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Is intravenous iron and darbepoetin more effective than oral iron in reducing blood transfusion requirements for patients undergoing cardiac surgery?

Submission date
23/07/2012

Recruitment status
No longer recruiting

Registration date
28/08/2012

Overall study status
Completed

Last Edited
09/09/2020

Condition category
Surgery

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

Plain English summary of protocol

Background and study aims
About 25% of patients undergoing planned, elective heart surgery have an abnormally low blood count (hemoglobin). These patients are more likely to need a blood transfusion during and after surgery. They are also more likely to have complications after surgery. Most patients who have a low blood count have low levels of iron. Iron treatment in these patients can increase the blood count if it is given several weeks before surgery. Undergoing surgery at a higher blood count will lower the risk of needing a blood transfusion after surgery. The standard method of treating low iron is to take iron tablets, but iron can also be given by injection and this might be more effective. Additionally, drugs such as darbepoetin that stimulate the bone marrow can speed up the increase in blood count. This study will test whether the combination of intravenous iron and darbepoetin will more effectively raise the blood count before surgery and lead to a lower rate of blood transfusion compared to taking iron tablets alone.

Who can participate?
Patients undergoing elective heart surgery at our institution.

What does the study involve?
Patients who are seen in the outpatient clinic when first referred for surgery have their hemoglobin (Hb) level measured routinely. Those with an Hb between 10 and 13 g/dl will be invited to participate in the study. Tests will be performed to measure iron levels in the blood. Those with a low iron level will be randomly allocated to either iron tablets or to attend the hospital for a few hours to receive intravenous iron and darbepoetin. The participants will be scheduled for surgery in the usual way between 2 and 10 weeks after the start of iron treatment. During and after surgery, participants will be looked after according to our normal practice. Red blood cells will be transfused when the Hb is less than 7 g/dl, or higher if there are specific clinical reasons. In addition to monitoring for serious complications after surgery, we will assess the participants' general well being, mental function, mood and fatigue levels before and after iron treatment and after surgery.

What are the possible benefits and risks of participating?
Benefits include investigation and treatment of low Hb level before surgery. A higher Hb before surgery will decrease blood transfusion and may reduce postoperative complications. Risks include side effects from oral iron - constipation or diarrhoea may occur occasionally. Intravenous iron can cause blood pressure to increase or fall during infusion, muscle aches the following days, and very rarely an allergic reaction which may require hospital admission and antihistamine drugs to be given.

Where is the study run from?
The Royal Sussex County Hospital in Brighton (UK)

When is the study starting and how long is it expected to run for?
September 2012 to May 2017

Who is funding the study?
Royal College of Surgeons of England (UK), Sussex Heart Charity (UK) and Pharmacosmos A/S (Denmark)

Who is the main contact?
Dr Robert Kong
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number
2011-003695-36

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

11/104KON

Study information

Scientific Title
Is intravenous iron and darbepoetin more effective than oral iron in reducing blood transfusion requirements for patients undergoing cardiac surgery? A pragmatic randomised trial

Acronym
INITIATE

Study objectives
In patients who have a low hemoglobin before elective cardiac surgery, treatment with a combination of intravenous iron and darbepoetin several weeks before surgery will reduce perioperative red cell transfusion compared to oral iron alone.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee London - Bentham, 11/01/2012, ref: 11/LO/1310

Study design
Pragmatic open-label randomised parallel group 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
Preoperative anemia, cardiac surgery

Interventions
1. Monofer® [iron isomaltoside 1000] 1000mg, single dose, i.v. (or Ferinject® [ferric carboxymaltose] 1000mg, single dose i.v. if Monofer® contraindicated) AND Aranesp® (darbepoetin) 200 µg, single dose, s.c.
2. Compared to ferrous sulphate 200mg, three times daily, oral

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Iron isomaltoside, ferric carboxymaltose, darbepoetin, ferrous sulphate

Primary outcome measure
Proportion of participants in each study arm that receives one or more packed red cell transfusion between the start of surgery until the end of the fifth postoperative day

Secondary outcome measures
1. Hemoglobin increase between randomisation and surgery
2. Total number of packs and volume of red cells transfused from the start of surgery until hospital discharge
3. Postoperative blood loss at 12 and 24 hours after surgery
4. Significant postoperative myocardial injury as measured by Troponin level 18-24h after surgery
5. Acute renal failure as defined by greater than 1.5 times increase in creatinine level after surgery
6. Length of hospital stay

Overall study start date
15/09/2012

Completion date
16/05/2019

Eligibility

Key inclusion criteria
1. Preoperative Hb 10-13 g/dl
2. Serum ferritin <100µg/l or 100-800 µg/L with transferrin saturation <30%
3. First time cardiac surgery involving one or more of the following: coronary artery bypass grafting, repair or replacement of cardiac valve/s or ascending aorta
4. Surgery is elective - not an emergency or patient is not an inpatient immediately prior to surgery

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
320

Key exclusion criteria
1. Hb <10 g/dl or >13 g/dl
2. Patient intends to refuse allogeneic blood transfusion
3. Patient is receiving renal replacement therapy (peritoneal or hemodialysis) before surgery
4. Patient has a history of allergic or toxic reaction to any of the study drugs
5. Patient has significant acute or chronic hepatic disease
6. Patient is undergoing chemotherapy
7. Redo cardiac surgery (i.e. second time or more)
8. Proposed surgery will require hypothermic circulatory arrest
9. Pregnant
10. Age <18
11. Lacks mental capacity to give consent
12. Already participating in another clinical trial that could interfere with this study

Date of first enrolment
15/09/2012

Date of final enrolment
30/05/2017

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Royal Sussex County Hospital
Brighton
United Kingdom
BN2 5BE

Sponsor information

Organisation
Brighton & Sussex University Hospitals NHS Trust (UK)

Sponsor details
c/o R & D Manager
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Sponsor type
Hospital/treatment centre

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

Funder(s)

Funder type
Research organisation

Funder Name
Royal College of Surgeons of England (UK)

Alternative Name(s)
RCS

Funding Body Type
Private sector organisation

Funding Body Subtype
Associations and societies (private and public)

Location
United Kingdom

Funder Name
Sussex Heart Charity (UK)

Funder Name
Pharmacosmos A/S (Denmark)

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