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A randomised controlled trial of patient-specific oxygen monitoring to reduce blood transfusion during heart surgery

Submission date
13/01/2009

Recruitment status
No longer recruiting

Registration date
27/02/2009

Overall study status
Completed

Last Edited
04/10/2017

Condition category
Surgery

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

Plain English summary of protocol

Background and study aims
During on-pump cardiac surgery it is important to ensure that a patient's organs are receiving the correct amount of oxygen. At present, counting a patient's red blood cells (the 'haematocrit' level) is the standard method of measuring the oxygen level. When the haematocrit drops below a certain level (threshold) a transfusion is given. This threshold is the same in all patients. This may not be the best method because the oxygen supply to an individual organ can be low (which can cause injury) while the overall haematocrit level remains within the normal range. On the other hand, transfusing blood unnecessarily may cause the body more stress and reduce its ability to fight infection. In this study a patient-specific method for deciding when to transfuse, based on the amount of oxygen reaching the brain during the operation, is being compared with the standard method using the same threshold for transfusion for all patients. 'Near infra-red spectroscopy' (NIRS) is used to monitor oxygen levels in the brain and help guide surgeons in transfusion decisions. This is a non-invasive technology that is thought to be the best device for measuring oxygen supply.

Who can participate?
Patients over 16 years of age who are having valve or combined valve and coronary surgery at one of three UK hospitals (Bristol Royal Infirmary, Castle Hill Hospital or Glenfield Hospital)

What does the study involve?
Participants are randomly allocated to one of two groups: standard method or new method. In the standard method group, during surgery, the amount of oxygen being supplied to the body is monitored in the normal way. The doctor takes the normal steps to ensure that the oxygen supply is kept at the right levels and patients receive a blood transfusion if their haematocrit falls to the pre-set value normally used at this hospital (23%). In the new method group, during surgery, the amount of oxygen being supplied to the body is monitored in the normal way. In addition, two sensors are attached to the skin on the forehead. These monitor the oxygen levels in the brain during surgery. A blood transfusion is only given if the oxygen level in your brain starts to drop and the doctors cannot improve this using other methods. However, oxygen levels in the brain are not used as the only guide to transfusion and a transfusion is still given if the

haematocrit reaches a low level (18%). Before the operation participants complete some short questionnaires about their general health and undergo a series of short tests to check their memory, co-ordination and levels of attention. These tests in total take about an hour. After heart surgery some patients may become confused and disorientated. The aim is to find out whether monitoring the level of oxygen in the brain during the operation can reduce these side effects. Patients taking part are asked to give blood and urine samples. These samples are tested for several chemicals that give an idea of how well different parts of the body, e.g. the brain, heart and kidneys, worked during and after the operation. Blood samples are taken at six time points and urine samples at four time points during the hospital stay. Five days after the operation, participants complete the questionnaires again and repeat the tests. During their stay in hospital, they may also be asked some short questions about how well their operation wounds are healing. Other information is collected from their medical records.
After they are discharged from hospital, participants complete a short postal questionnaire about their general health about 6 weeks after their operation. Participants attend a special follow-up appointment about 3 months after their operation. At this visit, their memory, co-ordination and levels of attention are tested again, and they complete the health questionnaires and answer some other questions about their health since the operation.

What are the possible benefits and risks of participating?
Monitoring oxygen levels may ensure better oxygen supply to the brain and other organs. Taking part in the study may change the chance of having a blood transfusion, depending on the allocated group. It is not thought that taking part in this study exposes participants to an increased risk. There is a risk that patients put into the 'standard method' group may experience higher transfusion rates, as well as possibly lower oxygen levels in the tissues. This risk is no different to that experienced by patients undergoing cardiac surgery on a day-to-day basis. The only way that to be sure that monitoring oxygen levels in the brain is better than the method currently used is by carrying out a study of this kind. As an additional safety measure a minimum haematocrit level (18%) has been set for patients cared for using the 'new method'. If this level is reached, patients receive a blood transfusion even if oxygen levels in the brain are normal. This minimum haematocrit level is routinely used in some hospitals in the UK and elsewhere. This has been done to avoid any patient having a very low haematocrit, which might be harmful.

Where is the study run from?
The main site is Bristol Heart Institute. The additional sites are Castle Hill Hospital and Glenfield Hospital (UK).

When is the study starting and how long is it expected to run for?
December 2009 to April 2014

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

Who is the main contact?
Prof. Barney Reeves
barney.reeves@bristol.ac.uk

Contact information

Type(s)
Scientific

Contact name
Prof Barney Reeves

Contact details
Bristol Heart Institute
University of Bristol
Level 7
Bristol Royal Infirmary
Upper Maudlin Street
Bristol
United Kingdom
BS2 8HW

Additional identifiers

Protocol serial number
CS/2008/3057

Study information

Scientific Title
Patient-specific cerebral oxygentation monitoring as part of an algorithm to reduce transfusion during heart valve surgery: a randomised controlled trial

Acronym
PASPORT

Study objectives
The hypothesis for the trial is that a patient-specific, goal-directed algorithm (based on optimising regional cerebral oxygen saturation), combined with a pre-specified "restrictive" haematocrit transfusion threshold of 18, will result in fewer red blood cell (RBC) transfusions and will reduce complications arising from unnecessary transfusion and from low oxygen levels during cardiopulmonary bypass, when compared with the currently used "generic" algorithm for monitoring and optimising oxygen levels.

Ethics approval required
Old ethics approval format

Ethics approval(s)
The local Research Ethics Committee (REC) approved on 15/06/2009. Amendments to the protocol were approved on 09/11/2009, 19/01/2010,12/02/2010, 17/05/2011 and 27/07/2011. Amendment 9 approved by REC on 24/08/2012. Amendment 10 was approved on 07/08/2013. Amendment 11 was approved on 17/07/2015.

Study design
Randomised controlled multi-centre trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Oxygen monitoring/blood transfusion in patients having heart valve replacement surgery

Interventions
The trial will compare two different algorithms for optimising tissue oxygenation during cardiopulmonary bypass (CPB), as follows:

1. "Generic algorithm" (including a standard transfusion threshold):
A generic algorithm for optimising tissue oxygenation based on global measures of oxygen utilisation and including a pre-defined intraoperative haematocrit transfusion threshold of 23 (current "standard practice", i.e. our existing protocol).

2. "Patient-specific algorithm" (including a restrictive transfusion threshold):
A patient-specific, goal-directed, algorithm based on monitoring and optimisation of regional cerebral oxygen saturation, combined with a predefined "restrictive" intraoperative haematocrit transfusion threshold of 18 (experimental arm).

Intervention Type
Procedure/Surgery

Phase
Not Applicable

Primary outcome(s)
Current primary outcome measures as of 12/08/2015:
Cognitive function:
Recommended cognitive domains will be tested as follows:
1. Verbal memory: Rey Auditory Verbal Learning Test (AVLT)
2. Attention: First trial of the AVLT, Sustained and divided attention: Trail- Making Test parts A and B
3. Visuo-spatial: Block Design from the Wechsler Adult Intelligence Scale - Revised (WAIS-R) test
4. Motor coordination: Grooved Pegboard Test, dominant and non dominant hand
5. Executive function/Verbal fluency: Controlled Oral Word Association Test (COWAT)

Primary outcome measures from 17/11/2010 to 12/08/2015:
1. Cognitive function: recommended cognitive domains will be tested as follows:
1.1. Verbal memory: Rey Auditory Verbal Learning Test (AVLT)
1.2. Attention: First trial of the AVLT, Sustained and divided attention: Trail- Making Test parts A and B
1.3. Visuo-spatial: Block Design from the Wechsler Adult Intelligence Scale - Revised (WAIS-R) test
1.4. Motor coordination: Grooved Pegboard Test, dominant and non dominant hand
1.5. Executive function/Verbal fluency: Controlled Oral Word Association Test (COWAT)
2. Infectious complications: a cumulative infection score will be calculated by supplementing data on wound infections (the ASEPSIS score that describes signs and symptoms of wound infection on a continuous scale) with data describing the severity of sepsis

Primary outcome measures at time of registration:
1. Cognitive function: recommended cognitive domains will be tested as follows:
1.1. Verbal memory: Rey Auditory Verbal Learning Test (AVLT)
1.2. Attention: First trial of the AVLT, Sustained and divided attention: Trail- Making Test parts A and B
1.3. Psychomotor speed: Digit Symbol Test from the Weschler Adult Intelligence Scale - Revised (WAIS-R) test
1.4. Motor coordination: Grooved Pegboard Test, dominant and non dominant hand
1.5. Executive function/Verbal fluency: Controlled Oral Word Association Test (COWAT)
2. Infectious complications:
2.1. Septicaemia
2.2. Lower respiratory tract infection
2.3. Urinary sepsis
2.4. Wound infection

Key secondary outcome(s))

Current secondary outcome measures as of 12/08/2015:
1. Units of RBC and other blood components transfused during the operative period and post-operative hospital stay
2. Cerebral oxygenation during the operative period
3. Oxygen delivery and utilisation during CPB
4. Euroqol EQ-5D at baseline and 6 weeks and 3 months after surgery
5. Length of intensive care unit (ICU)/high dependency unit (HDU) stay
6. Length of hospital stay
7. Clinical outcomes (defined as: stroke, ST elevation myocardial infarction, post-operative acute kidney injury, respiratory complications) during the post-operative hospital stay
8. Cumulative resource use, cost and cost-effectiveness
9. All-cause mortality within 30 days of surgery
10. Biochemical markers of organ injury during first 96 hours post-surgery
11. The occurrence of an infectious complication

Secondary outcome measures from 17/11/2010 to 12/08/2015:
1. Units of RBC and other blood components transfused during the operative period and post-operative hospital stay
2. Cerebral oxygenation during the operative period
3. Oxygen delivery and utilisation during CPB
4. Euroqol EQ-5D at baseline and 6 weeks and 3 months after surgery
5. Length of intensive care unit (ICU)/high dependency unit (HDU) stay
6. Length of hospital stay
7. Clinical outcomes (defined as: stroke, ST elevation myocardial infarction, post-operative acute kidney injury, respiratory complications) during the post-operative hospital stay
8. Cumulative resource use, cost and cost-effectiveness
9. All-cause mortality within 30 days of surgery
10. Biochemical markers of organ injury during first 96 hours post-surgery

Initial secondary outcome measures at time of registration:
1. Units of RBC and other blood components transfused during the operative period and post-operative hospital stay
2. Cerebral oxygenation during the operative period
3. Oxygen delivery and utilisation during CPB
4. Euroqol EQ-5D at baseline and 6 weeks and 3 months after surgery

5. Length of intensive care unit (ICU)/high dependency unit (HDU) stay
6. Length of hospital stay
7. Clinical outcomes (defined as: stroke, ST elevation myocardial infarction, post-operative renal dysfunction, respiratory complications) during the post-operative hospital stay
8. Cumulative resource use, cost and cost-effectiveness
9. All-cause mortality within 30 days of surgery
10. Biochemical markers of organ injury during first 48 hours post-surgery

Completion date
30/04/2014

Eligibility

Key inclusion criteria
Current information as of 17/11/2010:
1. Adults ≥ 16 years of either sex undergoing valve or combined coronary artery bypass graft (CABG) and valve surgery at the Bristol Royal Infirmary
2. Patients giving informed consent to participate and who are suitable for allocation to either transfusion protocol

Initial information at time of registration:
1. Adults (>= 16 years and <80 years) of either sex undergoing valve or combined coronary artery bypass graft (CABG) and valve surgery at the Bristol Royal Infirmary
2. Patients giving informed consent to participate and who are suitable for allocation to either transfusion protocol

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
Current exclusion criteria as of 09/08/2011:
1. Patients undergoing emergency cardiac surgery (emergency surgery defined as surgery taking place before the end of the same working day as admission).
2. Patients who are prevented from having blood and blood products according to a system of beliefs (e.g. Jehovah's Witnesses).
3. Patients who may have higher perioperative haemoglobin requirements (e.g. preoperative ejection fraction < 30%, cerebrovascular occlusive disease [arterial stenosis > 75%] or critical limb ischemia).
4. Patients with congenital or acquired RBC, platelet or clotting factor disorders, (excluding those receiving antiplatelet therapy, warfarin or other systemic oral anticoagulants).
5. Patients with a neurological disorder (e.g. epilepsy, Alzheimer's, dementia and Parkinson's disease)

6. Patients with a diagnosed psychiatric disorder (e.g. schizophrenia, psychosis), drug or alcohol addiction.
7. Patients with an already identified cognitive impairment (e.g. memory and/or attentional deficits) as defined by psychometric assessment or a preoperative Mini-Mental State Examination score < 24 [37].
8. Patients who have previously sustained a stroke, intra-cerebral haemorrhage, acquired brain injury.
9. Patients with a pre-existing inflammatory state (e.g. sepsis, active inflammatory disease including active rheumatoid arthritis, colitis, Lupus, or Crohn's disease. NB consider latter conditions as active conditions when a patient is taking a high dose of oral steroids, for example > 10 mg/day of prednisolone/prednisone).
10. Patients with end stage renal failure or patients who have undergone renal transplantation.
11. Patients unable to complete the cognitive assessments required for the trial e.g. due to language difficulties, visual or hearing impairment.
12. Patients who were unable to give full informed consent for the study (e.g. language difficulties).
13. Patients already participating in another clinical (interventional) study.

Previous exclusion criteria (added 17/11/2010):
1. Patients undergoing emergency cardiac surgery (emergency surgery defined as surgery taking place before the end of the same working day as admission)
2. Patients who are prevented from having blood and blood products according to a system of beliefs (e.g. Jehovahs Witnesses)
3. Patients who may have higher perioperative haemoglobin requirements (e.g. preoperative ejection fraction < 30%, cerebrovascular occlusive disease [arterial stenosis > 75%] or critical limb ischemia)
4. Patients with congenital or acquired RBC, platelet or clotting factor disorders (excluding those receiving antiplatelet therapy, warfarin or other systemic oral anticoagulants)
5. Patients with neuropsychological impairment as defined by previous psychiatric illness, stroke, intra-cerebral haemorrhage, preoperative Mini-Mental State Examination score >24 [37], and/or alcohol or drug addiction
6. Patients with a pre-existing inflammatory state (e.g. sepsis, active inflammatory disease including active rheumatoid arthritis, colitis, Lupus, or Crohn's disease. NB consider latter conditions as active conditions when a patient is taking a high dose of oral steroids, for example > 10 mg/day of prednisole)
7. Patients with end stage renal failure or patients who have undergone renal transplantation
8. Patients unable to complete the cognitive assessments required for the trial e.g. due to language difficulties, visual or hearing impairment
9. Patients who were unable to give full informed consent for the study (e.g. language difficulties)
10. Patients already participating in another clinical (interventional) study

Initial exclusion criteria at time of registration:
1. Patients who are prevented from having blood and blood products according to a system of beliefs (e.g., Jehovah's Witnesses)
2. Patients who may have higher perioperative haemoglobin requirements (e.g., emergency cases, preoperative ejection fraction <30%, cerebrovascular occlusive disease [arterial stenosis >75%] or critical limb ischaemia)
3. Patients with congenital or acquired RBC, platelet or clotting factor disorders (excluding those receiving antiplatelet therapy, warfarin or other systemic oral anticoagulants)
4. Patients with neuropsychological impairment as defined by previous psychiatric illness, stroke, transient ischaemic attacks, intra-cerebral haemorrhage, preoperative Mini-Mental State

Examination score <24, and/or alcohol or drug addiction
5. Patients with a pre-existing inflammatory state (e.g., sepsis, active inflammatory disease)
6. Patients at risk of impaired cerebral autoregulation (e.g., diabetics requiring insulin, patients aged >80 years, untreated malignant hypertension)
7. Patients who were unable to give full informed consent for the study (e.g., learning or language difficulties)
8. Patients already participating in another clinical (interventional) study

Date of first enrolment
01/12/2009

Date of final enrolment
31/12/2013

Locations

Countries of recruitment
United Kingdom

England

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

Study participating centre
Glenfield Hospital
Department of Cardiothoracic Surgery
Groby Road
Leicester
United Kingdom
LE3 9QP

Study participating centre
Castle Hill Hospital
Department of Anaesthesia
Castle Road
United Kingdom
HU16 5JQ

Sponsor information

Organisation
University Hospitals Bristol NHS Foundation Trust (UK)

ROR
https://ror.org/04nm1cv11

Funder(s)

Funder type
Government

Funder Name
NIHR Programme Grant for Applied Research (UK) (ref: RP-PG-0407-10384)

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	01/09/2017		Yes	No
Protocol article	protocol	18/12/2015		Yes	No