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A randomised controlled trial to compare normoxic versus standard cardiopulmonary bypass in cyanotic children undergoing cardiac surgery

Submission date
20/05/2008

Recruitment status
No longer recruiting

Registration date
10/07/2008

Overall study status
Completed

Last Edited
21/08/2019

Condition category
Surgery

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

Plain English summary of protocol

Background and study aims
Some children are born with a heart defect that causes the levels of oxygen in the blood to be lower than expected for a healthy child. We call children with this condition cyanotic children. Often, the only way of improving the levels of oxygen in the childs blood is by operating on the heart.
When children undergo heart surgery, the job of pumping blood around the body is taken over by a heart-lung bypass machine. This machine also provides the blood with oxygen and allows surgical staff to decide how much oxygen the child gets during surgery.
Currently we give cyanotic children 100% oxygen from the beginning of surgery (when they are attached to the heart-lung bypass machine) and then throughout their surgery. This is widely accepted standard practice. However, after the operation cyanotic children sometimes suffer damage to the cells of their heart and other organs. This is thought to be caused by introducing 100% oxygen at the beginning of surgery when the childs body is not used to it.
Some evidence suggests it may be better to give lower levels of oxygen at the start of the operation, similar to the level the child is used to, and then slowly bring up the level of oxygen by the end of the operation. The level the oxygen given at the end of the operation depends on the childs specific condition.
The Oxic2 study aims to find out which is the best method of giving oxygen to a cyanotic child during surgery by seeing if it leads to any differences in how the child recovers from the operation.

Who can participate?
Cyanotic children undergoing heart surgery.

What does the study involve?
To join the study parents or guardians are required to sign a consent form. After this, and as close as possible to the time of surgery, children will be randomly allocated to one of two groups:
1. Children in the first group will get the higher level of oxygen (100%) at the start of surgery

and throughout their operation;
2. Children in the second group will be given the level of oxygen they are used to at the start of surgery and then slowly given more until they reach a level we would expect to see by the end of the operation.
Everything else about the operation and after care is the same, regardless of which group a child is in.
With permission, any waste heart tissue removed during the operation will be kept for examination to see if the different oxygen levels affect the way heart muscle tissue makes protein and other chemicals. The samples will be stored for the duration of the study and destroyed at the end.
After the operation, information will be collected about the type and amount of care and medical support each child needs while recovering in hospital. This information will be used to compare how fast children recover in each group.
Parents/guardians will also be contacted at 3 months and 12 months after the operation to ask if their child has been admitted to hospital for any reason.
Children aged 2½ years or younger will be assessed for their current stage of development using the Bayley Infant Development Scale to see whether the way their oxygen was managed during the operation has any effect on their development after the operation. The assessments take place at the childs home (or an alternative place to suit) and will be performed before the operation, at 3 months after the operation and again at 12 months after the operation. Children who are less than a month old at the time of their operation will not have an assessment before the operation, but may still have the assessments at 3 and 12 months.The test involves a play session lasting between an hour and 90 minutes depending on the age of the child. Objects and toys are used to see how a child makes sense of the world, how they communicate, and to assess their physical development. The assessment also includes some questions for the parents /guardians to answer about their childs behaviour.
When a child reaches school age, we may ask permission to access their school entry results, which along with the Bayley assessments will provide information about the long term effects of the two oxygen levels.

What are the possible benefits and risks of participating?
Giving high levels of oxygen during a heart operation is standard practice at our hospital so if a child is in the group where the high level of oxygen is used from the beginning of surgery then the risks and benefits are the same as if they were not participating in the study.
The risks and benefits for the lower level of oxygen have not been directly compared with the higher levels of oxygen before. We are doing the study in order to be able to make this comparison. However, we do not believe there is any extra risk as a result of taking part in this study.
One possible benefit is that some parents/guardians find it reassuring for their child to have the Bayley assessments as this is an extra assessment to what the child would normally receive. However, parents/guardians may feel they are unable to give the time required for the assessments.

Where is the study run from?
The study is run by the University of Bristol from the Bristol Royal Hospital for Children at the University Hospitals Bristol NHS Trust (UK).

When is study starting and how long is it expected to run for?
The study started in 2008 and is expected to run until approximately September 2014.

Who is funding the study?
The research is funded by two medical research charities, The BUPA Foundation and the Garfield Weston Trust (UK).

Who is the main contact?
Research Nurse: Karen Sheehan
Trial Coordinator: Lucy Dabner / Lucy Ellis
Chief Investigator: Prof. Massimo Caputo
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2010-019713-21

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
CS/2007/2678

Study information

Scientific Title
A randomised controlled trial to compare normoxic versus standard cardiopulmonary bypass in cyanotic children undergoing cardiac surgery

Acronym
OXIC-2

Study objectives
The principal hypothesis is that using lower levels of oxygen during cardiopulmonary bypass will reduce the levels of re-oxygenation injury to paediatric patients, measured both in terms of

clinical outcomes (e.g., length of post-operative hospital stay and type of care required) and in long term behavioural outcomes (measured preoperatively and 3 and 12 months post-operatively using the Bayley III Infant Development Scales).

As of 26/07/2012 the anticipated end date of this trial was updated from 01/06/2012 to 01/09/2014

Ethics approval required
Old ethics approval format

Ethics approval(s)
North Somerset and South Bristol Research Ethics Committee. Date of approval: 19/12/2007 (ref: 07/HO106/153)

Study design
Single-centre open 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
Children with a congenital heart defect which results in cyanosis and which are amenable to surgical repair

Interventions
All children will undergo surgery for repair of congenital cyanotic heart disease. All operations will be performed using cardiopulmonary bypass (CPB) with ascending aortic cannulation and bicaval venous cannulation. The experimental group will have normoxic (70-100 mmHg) CPB and the control group will have standard (relatively hyperoxic) (150-200 mmHg) CPB. Equal numbers of participants will be allocated to the two arms of the trial, stratified by age.

Intervention Type
Procedure/Surgery

Phase
Not Applicable

Primary outcome measure

Clinical outcomes:
1. Duration of inotropic support
2. Intubation time
3. Length of intensive care unit (ICU) stay
4. Length of hospital stay

Secondary outcome measures
1. In-hospital mortality and morbidity (e.g., blood loss, transfusion requirement, abnormal echocardiographic findings, abnormal post-operative blood test results)
2. Developmental assessments using the Bayley III Infant Development Scales measured pre-operatively and at 3 and 12 months after surgery (children aged up to 42 months only)
3. Assessment of brain injury using a biochemical marker (astroglial S100) measured pre-operatively, 10 and 30 minutes after starting CPB, 10 minutes after the end of surgery, and 4 and 24 hours after surgery
4. Renal function, measured by plasma creatinine and urea nitrogen levels taken every 24 hours for the first 5 days after surgery
6. Gene expression profiles associated with rexoygenation injury to the heart muscle

Overall study start date
01/06/2008

Completion date
05/06/2015

Eligibility

Key inclusion criteria
Current inclusion criteria as of 08/03/2013:
1. Cyanotic children undergoing operations to repair or palliate a heart defect
2. Children must be ≥1 month old to be eligible for all the neurocognitive assessments. Children <1 month old are eligible only for the 3 and 12 month post-operative neurocognitive assessments

Previous inclusion criteria until 08/03/2013:
1. Cyanotic children undergoing operations to repair or palliate a heart defect
2. Children aged >= 1 month of age

Previous inclusion criteria until 26/07/2012:
1. Cyanotic children (both males and females) undergoing operations to repair a heart defect
2. Children aged >= 1 month of age

Participant type(s)
Patient

Age group
Child

Sex
Both

Target number of participants

Key exclusion criteria
Current exclusion criteria as of 08/03/2013:
1. Children with a preoperative diagnosis of Downs syndrome or other developmental disorders are excluded from the neurocognitive assessments as part of the trial, but may be included in the main study
2. Emergency operations
3. Children requiring cardiovascular and/or respiratory support prior to study entry

Previous exclusion criteria until 08/03/2013:
1. Children with a preoperative diagnosis of Down's syndrome or other developmental disorders are excluded from the neurocognitive assessments as part of the trial, but may be included in the main study
2. Emergency operations
3. Patients undergoing arterial switch procedure
4. Neonatal patients (<1 month old)

Previous exclusion criteria as of 26/07/2012:
1. Preoperative diagnosis of Down's syndrome or other developmental disorders

Date of first enrolment
01/06/2008

Date of final enrolment
29/05/2014

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Bristol Royal Hospital for Sick Children
University Hospitals Bristol NHS Foundation Trust
Upper Maudlin Street
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Sponsor information

Organisation
University Hospitals Bristol NHS Foundation Trust

Sponsor details
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Sponsor type
Hospital/treatment centre

Website
http://www.uhbristol.nhs.uk/research-innovation/

ROR
https://ror.org/04nm1cv11

Funder(s)

Funder type
Charity

Funder Name
Bupa Foundation (UK) (ref: 5 FEB06)

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Funder Name
Garfield Weston (UK) (ref: PMS/MMS, 07/08, 3014)

Results and Publications

Publication and dissemination plan
The findings will be disseminated by presentation at international meetings, by peer-reviewed publications and through newsletters to participants.

Intention to publish date

Individual participant data (IPD) sharing plan
At the time of the research, parents/guardians of participants were not asked to consent to data sharing for future ethically approved studies. However, anonymised individual patient data may be made available for secondary research if further consent is obtained from participants /families and on condition of assurance from the secondary researcher that the proposed use of the data is compliant with the MRC Policy on Data Preservation and Sharing regarding scientific quality, ethical requirements and value for money. Please contact Professor Chris Rogers (chris.rogers@bristol.ac.uk) to discuss any data requests.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/07/2009		Yes	No