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Progenitor cell response following Myocardial Infarction Study (ProMIS)

Submission date
16/12/2011

Recruitment status
No longer recruiting

Registration date
05/03/2012

Overall study status
Completed

Last Edited
12/12/2017

Condition category
Circulatory System

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

Plain English summary of protocol

Background and study aims
Stem cells produced in the bone marrow are able to heal parts of the body that have lost their blood supply. After a heart attack, these stem cells are released into the blood stream in large amounts. Although there is previous research evaluating the effects of injecting these stem cells as a treatment to promote the growth of new blood vessels, little is known about the body's natural release of these cells and their ability to travel to the damaged parts of the body following a heart attack. This study aims to assess how natural repair mechanisms respond after a heart attack and whether diabetes interferes with these natural responses, potentially worsening the patient's clinical outcome. We know that after a heart attack the body produces more stem cells that are designed to help new blood vessels to grow and thereby repair the damaged heart. We want to find out whether the increase in these stem cells is influenced by the amount of damage to the heart and, if so, whether this relationship between the response and amount of damage is lost in patients with diabetes. The incidence of diabetes is rising and represents one of the greatest medical challenges worldwide. Heart disease is a leading cause of death in patients with diabetes and these patients have a worse outcome after a heart attack. Understanding better why patients with diabetes do less well is currently a topic of intensive research, with the hope of finding new effective treatments. The aim of this study is to assess the number of stem cells and their ability to reach damaged parts of the body after a heart attack.

Who can participate?
Patients aged 40 to 75 who have had either a sudden (STEMI) or 'grumbling' heart attack (NSTEMI) and both diabetic and non-diabetic patients.

What does the study involve?
Participants will give blood samples within the first four days after their heart attack and will undergo MRI scans four days and 3 months after their heart attack. 12 months later the participants will be contacted by telephone to ask about any adverse events, hospital admissions or changes to medication.

What are the possible benefits and risks of participating?
There is no direct benefit for participants, although the information collected from this study

will help to improve our understanding of the body's natural responses during and after a heart attack, and their impact on heart function. This work will also increase our knowledge of how these natural responses vary in people with and without diabetes. Counting these stem cells in a blood sample and their ability to reach damaged heart muscle may help us to identify which patients need more aggressive treatment after a heart attack.

Where is the study run from?
Bristol Royal Infirmary (UK).

When is study starting and how long is it expected to run for?
February 2010 to February 2014.

Who is funding the study?
NIHR Bristol Biomedical Research Unit (UK).

Who is the main contact?
Dr Andreas Baumbach

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
CS/2009/3297

Study information

Scientific Title

Progenitor cell response following coronary intervention for unstable angina and ST elevation myocardial infarction in diabetic and nondiabetic cohorts

Acronym
ProMIS

Study objectives
The aim of the study is to characterise the number and migratory capacity of circulating progenitor cells (CPCs) in patients with or without Diabetes Mellitus (DM) who have had either a ST segment elevation Myocardial Infarction (STEMI) or a non-ST segment elevation Myocardial Infarction (NSTEMI).

Objectives:
1. To measure the number and migratory capacity of CPCs on day 4 after the onset of symptoms and then to test the hypotheses that:
1.1. The number of CPCs differs after STEMI compared to NSTEMI
1.2. The migratory capacity of CPCs differs in patients with or without DM
1.3. The number and migratory capacity of CPCs are associated with covariates characterising the severity of the initial STEMI or NSTEMI (e.g. troponin I, hsCRP) or the quality of glucose control (HbA1c)
2. To test the hypothesis that the number and migratory capacity of CPCs after a STEMI or NSTEMI influence the size of the myocardial scar and myocardial contractility three months after the initial cardiac event.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Wiltshire Research Ethics Committee, 13/10/2009, ref: 09/H0104/58

Study design
Single-centre cohort study

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Treatment

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

Myocardial infarction (STEMI/NSTEMI) and diabetes mellitus (DM)

Interventions
In order to characterise the response of CPCs, blood samples are taken on day 0 (up to 24hrs after patient's presentation of symptoms) and day 4. MRI scans are performed at baseline (day 4) and three months after patients' presentation of symptoms. Involvement in the study concludes 12 months after the index event, when the participant will be contacted by telephone to ascertain any adverse events, hospital admissions or changes to medication occurring since the index admission.

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
1. For objective 1 - the number of CPCs measured in a peripheral blood sample or the migratory ability of CPCs expressing CXCR4 to the chemo-attractant stromal cell-derived factor-1 (SDF-1) (assessed in a test tube by a migration assay).
2. For objective 2 - the size of myocardial scar (volume or mass of affected myocardium) three months after symptom onset

Secondary outcome measures
1. For objective 1:
1.1. Number of CPCs expressing cell surface markers: CD34, CD133, c-kit, KDR, trkA, beta-2, CD14 and CD16, either viable, apoptotic or necrotic
1.2. Migratory ability of Peripheral Blood Mononuclear Cell Culture (PBMNC) expressing CPC surface markers: CD34, CD133, c-kit, KDR, trkA, beta-2, CD164, CD14, CD16. For migration assays, we will use SDF-1 and Nerve growth factor (NGF) as chemo-attractants and PBS as vehicle control
1.3. Viability of CPCs on Day 4 for CPCs expressing CXCR4 and sub-populations of CPCs expressing cell surface markers: CD34, CD133, c-kit, KDR, trkA, beta-2, CD164, CD14 and CD16)
2. For objective 2:
2.1. Myocardial contractility / wall thickening three months after the index STEMI or NSTEMI
2.2. Left ventricular (LV) wall motion
3. The following clinical outcomes will be evaluated at day 4, 3 and 12 months after the index admission:
3.1. Incidence of peri-procedural myocardial damage, assessed by analysis of creatinine kinase
3.2. Major adverse cardiac-related events (death, new MI, further revascularisation, recurrent angina as defined by repeat coronary angiogram for chest pain symptoms)
3.3. Hospitalisation rates

Overall study start date
19/02/2010

Completion date
28/02/2014

Eligibility

Key inclusion criteria
1. Presentation to a Bristol Heart Institute cardiologist within 24 hours after the onset of symptoms
2. Admission with STEMI or NSTEMI (troponin positive acute coronary syndromes)
3. Aged 40 to 75 at admission
4. Reside within 40 miles of the Bristol Royal Infirmary

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
Total: 80 participants (STEMI - without DM: 32 participants; NSTEMI - without DM: 16 participants; STEMI - DM: 16 participants; NSTEMI - DM: 16 participants)

Key exclusion criteria
1. Anaemia, i.e. haemoglobin <10mg/dl
2. Cardiogenic shock on presentation
3. Renal impairment [Glomerular filtration rate (GfR) <50ml]
4. Haemodynamic instability
5. Contraindications to having the MRI scan (e.g. metallic implant, pacemakers, screws, claustrophobia, etc)
6. Previous coronary event within the last 12 weeks
7. Participation in another clinical study
8. Patients who are unable or unwilling to return for follow-up in accordance with the study schedule on day 4, or after three months
9. Heightened anxiety during recruitment

Date of first enrolment
19/02/2010

Date of final enrolment
01/11/2012

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University Hospitals Bristol NHS Foundation Trust
Bristol

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Sponsor information

Organisation
University Hospitals Bristol NHS Foundation Trust (UK)

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Sponsor type
University/education

Website
http://www.uhbristol.nhs.uk/

ROR
https://ror.org/04nm1cv11

Funder(s)

Funder type
Government

Funder Name
NIHR Bristol Biomedical Research Unit (UK) ref: 2008/SS/BRU

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date
01/02/2014

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	01/07/2012		Yes	No