Sponsor information

Organisation
Record Provided by the NHSTCT Register - 2006 Update - Department of Health

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Funder(s)

Funder type
Government

Funder Name
Cambridge Consortium - Addenbrooke's (UK), NHS R&D Support Funding

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