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A multi-centre randomised controlled trial of the effects of a reduction in the threshold for blood transfusion following heart surgery

Submission date
01/09/2008

Recruitment status
No longer recruiting

Registration date
09/09/2008

Overall study status
Completed

Last Edited
22/02/2018

Condition category
Surgery

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

Plain English summary of protocol

Background and study aims
Unnecessary blood transfusions increase healthcare costs both directly, because blood is an increasingly scarce and expensive resource, and indirectly, due to complications associated with transfusion. Transfusion may cause complications by reducing patients' ability to fight off infection and respond to the stress that surgery puts on the body, as well as (rarely) by transmitting viral infections present in donor blood. In the UK, cardiac (heart) surgery uses more than 6% of all donor blood. Although the benefits of red cells for managing life-threatening bleeding are clear, the majority of decisions to transfuse after surgery are made on the basis of a patient's haemoglobin (Hb) level - a measure of the ability of the blood to transport oxygen around the body. The level that causes a doctor to transfuse a patient varies widely, and studies in non-cardiac surgical fields have shown that lowering the level that 'triggers' transfusion (threshold) reduces complications as well as the use of blood. The aim of this study is to find out whether lowering the threshold for red cell transfusion reduces complications and NHS costs.

Who can participate?
Patients aged over 16 undergoing cardiac surgery, whose Hb level drops below the level at which transfusion is conventionally given

What does the study involve?
Participants are randomly allocated either to have decisions made about transfusion more or less as they are now, or to only have a transfusion when their Hb level drops to a lower 'restrictive' level. We assess the number of infectious complications (septicaemia, wound or chest infection) and ischaemic complications (stroke, heart attack or kidney failure) that occur during the first 3 months after surgery.

What are the possible benefits and risks of participating?
We believe that withholding transfusion until the lower Hb level is reached will reduce both complications and hospital costs. Participants will not need to have any special investigations or extra hospital visits.

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

When is the study starting and how long is it expected to run for?
December 2008 to November 2011

Who is funding the study?
Health Technology Assessment Programme (UK)

Who is the main contact?
Prof. Barney Reeves

Contact information

Type(s)
Scientific

Contact name
Prof Barney Reeves

Contact details
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
HTA 06/402/94

Study information

Scientific Title
A multi-centre randomised controlled trial of Transfusion Indication Threshold Reduction on transfusion rates, morbidity and healthcare resource use following cardiac surgery

Acronym
TITRe 2

Study objectives
Current information as of 01/09/2009:
The hypothesis for the trial is that lowering the transfusion threshold for red cell transfusion from a haemoglobin (Hb)/haematocrit (Hct) level of 9 g/dL / 27 ('liberal', similar to current practice) to 7.5 g / dL / 22 ('restrictive') will reduce postoperative morbidity and NHS costs.

Information at time of registration:
The hypothesis for the trial is that lowering the transfusion threshold for red cell transfusion from a haemoglobin (Hb) level of 9 g/dL ('liberal', similar to current practice) to 7.5 g/dL ('restrictive') will reduce postoperative morbidity and NHS costs.

More details can be found at: http://www.nets.nihr.ac.uk/projects/hta/0640294
Protocol can be found at: http://www.nets.nihr.ac.uk/__data/assets/pdf_file/0003/51393/PRO-06-402-94.pdf

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. First approved by Oxfordshire Regional Ethics Committee (REC) C on 31/10/2008 (ref: 08/H0606/125). Subsequent amendments were approved on 19/05/2009 and 14/07/2009.
2. The latest amendments included in this record were approved by the REC on 30/07/2010. Two further amendments were approved by the REC on 09/10/2009 and 12th April. These amendments do not affect the information shown on the ISRCTN page.

Study design
Multicentre randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

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
Patients undergoing cardiac surgery

Interventions
Current information as of 01/09/2009:
The trial will compare two Hb thresholds for blood transfusion, 'liberal' and 'restrictive'. The thresholds are defined as follows:

A: Liberal (control, similar to current practice): participants randomised to this group will be eligible for transfusion if their post-operative nadir Hb / Hct level falls below 9.0 g / dL / 27. One unit of RBC should be transfused and the Hb level checked before transfusing another unit. The objective should be to maintain the Hb / Hct level above 9.0 g / dL / 27.

B: Restrictive (experimental): participants randomised to this group will be eligible for transfusion if their post-operative nadir Hb / Hct level falls below 7.5 g / dL / 22. One unit of RBC should be transfused and the Hb level checked before transfusing another unit. The objective should be to maintain the Hb / Hct level above 7.5 g / dL / 22.

Clinicians will be allowed to transfuse, or refuse to transfuse, in contravention of these thresholds but must document the reason(s).

The total duration of follow-up for each participant is 3 months post randomisation, at which point participants will leave the study. However, we are hoping to collect long-term mortality data from data held routinely by the NHS and will be seeking consent from participants for this.

Initial information at time of registration:
The trial will compare two Hb thresholds for blood transfusion, 'liberal' and 'restrictive'. The thresholds are defined as follows:

A: Liberal (control, similar to current practice): participants randomised to this group will be eligible for transfusion if their post-operative nadir Hb level falls below 9.0 g/dL. One unit of RBC should be transfused and the Hb level checked before transfusing another unit. The objective should be to maintain the Hb level above 9.0 g/dL.

B: Restrictive (experimental): participants randomised to this group will be eligible for transfusion if their post-operative nadir Hb level falls below 7.5 g/dL. One unit of RBC should be transfused and the Hb level checked before transfusing another unit. The objective should be to maintain the Hb level above 7.5 g/dL.

Clinicians will be allowed to transfuse, or refuse to transfuse, in contravention of these thresholds but must document the reason(s).

The total duration of follow-up for each participant is 3 months post randomisation, at which point participants will leave the study. However, we are hoping to collect long-term mortality data from data held routinely by the NHS and will be seeking consent from participants for this.

Intervention Type
Procedure/Surgery

Phase
Not Specified

Primary outcome measure
Current information as of 01/09/2009:
A composite of serious infectious or ischaemic events in the first 3 months after randomisation. The infectious and ischaemic events to be recorded will include the following:
1. Infectious events:
1.1. Sepsis
1.2. Wound infection

2. Ischaemic events:
2.1. Permanent stroke
2.2. Myocardial infarction
2.3. Acute kidney injury
2.4. Gut infarction

Initial information at time of registration:
A composite of serious infectious or ischaemic events in the first 3 months after randomisation. The infectious and ischaemic events to be recorded will include the following:

1. Infectious events:
1.1. Septicaemia
1.2. Lower respiratory tract infection
1.3. Urinary sepsis
1.4 Wound infection
2. Ischaemic events:
2.1. Permanent stroke
2.2. Myocardial infarction
2.3. Renal failure
2.4. Gut infarction

Secondary outcome measures
Current information as of 01/09/2009:
1. Units of red blood cells transfused, recorded for the duration of hospital stay post-randomisation
2. Proportion of patients experiencing an infectious event
3. Proportion of patients experiencing an ischaemic event
4. EuroQol EQ-5D
5. Duration of ICU/HDU stay post-operatively
6. Duration of post-operative hospital stay
7. All cause mortality, recorded for duration of participation in study (3 months post-randomisation)
8. Cumulative resource use, cost, and cost-effectiveness, assessed for duration of participation in study (3 months post-randomisation)

Initial information at time of registration:
1. Units of red blood cells transfused, recorded for the duration of hospital stay post-randomisation
2. Frequency of infectious events, recorded for the duration of hospital stay post-randomisation
3. Frequency of ischaemic events, recorded for the duration of hospital stay post-randomisation
4. EuroQol EQ-5D, assessed at baseline (pre-randomisation) and 3-months follow-up
5. Length of ICU stay, recorded for the duration of hospital stay post-randomisation
6. Length of hospital stay
7. All cause mortality, recorded for duration of participation in study (3 months post-randomisation)
8. Cumulative resource use, cost, and cost-effectiveness, assessed for duration of participation in study (3 months post-randomisation)

Overall study start date
01/12/2008

Completion date
30/11/2011

Eligibility

Key inclusion criteria
Current inclusion criteria as of 24/08/2010:
1. Adults of either sex, aged ≥16
2. Post-operative nadir Hb / Hct level below 9.0 g / dL / 27

Previous inclusion criteria from 01/09/2009 to 24/08/2010:
1. Adults of either sex, aged ≥16 and <80 years
2. Post-operative nadir Hb / Hct level below 9.0 g / dL / 27

Initial information at time of registration:
1. Adults of either sex, aged ≥16 and <80 years
2. Post-operative nadir Hb level below 9.0 g/dL

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
2,000

Key exclusion criteria
Current information as of 01/09/2009:
1. Patients who are prevented from having blood and blood products according to a system of beliefs (e.g., Jehovah's Witnesses)
2. Patients with congenital or acquired platelet, red cell or clotting disorders
3. Patients with ongoing or recurrent sepsis
4. Patients who were unable to give full informed consent for the study (e.g., learning or language difficulties)
5. Patients with critical limb ischaemia
6. Patients undergoing emergency surgery
7. Patients already participating in another interventional research study

Initial information 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 with congenital or acquired platelet, red cell or clotting disorders
3. Patients with ongoing or recurrent systemic sepsis
4. Patients who were unable to give full informed consent for the study (e.g., learning or language difficulties)

5. Patients with a critical carotid artery stenosis (>75%) or critical limb ischaemia
6. Patients with flow limiting (>70% luminal stenosis) coronary artery disease not undergoing complete revascularisation

Date of first enrolment
01/12/2008

Date of final enrolment
30/11/2011

Locations

Countries of recruitment
England

United Kingdom

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

Sponsor information

Organisation
University Hospitals Bristol NHS Foundation Trust (UK)

Sponsor details
Research and Development Department
Education Centre
Level 3
Upper Maudlin Street
Bristol
England
United Kingdom
BS2 8AE

Sponsor type
Hospital/treatment centre

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

ROR

https://ror.org/04nm1cv11

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

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?
Protocol article	protocol	01/06/2014		Yes	No
Statistical Analysis Plan	statistical analysis plan	22/02/2015		No	No
Results article	results	12/03/2015		Yes	No
Results article	results	01/08/2016		Yes	No