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Propofol cardioplegia for Myocardial Protection Trial: ProMPT

Submission date	Recruitment status	[X] Prospectively registered
18/08/2009	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
11/11/2009	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
07/09/2018	Circulatory System	

Plain English summary of protocol

Background and study aims.
Propofol is a general anaethestic drug widely used in heart surgery. Propofol has been shown to protect the muscles of the heart against injury. During heart surgery a cardioplegia solution is infused into the heart's circulation, which causes the heart to stop beating so that the surgery can be performed. There is a vast amount of evidence that propofol protects against the damaging effects of placing the heart under a state of cardioplegic arrest during surgery, but there are still conflicting reports of its benefits. In this study we plan to investigate the protective action of propofol added to blood cardioplegia in patients undergoing isolated coronary artery bypass grafting (CABG) or aortic valve replacement surgery (AVR).

Who can participate?
96 patients aged 18 to 80 undergoing CABG or AVR with cardiopulmonary bypass at the Bristol Heart Institute (BHI).

What does the study involve?
Participants will be randomly allocated to one of two groups. During surgery one group will receive cardioplegia solution with propofol supplementation and the other group will receive a cardioplegia solution with placebo (dummy drug) supplementation. We will measure the markers of heart muscle stress and injury from biopsies (small pieces of tissue) taken from the heart. We will also look at markers of whole body stress and inflammation which can tell us about damage to the heart. After 3 months all patients will complete a health status questionnaire.

What are the possible benefits and risks of participating?
If benefits are shown from this study we will improve outcomes for patients undergoing heart surgery and reduce hospital costs.

Where is the study run from?
Bristol Heart Institute (UK).

When is the study starting and how long is it expected to run for?
From February 2010 to September 2015.

Who is funding the study?
National Institute for Health Research (NIHR) (UK).

Who is the main contact?
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Contact information

Type(s)
Scientific

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Clinical Trials Information System (CTIS)
2009-015779-28

Protocol serial number
CS/2008/3029

Study information

Scientific Title
A single-centre randomised controlled trial of propofol cardioplegia on blood and myocardial biomarkers of stress and injury in patients having isolated coronary artery bypass grafting (CABG) or aortic valve replacement (AVR) using cardiopulmonary bypass (CPB)

Acronym
ProMPT

Study objectives
The ProMPT trial aims to test the hypothesis that supplementation of the cardioplegic solution with propofol will be cardioprotective for patients undergoing isolated coronary artery bypass grafting (CABG) or aortic valve replacement surgery (AVR) with cardiopulmonary bypass (CPB).

On 01/02/2011 the overall trial start date was changed from 01/09/2009 to 15/02/2010 and the overall trial end date was changed from 28/02/2012 to 31/03/2012.

On 20/12/2012 the overall trial end date was changed from 31/03/2012 to 30/09/2012. Data analysis and report writing will continue until 30/09/2013.

On 01/10/2014 the overall trial end date for this trial was changed from 30/09/2012 to 30/09 /2015. Data analysis and report writing will continue until 30/09/2015.

Ethics approval required
Old ethics approval format

Ethics approval(s)
16th November 2009 (West Midlands)

Primary study design
Interventional

Study design
Single-centre blinded placebo-controlled randomised controlled trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Cardiac disease/coronary surgery

Interventions
Eligible patients undergoing coronary artery bypass grafting (CABG) or aortic valve replacement (AVR) with cardiopulmonary bypass (CPB) and who consent to participate will be randomly allocated to either:
1. Control: cardioplegia with placebo (intralipid) supplementation. Warm blood cardioplegia will be used for CABG participants and cold blood cardioplegia for participants having AVR.
2. Intervention: cardioplegia with propofol supplementation (6 µg/ml). Warm blood cardioplegia will be used for participants having isolated CABG and cold blood cardioplegia for participants having AVR.

Method of administration will be through either antegrade or retrograde cardioplegia delivery according to local protocol. Several 'doses' may be given but this varies according to the length of surgery time. The duration of treatment is the time on cardiopulmonary bypass and a 3-month postal health status questionnaire follow-up will be completed for all patients.

Intervention Type
Drug

Phase
Phase IV

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

Primary outcome(s)

Current primary outcome measure(s) as of 01/02/2011:
The primary outcome will be myocardial injury, assessed by measuring myocardial Troponin T in serum from blood samples collected pre-operatively and at 1, 6, 12, 24 and 48 hours post chest closure.

Previous primary outcome measure(s):
Myocardial injury, assessed by measuring myocardial Troponin T in serum from blood samples collected pre-operatively and 1, 6, 12, 24 and 48 hours post cross-clamp release

Key secondary outcome(s)

Current secondary outcome measure(s) as of 01/02/2011:
1. Myocardial ischaemic stress assessed using biopsies taken from left and right ventricles immediately prior to aortic cross-clamping and 10 minutes post chest closure. Gene expression and cellular changes associated with stress and injury signalling pathways will be measured from metabolite/RNA extracts.
2. Systemic metabolic stress, assessed by measuring lactate in blood samples collected pre-operatively, 10 minutes after aortic chest closure and 1, 6, 12, 24 and 48 hours post chest closure.
3. Blood pH, measured using each sample collected for (b).
4. Renal function, assessed by measuring creatinine in serum from blood samples collected pre-operatively and 1, 6, 12, 24 and 48 hours post chest closure.
5. The concentration of plasma propofol, measured in blood samples collected immediately before aortic cross-clamping, once during cardioplegia (after blood/cardioplegia mixing) and 10 minutes post cross-clamp release. Blood will be taken from the cardioplegia/bypass circuit.
6. Length of intensive care unit (ICU)/high dependency unit (HDU) stay.
7. Clinical outcomes and serious adverse events, i.e. serious post-operative complications (e.g. myocardial infarction, permanent stroke, renal failure defined as new need for haemodialysis) and death from any cause.
8. Patient health status, monitored using specialist questionnaires administered pre-operatively and 3 months post-operatively. CABG patients will be asked to complete the Coronary Revascularisation Outcome Questionnaire (CROQ) and AVR patients will be asked to complete the Minnesota Living with Heart Failure (MLHF) Questionnaire. The EQ-5D™ health questionnaire will also be administered to all patients.

Previous secondary outcome measure(s):
1. Myocardial ischaemic stress assessed using biopsies taken from left and right ventricles immediately prior to aortic cross-clamping and 10 minutes after cross-clamp release. Gene expression and cellular changes associated with stress and injury signalling pathways will be measured from metabolite/RNA extracts.
2. Systemic oxidative stress assessed by measuring 8-Isoprostane in serum from blood samples collected pre-operatively and 1, 6, 12, 24 and 48 hours post cross-clamp release
3. Systemic metabolic stress assessed by measuring lactate in blood samples collected pre-operatively, 10 minutes after aortic cross-clamp release and 1, 6, 12, 24 and 48 hours post cross-clamp release
4. Blood pH measured using each sample collected for point 3 above
5. The inflammatory response characterised by measuring IL-6, IL-8, IL-10, C3a, C5a, and TNF1alpha in serum from blood samples collected pre-operatively and 1, 6, 12, 24 and 48 hours post cross-clamp release
6. Renal function assessed by measuring creatinine in serum from blood samples collected pre-operatively and 1, 6, 12, 24 and 48 hours post cross-clamp release
7. Renal injury assessed by measuring Neutrophil Gelatinase Associated Lipocalin (NGAL) in

serum from blood samples collected pre-operatively and at 1, 6, 12, 24 and 48 hours post cross-clamp release
8. The concentration of circulating microparticles measured in plasma from blood samples collected pre-operatively and 1, 6, 12, 24 and 48 hours post cross-clamp release
9. The concentration of plasma propofol measured in plasma from blood samples collected immediately before aortic cross-clamping, once during cardioplegia (after blood/cardioplegia mixing) and 10 minutes after cross-clamp release. Blood will be taken from the cardioplegia /bypass circuit.
10. Length of intensive care unit (ICU)/high dependency unit (HDU) stay will be recorded
11. Clinical outcomes and serious adverse events, i.e. serious post-operative complications (e.g. myocardial infarction, permanent stroke, renal failure defined as new need for haemodialysis) and death from any cause will be recorded
12. Patient health status monitored using specialist questionnaires pre-operatively and 3 months post-operatively. CABG patients will be asked to complete the Coronary Revascularisation Outcome Questionnaire (CROQ) and AVR patients will be asked to complete the Minnesota Living with Heart Failure (MLHF) Questionnaire. The EQ-5D™ health questionnaire will also be administered to all patients pre-operatively and at 3 months post-operatively.

Completion date
31/12/2016

Eligibility

Key inclusion criteria
Current inclusion criteria as of 01/02/2011:
1. Male or female
2. Age ≥18 to ≤80 years
3. Having elective or urgent CABG or AVR with CPB at the BHI
4. Able to give full informed consent for the study

Previous inclusion criteria:
1. Male or female
2. Aged greater than or equal to 16 years to less than or equal to 80 years
3. Having elective or urgent CABG or AVR with CPB at the Bristol Heart Institute (BHI)
4. Able to give full informed consent for the study

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria
Current inclusion criteria as of 01/02/2011:
1. Previous cardiac surgery
2. Combined CABG and AVR
3. Emergency or salvage operation
4. Chronic renal failure requiring dialysis
5. Current congestive heart failure
6. Left ventricular ejection fraction less than 30% (i.e. poor LV function)
7. Allergy to peanuts, eggs, egg products, soybeans or soy products
8. Already participating in another clinical (interventional) study

Previous inclusion criteria:
2. Concomitant CABG/AVR procedure

Date of first enrolment
15/02/2010

Date of final enrolment
06/07/2012

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Bristol Heart Institute
Bristol
United Kingdom
BS2 8HW

Sponsor information

Organisation
University Hospitals Bristol NHS Foundation Trust (UK)

ROR
https://ror.org/04nm1cv11

Funder(s)

Funder type

Government

Funder Name
National Institute for Health Research (NIHR) (UK) - Biomedical Research Unit (ref: 2008/SS/BRU)

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	08/07/2014		Yes	No
Basic results				No	No