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Intermittent antegrade warm blood versus cold blood cardioplegia in children undergoing open heart surgery

Submission date
19/03/2018

Recruitment status
No longer recruiting

Registration date
05/04/2018

Overall study status
Completed

Last Edited
20/02/2023

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
Congenital heart disease is a problem in the structure of the heart that is present at birth. It is not uncommon and morbidity (illness) following heart surgery in children remains significant. Surgical repair of congenital heart defects usually requires the heart to be stopped using a cold solution containing potassium (cardioplegia) which protects the heart and keeps it still when operating. Cold cardioplegia solutions may have negative effects on the recovery of the heart after surgery in adults. However, very little is known about the effects of using warm cardioplegia solutions in children. The aim of this study is to compare warm and cold cardioplegia in children undergoing open heart surgery. Temperature monitoring is essential and always measured during the treatment of critically ill children. Rectal temperature monitoring is currently the most commonly used method for estimation of core body temperature in ill children. Multiple studies in adults and children have questioned the accuracy of rectal temperature monitoring when compared to pulmonary artery or urinary catheter monitoring. However, these studies are limited by small numbers. The study therefore also compares measurements of core body temperature obtained using a temperature sensing urinary catheter, a rectal temperature probe, and other temperature measuring devices such as axillary (armpit), oral (mouth), aural (ear) and oesophageal (food pipe) probes.

Who can participate?
Patients undergoing a congenital heart operation requiring cardiopulmonary bypass and cardioplegic arrest

What does the study involve?
Participants are randomly allocated to one of two groups to be treated with either warm or cold cardioplegia solutions to stop and protect the heart. Recovery and complications after surgery are compared between the two groups.

What are the possible benefits and risks of participating?
Participants in the cold cardioplegia group receive the same surgical procedure as patients not participating in the study and receive the same benefits inherent in cardiac surgery. Participants

in the warm cardioplegia group receive the same benefits. Recent evidence suggests that warm cardioplegia is safe in children and may improve outcomes.

Where is the study run from?
Bristol Royal Hospital for Children (UK)

When is the study starting and how long is it expected to run for?
December 2017 to September 2021 (updated 30/03/2021, previously: February 2021 (updated 29 /06/2020, previously: August 2020))

Who is funding the study?
British Heart Foundation (UK)

Who is the main contact?
Ms Lucy Dabner, thermic3-trial@bristol.ac.uk
(updated 29/06/2020, previously: Miss Rachael Heys, rh13369@bristol.ac.uk)

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number
211278

ClinicalTrials.gov number

Secondary identifying numbers
37109, IRAS 211278

Study information

Scientific Title
Intermittent antegrade warm blood versus cold blood cardioplegia in children undergoing open heart surgery: a randomised controlled trial (THERMIC-3)

Acronym
THERMIC-3

Study objectives
Congenital heart disease is not uncommon and morbidity following cardiac surgery in children remains significant. Surgical repair of congenital heart defects usually requires the heart to be stopped using a cold solution containing potassium (cardioplegia) which protects the heart and keeps it still when operating. Cold cardioplegia solutions may have deleterious effects on the recovery of the heart after surgery in adults. However, very little is known about the effects of using warm cardioplegia solutions in children. Therefore, children undergoing open heart surgery will be assigned by chance to one of two groups, using either warm or cold cardioplegia solutions to stop and protect the heart. Clinical and biochemical measures of recovery and complications following surgery will be compared between the two groups.

A sub-study will also look at methods for measuring core body temperature monitoring in children undergoing cardiac surgery with cardiopulmonary bypass. Temperature monitoring is an essential and a universally measured sign in the management of critically ill children. Rectal temperature monitoring is currently the most commonly used method for estimation of the core body temperature in ill children. Multiple studies in adults and children have questioned the accuracy of rectal temperature monitoring when compared to pulmonary artery or urinary catheter monitoring. However, these studies are limited by small numbers. The sub-study is a proof of concept study which will compare measurements of core body temperature obtained using a temperature sensing urinary catheter and a rectal temperature probe and other temperature measuring devices such as axillary, oral, aural and oesophageal probes.

Ethics approval required
Old ethics approval format

Ethics approval(s)
London Central Research Ethics Committee, 07/03/2018, ref: 18/LO/0205

Study design
Randomised; Interventional; Design type: Process of Care, Surgery

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 to request a patient information sheet

Health condition(s) or problem(s) studied
Congenital malformations of cardiac chambers and connections

Interventions
Eligible patients requiring congenital heart operations who give consent will be randomised to receive either warm blood cardioplegia or cold blood cardioplegia during their cardiac surgery. Clinical and biochemical measures of recovery and complications following surgery will be compared between the two groups.

Sub-study:
The sub-study is a proof of concept study which will compare measurements of core body temperature obtained using a temperature sensing urinary catheter and a rectal temperature probe and investigate the lag in changes in temperature with the two methods during therapeutic or pathological rapid changes in body core temperature. It will also investigate changes in the relationship between urinary bladder and rectal temperature measurements during low urinary output state (defined as urine output of less than 0.5ml/kg/hr) and compare the accuracy of these measurements with other temperature measuring devices such as axillary, oral, aural and oesophageal probes in the same cohort.

Intervention Type
Procedure/Surgery

Primary outcome measure
Troponin T (cTnT) levels over the first 48 postoperative hours

Secondary outcome measures
Current secondary outcome measures as of 18/03/2020:
1. Cardiac function, assessed by measuring cardiac output and cardiac index. Central venous saturations (ScvO2), arterial saturations, base deficit & blood lactate will also be recorded as indirect measures of cardiac index. Central venous saturations (ScvO2), arterial saturations, base deficit and blood lactate recorded as indirect measures of cardiac index up to 48 hours postoperatively
2. Routine blood gas and blood sample/test results measured before, during and after surgery (up to 48 hours postoperatively). Results collected will include pH, PO2, PCO2, base excess and lactate from blood gases and serum creatinine and urea nitrogen (measures of renal function), c-reactive protein (CRP), haemoglobin (Hb), haematocrit (Hct), white cell count (WCC) and alanine aminotransferase (ALT) from blood samples.
3. Renal function measured by urinary albumin, urinary creatinine, retinal binding protein (RBP), N- acetyl- β-glucosaminidase (NAG) and neutrophil gelatinase-associated lipocalin (n-GAL) in urine samples, measured before surgery and at 4 hours, 24 hours and 48 hours postoperatively
4. Cardiac and electrical activity on removal off cross clamp and chest closure (arrhythmias including; atrial fibrillation/flutter, ventricular tachycardia, ventricular fibrillation, nodal, junctional ectopic tachycardia (JET) or AV block)
5. Postoperative blood loss in the first 12 hours
6. New onset of arrhythmia post-operatively (either supraventricular tachycardia/atrial fibrillation or ventricular fibrillation/ventricular tachycardia, JET or heart block)
7. Vasoactive-inotrope score (VIS) over the first 48 hours after admission to PICU

8. Intubation time
9. Time from return from theatre until fit for discharge to the ward/high dependency unit (HDU) from the paediatric intensive care unit (PICU). Fit for discharge to the ward/HDU will reflect current HDU/ward admission criteria.
10. Chest and wound infections, recorded post-operatively
11. All-cause mortality to 3 months post-surgery
12. Length of postoperative hospital stay
13. Myocardial injury at the molecular and cellular level (e.g. transciptomics, proteonomics and metabonomics) measured in samples considered clinical waste during surgery
14. Body temperature from rectal, esophageal and urinary bladder and from oral, axillary and aural sites where possible for 8 hours after surgery (sub-study)

Previous secondary outcome measures:
1. Cardiac function, assessed by measuring cardiac output, cardiac index and myocardial contractility using trans-oesophageal echocardiography (TOE) during surgery and transthoracic echocardiography (TTE) pre-operatively and at 24 hours postoperatively. Central venous saturations (ScvO2), arterial saturations, base deficit and blood lactate recorded as indirect measures of cardiac index up to 48 hours postoperatively
2. Routine blood gas and blood sample/test results measured before, during and after surgery (up to 48 hours postoperatively)
3. Cerebral function/injury measured by Glial Fibrillary Acidic Protein (GFAP) before, during surgery and at 2 hours, 6 hours, 24 hours and 48 hours postoperatively
4. Renal function measured by urinary albumin, urinary creatinine, retinal binding protein (RBP), N- acetyl- β-glucosaminidase (NAG) and neutrophil gelatinase-associated lipocalin (n-GAL) in urine samples, measured before surgery and at 4 hours, 24 hours and 48 hours postoperatively
5. Cardiac and electrical activity on removal off cross clamp and chest closure (arrhythmias including; atrial fibrillation/flutter, ventricular tachycardia, ventricular fibrillation, nodal, junctional ectopic tachycardia (JET) or AV block)
6. Postoperative blood loss in the first 12 hours
7. New onset of arrhythmia post-operatively (either supraventricular tachycardia/atrial fibrillation or ventricular fibrillation/ventricular tachycardia, JET or heart block)
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Overall study start date
01/12/2017

Completion date
30/09/2021

Eligibility

Key inclusion criteria
Patients undergoing a congenital heart operation requiring CPB and cardioplegic arrest at the BRHC

Participant type(s)
Patient

Age group
Child

Sex
Both

Target number of participants
Planned Sample Size: 94; UK Sample Size: 94

Total final enrolment
97

Key exclusion criteria
1. Patient weighing < 3 kg
2. Patient requires an emergency operation (patient with haemodynamic instability who require immediate surgical intervention defined as operation within 24 hours of admission)
3. Patient requires secundum atrial septal defect repair (ASD) as an isolated procedure
4. Patient judged pre-operatively by surgeon to require deep hypothermic circulatory arrest (e.g. aortic arch repair, repair of total anomalous pulmonary venous drainage (TAPVD), Norwood procedure)
5. Patient judged pre-operatively by the surgeon to require deep hypothermic CPB
6. Patient judged by the surgeon pre-operatively to be too complex. This could be procedure related or patient related (e.g. complex tailor made surgery; necrotising enterocolitis; pre-operative brain haemorrhage; or generalised bleeding state/ongoing major bleeding)
7. Patient of consenting/assenting age lacking capacity to consent/assent
8. Patient under the care of social services and/or parent/guardian unavailable for consent

For the sub-study, the following additional exclusion criteria will apply:
9. Patient aged < 4 months
10. Patient weighing < 6 kg
11. Patient has contraindication for urethral catheterisation due to urethral obstruction or haemorrhage.

Date of first enrolment
08/05/2018

Date of final enrolment
01/04/2020

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Bristol Royal Hospital for Children
24 Upper Maudlin St
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United Kingdom
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Sponsor information

Organisation
University Hospitals Bristol NHS Foundation Trust

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Research and Innovation
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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/04nm1cv11

Funder(s)

Funder type
Charity

Funder Name
British Heart Foundation (BHF); Grant Codes: CH/1992027/7163 & CH/17/1/32804

Alternative Name(s)
the_bhf, The British Heart Foundation, BHF

Funding Body Type
Private sector organisation

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

Location
United Kingdom

Results and Publications

Publication and dissemination plan
The trialists plan to publish a protocol paper in the near future. The findings will be disseminated by the usual academic channels around one year after the overall trial end date, i.e. presentation at international meetings, as well as by peer-reviewed publications and through patient organisations and newsletters to patients, where available.

Intention to publish date
31/03/2022

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	14/10/2020	22/10/2020	Yes	No
Results article		17/02/2023	20/02/2023	Yes	No
HRA research summary			28/06/2023	No	No