ISRCTN27767229 https://doi.org/10.1186/ISRCTN27767229

Ciclosporin to reduce reperfusion injury in primary percutaneous coronary intervention

Submission date
23/06/2015

Recruitment status
No longer recruiting

Registration date
01/07/2015

Overall study status
Completed

Last Edited
28/05/2020

Condition category
Circulatory System

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

Plain English summary of protocol

Background and study aims
Coronary heart disease is a condition in which the supply of blood and oxygen to the heart is reduced due to the narrowing of the arteries (blood vessels) supplying the heart. A heart attack is caused when one of these arteries becomes blocked. The modern treatment for a heart attack is called primary percutaneous coronary intervention (PPCI). PPCI involves opening the blocked artery with a balloon and placing a stent (a small metal tube) in the artery to hold it open. Research has shown that after opening the blocked artery, inflammation develops within the heart. This inflammation is generated by the immune system. Initial studies have suggested that certain immune system cells (T-cells) may be involved in causing much of the damage that occurs in the heart following a heart attack. The drug ciclosporin temporarily inhibits the immune system and it has been shown in a small number of patients that it reduces the size of the heart attack. The aim of this study is to investigate in a larger number of patients whether the size of the heart attack is reduced in patients treated with the drug ciclosporin immediately before PPCI compared to patients treated with a dummy drug.

Who can participate?
To participate in the study you must be having a large heart attack (STEMI) and be undergoing a PPCI to unblock your artery. You must also be aged over 18.

What does the study involve?
You will be randomly allocated to receive either a single dose of the drug ciclosporin or a dummy drug before your blocked artery is opened. This will allow us to compare the results to see whether treatment with ciclosporin reduces the size of the heart attack compared with treatment with a dummy drug. You will need to come back to the hospital after 2 weeks for a blood test. After 3 months you will need to come back to the hospital for a heart magnetic resonance imaging (MRI) scan and a blood test. After 12 months you will have a telephone follow-up call.

What are the possible benefits and risks of participating?
There may be no immediate benefit from taking part in the study but the information we get will help improve the treatment of people having a heart attack in the future. As far as we know there are no disadvantages of taking part in the study. There is a very small risk of side effects

from ciclosporin, such as high blood pressure and slight worsening of kidney function. We do not expect any side effects as the ciclosporin is only given once in the study. On rare occasions allergic reactions have been observed. If any ciclosporin-related side effects were to occur, they would be expected soon after the drug was given.

Where is the study run from?
This study is run from the Freeman Hospital, Newcastle upon Tyne, UK.

When is the study starting and how long is it expected to run for?
The study started in March 2015 and it is aiming to recruit 68 patients over a period of 18 months. Each patient will be in the trial for 12 months.

Who is funding the study?
The study is being funded by the National Institute for Health Research Newcastle Biomedical Research Centre

Who is the main contact?
Alison J Steel, PhD
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Contact information

Type(s)
Public

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Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2014-002628-29

ClinicalTrials.gov (NCT)
NCT02390674

Protocol serial number
R&D 6327

Study information

Scientific Title
Evaluating the effectiveness of intravenous ciclosporin on reducing reperfusion injury in patients undergoing primary percutaneous coronary intervention: a double-blind randomised controlled trial

Acronym
CAPRI

Study objectives
Whether an intravenous infusion of ciclosporin prior to reperfusion by coronary stenting will affect infarct size in patients with acute myocardial infarction.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee North East - Newcastle & North Tyneside 2, 24/07/2014, ref: 14/NE/1070

Study design
Interventional single-centre double-blind randomised controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Myocardial reperfusion injury

Interventions
Active comparator: single intravenous administration of ciclosporin (2.5 mg per kilogram body weight) immediately prior to reperfusion during primary percutaneous coronary intervention. Ciclosporin is dissolved in saline (maximum concentration 2.5 mg per millilitre)
Placebo comparator: single intravenous administration of saline immediately prior to reperfusion during primary percutaneous coronary intervention

Intervention Type
Drug

Phase
Phase II/III

Drug/device/biological/vaccine name(s)
Ciclosporin

Primary outcome(s)
Infarct size at 12 weeks post-PPCI as measured by cardiac magnetic resonance imaging (MRI).

Key secondary outcome(s))
1. Microvascular obstruction after 2-7 days as measured by a single cardiac MRI scan
2. Salvage index after 2-7 days as measured by a single cardiac MRI scan
3. Change in T lymphocyte counts relative to baseline at 5, 15, 30, 60 and 90 minutes post-reperfusion
4. Number of clinical events (death, stroke or myocardial infarction) after 12 months

Completion date
15/09/2017

Eligibility

Key inclusion criteria
1. Patients presenting with acute myocardial infarction (STEMI) and undergoing primary percutaneous coronary intervention (primary PCI)
2. Age above 18 years
3. Presenting within 6 hours of the onset chest pain and ST segment elevation. The culprit coronary artery has to be a major coronary artery with a diameter of at least 3 mm and has to be proximally occluded (TIMI flow grade 0-1) at the time of admission coronary angiography

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
52

Key exclusion criteria

1. Patients with any disorder associated with immunological dysfunction (acute or chronic inflammatory or neoplastic co-existing disease, known positive serology for HIV, or hepatitis)
2. Clinically unstable patients (haemodynamically unstable, cardiogenic shock, unconscious patients)
3. Patients with evidence of coronary collaterals to the infarct area
4. Patients with an open (TIMI > 1) culprit coronary artery at the time of angiography
5. Previous myocardial infarction
6. Previous thrombolytic therapy
7. Patients with known hypersensitivity to ciclosporin or to egg, peanut or soya-bean proteins
8. Patients with known renal insufficiency (either known GFR <30 ml/min/1.73m2) or current medical care for severe renal insufficiency
9. Known liver insufficiency
10. Uncontrolled hypertension (>180/110 mmHg)
11. Patients treated with any compound containing hypericum perforatum, stiripentol, Aliskiren, Bosentan or Rosuvastatin or with an active treatment that might modify blood concentration of ciclosporin
12. Female patients currently pregnant or women of childbearing age who are not using contraception (verbal diagnosis). Female patients of childbearing potential who are using contraception but are subsequently found to have a positive urine pregnancy test (pregnancy test performed as soon as reasonably practicable after IMP administration)
13. Contraindication to cardiac MRI:
13.1. Pacemaker
13.2. Implantable defibrillator
14. Patients unable to undergo cardiac MRI for any of the following reasons:
14.1. Frailty - as judged by the clinician. Frailty is defined as meeting three out of the five following criteria: low grip strength, low energy, slowed walking speed, low physical activity and /or unintentional weight loss. Due to the tight time constraints and emergency setting of this trial the clinician cannot test all these parameters and will need to exercise their judgment
14.2. Claustrophobic - patients who cannot take elevators or who are afraid of narrow or enclosed spaces
14.3. Breathlessness - patients who suffer from breathlessness at rest or low exercise level (e.g. while walking on the level)
15. Use of other investigational study drugs within 30 days prior to trial entry (defined as date of randomisation into trial). Co-enrolment with other studies is not allowed
16. Lack of capacity to give initial verbal consent
17. Life expectancy <1 year due to non-cardiac illness

Date of first enrolment
16/03/2015

Date of final enrolment
15/09/2017

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Freeman Hospital
Freeman Road
Newcastle upon Tyne
United Kingdom
NE7 7DN

Sponsor information

Organisation
The Newcastle upon Tyne Hospitals NHS Foundation Trust

ROR
https://ror.org/05p40t847

Funder(s)

Funder type
Government

Funder Name
NIHR Newcastle Biomedical Research Centre

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?
Basic results			28/05/2020	No	No
HRA research summary			28/06/2023	No	No