ISRCTN70523327 https://doi.org/10.1186/ISRCTN70523327

The effects of cardiopulmonary bypass on the function of white blood cells

Submission date
04/11/2015

Recruitment status
No longer recruiting

Registration date
05/11/2015

Overall study status
Completed

Last Edited
28/10/2022

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 (CHD), also known as ischemic heart disease, is one of the leading causes of death worldwide. CHD develops because of the build-up of fatty deposits (plaque) on the walls of the coronary arteries (the arteries that supply the heart with oxygen-rich blood). When arteries are blocked or narrowed, the heart does not receive enough blood to function properly, which can cause pain and tightness in the chest (angina), or even lead to a heart attack. A coronary artery bypass graft (CABG) is an operation that is used to treat CAD. It works taking a blood vessel from another part of the body, and attaching it to the coronary artery above and below the blocked or narrowed area (graft). This graft diverts the blood around the blockage, improving the overall blood supply to the heart. In order to ensure that the heart is “motionless” during surgery, a cardiopulmonary bypass (CBP) is performed so that blood supply avoids the heart and lungs during the grafting procedure. It works by diverting blood away from the lungs and heart through an oxygenator machine (which adds oxygen and gets rid of carbon dioxide from blood) and lengths of plastic tubing. A common complication of CPB is that white blood cells (cells which fight infection) become “activated” when they come into contact with the plastic tubing. This can cause damage to the lungs when the blood is redirected to them after the procedure. During the surgery, the surgeon and anaesthetist have the option of inflating the lungs, which is thought to prevent this from happening. In some heart operations, the left lung is deflated (because the left side of the chest is opened), while the right lung is inflated by the anaesthetist. This provides a unique opportunity to look at the behaviour of white blood cells when they are returned to an inflated and a deflated lung at the same time. The aim of this study is to find out whether white blood cells known as neutrophils (which ingest foreign material such as bacteria) behave differently when returning to an inflated or a deflated lung after a CPB procedure.

Who can participate?
Adults who are having coronary artery bypass graft surgery (CABG).

What does the study involve?
Participants who have agreed to take part in the study have three 25ml blood samples taken at different timepoints during their CABG surgery. These blood samples are all taken from the central line (a long, thin tube that is inserted into a major vein so that medications can be given)

that they have fitted before their operation. After their surgery, two more 25ml blood samples are taken from the pulmonary veins (the veins which supply the lungs). All five blood samples are then analysed in the lab in order to look at the presence of activated white blood cells.

What are the possible benefits and risks of participating?
There are no direct benefits of taking part in this study, however it could help to improve care for patients undergoing a CABG in the future. Risks of participating include pain or bruising when blood samples are taken, as well as the general risks associated with undergoing a CABG procedure.

Where is the study run from?
Freeman Hospital Newcastle upon Tyne (UK)

When is the study starting and how long is it expected to run for?
November 2015 to July 2017

Who is funding the study?
Newcastle Biomedical research Centre in Aging and Chronic Disease (UK)

Who is the main contact?
1. Dr Wendy Funston (Public)
2. Professor John Simpson (Scientific)

Contact information

Type(s)
Public

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Protocol serial number
Nil known

Study information

Scientific Title
Lung Inflation and Deflation and the Effect on Neutrophils

Acronym
LIDEN

Study objectives
Neutrophil function (specifically neutrophil phagocytic function) will be reduced following a period of time on cardiopulmonary bypass and that this phagocytic function will be partially restored after travelling through an inflated lung.

Ethics approval required
Old ethics approval format

Ethics approval(s)
North East – York Research Ethics Committee, 17/11/2015, REC ref: 15/NE/0319

Study design
Single-centre observational cohort study

Primary study design
Observational

Study type(s)
Treatment

Health condition(s) or problem(s) studied
The role of lung inflation on neutrophil function in patients undergoing coronary artery bypass grafting

Interventions

Eligible patients will be adults having coronary artery bypass grafting (CABG) at the Freeman Hospital, Newcastle upon Tyne. A full explanation of what is involved will be given when the patients are seen in the pre-assessment clinic (or on the ward for patients admitted for non elective surgery), about a week or two prior to surgery. At that stage they will be given the Patient Information Sheet. Final consent will be taken at least 24 hours later, when they are admitted for the operation. Some patients undergoing non elective surgery will be included, and will be allowed a minimum of 4 hours to elapse between the initial explanation of the study and the signing of the consent form. We intend to obtain 5x25ml blood samples in total from each participant. Prior to surgery a 'central line' is inserted into a major vein after the patient is anaesthetised and we intend to obtain three of the blood samples from this central line at different time points in the surgery. We may however ask permission to obtain the first of these blood samples from an arm vein before the patient goes to theatre (ie a pre-cardiopulmonary bypass sample) if it is more convenient.

Following standard anaesthetic practice, an endotracheal tube will be inserted by the anaesthetist. A "bronchial blocker" (a balloon catheter) will be placed near the origin of the left main bronchus, and inflated gently in order to obstruct the bronchus and ensure deflation of the left lung. The right lung will be ventilated, using the safest form of lung ventilation (known as "low tidal volume ventilation"). The operation will then proceed as normal. The pleura on the patient's left side will be opened, ensuring full deflation of the left lung. This is standard practice during coronary artery bypass grafting, in order to access the left internal mammary artery (used to bypass occluded coronary arteries).

When the operation is over, with the patient having just come off CPB, blood samples will then be taken from the the right and left inferior pulmonary veins (25ml each sample) under direct vision by the operating surgeon. The total blood collected throughout the whole operation will amount to approximately 125ml.

The 5x25ml blood samples will be taken to Prof Simpson's research lab at Newcastle University. Blood will be used to study activation status of white blood cells and to isolate neutrophils for functional studies, and to measure cytokines.

Intervention Type
Procedure/Surgery

Primary outcome(s)
Differences in phagocytic capacity of neutrophils in blood is measured by way of direct microscopic visualisation of ingestion of Zymosan particles and by flow cytometric analysis using staph. aureus PHrodo bioparticles at baseline, during and after CPB.

Key secondary outcome(s))
1. Differences in neutrophil priming status is measured by differences in cell surface expression markers (CD11b and CD62L) and release of reactive oxygen species by flow cytometric analysis at baseline, during and after CPB
2. Differences in the serum cytokines of blood is measured using an ELISA assay at baseline, during and after CPB

Completion date
30/07/2017

Eligibility

Key inclusion criteria
1. Aged 18 or over
2. Patients undergoing coronary artery bypass graft surgery

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Patients under 18 years of age
2. Lack of informed, written consent
3. Emergency surgery precluding the capacity to give sufficient time for informed written consent
4. Redo surgery
5. Patients taking part in other interventional studies of CTIMPs that may significantly affect white blood cell function

Date of first enrolment
01/11/2015

Date of final enrolment
01/05/2017

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Freeman Hospital Newcastle Upon Tyne
Cardiothoracic Centre
Freeman Hospital
Newcastle upon Tyne
United Kingdom
NE7 7DN

Sponsor information

Organisation
Newcastle Upon Tyne Hospitals NHS Foundation Trust (UK)

ROR
https://ror.org/05p40t847

Funder(s)

Funder type
Research organisation

Funder Name
Newcastle Biomedical Research Centre in Aging and Chronic Disease (UK)

Results and Publications

Individual participant data (IPD) sharing plan
Not provided at time of registration

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		26/07/2022	28/10/2022	Yes	No
HRA research summary			28/06/2023	No	No