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Use of a new blood test and a special camera for recording flow in the small blood vessels to identify children with poor outcomes after cardiac surgery

Submission date
17/07/2018

Recruitment status
Stopped

Registration date
31/07/2018

Overall study status
Stopped

Last Edited
18/01/2023

Condition category
Circulatory System

[X] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Children undergoing heart surgery are critically ill after the operation due to reasons such as (i) the effects of the heart disease on the body prior to the surgery, (ii) the cutting and sewing into the heart as part of the surgery and finally the use of a heart lung bypass machine during the operation which may lead to an production of detrimental chemicals by the body with widespread harmful effects. All these mechanisms lead to either a reduced pumping action of the heart or a reduction in blood flow to the tissues due to changes in the calibre of blood vessels or both. This results in deprivation of oxygen and nutrients to essential organs such as brain, lungs, liver, kidney and gut. It is estimated that about 25-30% of children undergoing heart surgery will experience such a complication to a varied severity. Currently, the diagnosis of this low flow condition is based upon clinical examination, scan of the heart (echocardiography) and blood markers such as lactate or oxygen saturations.
However, studies have shown that clinical estimation of this low flow condition is inaccurate in these children, echocardiography is often technically difficult due to open chest wall and fluid in the chest wall. Lactate and oxygen saturations may also have a lag time to demonstrate these changes. Hence, new markers and technologies are constantly being evaluated to detect these changes early enough to initiate corrective treatment strategy and minimise illness.
Recently, a new marker based upon analysis of gases (carbon dioxide and oxygen levels) in the blood estimated by blood gas analysis (essential blood test performed repeatedly in all children after cardiac surgery as a routine) has shown promising results in detecting these changes earlier than the routine tests in adult patients with poor heart function and reduced blood flow due to sepsis. In addition, recent advancement in the technology has enabled us to assess the status of the blood flow in the small vessels by taking a photograph of these small blood vessels under the tongue. This is a non-invasive procedure and is not painful.
We aim to investigate the utility of this new marker and the imaging device in 100 children undergoing heart surgery in order to accurately detect the detrimental changes in blood flow and oxygen delivery to essential organs earlier then the current methods. This could lead to early initiation of correct treatment hence, reducing the severity of illness and associated complications among these critically ill children.

Background and study aims
After a heart operation, about 25-30% of children have either a reduced pumping action of the heart and/or a reduction in the blood flow. This is due changes in the size of the blood vessels. This results in reduced delivery of oxygen and essential nutrients to vital organs such as the liver and kidneys, leading to a delay in their recovery. Currently, early diagnosis of this reduced blood flow is considered challenging and involves a combination of clinical examinations, heart scans (echocardiography) and blood tests measuring acid (lactate) and oxygen levels in the blood. However, all of these methods have their own limitations, which can mean a delay in diagnosis. Therefore, new tests are constantly being evaluated to detect these changes early and to start treatment sooner, reducing illness.
Recently, a new test based upon the blood gas analysis (carbon dioxide and oxygen content) has shown promising results in detecting these changes in severely ill adults.
In addition, we are now able to study blood flow in small blood vessels by taking their photographs with the help of a special camera. The photographs are taken from the surface underneath the tongue or inside of the cheeks. This is a non-invasive procedure and is not painful.
This study aims to use these two tests in children undergoing a heart operation to detect changes in the blood flow earlier than the current methods. If proven successful, this could lead to an early start of correct treatment and reduce the severity or duration of illness in future children undergoing heart operations

Who can participate?
Children aged up to 16 years undergoing open heart surgery with a heart-lung bypass

What does the study involve?
Before the operation, we will photograph the blood vessels on the underside of the child's tongue or inside of the cheeks before and after they are given anaesthetic, and after they have been put on the bypass machine for the heart operation.
After the operation, participants will receive a heart scan immediately after and around 24 hours after the operation is complete. They will also have their small blood vessels under the tongue or inside the cheeks photographed again. There will be blood tests for the 1-2 days they spend in the ICU to monitor oxygen, carbon dioxide and lactate (acid) in the blood, and to monitor the effect of heart surgery on the function of other organs such as the liver and kidney.

What are the possible benefits and risks of participating?
There are no known benefits to participants taking part in this study. There are no known risks to participants taking part in this study aside from the standard risks of the operation. The additional tests carried out in this study are non-invasive and not painful.

Where is the study run from?
Paediatric Intensive Care Unit at Royal Bristol Children’s Hospital in Bristol, UK

When is the study starting and how long is it expected to run for?
January 2017 to December 2022

Who is funding the study?
David Telling Charitable Trust (UK)

Who is the main contact?
1. Dr Alvin Schadenberg, alvin.schadenberg@uhbristol.nhs.uk
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Contact information

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Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CH/2017/6298

Study information

Scientific Title

The role of novel carbon-dioxide and oxygen based blood markers and Incident dark field micro-circulation imaging (IDFI) to identify children with high risk of adverse outcomes after cardiac surgery

Acronym
COMIC

Study objectives
Proposed novel CO_2 and O_2 derived variables (ratio between mixed venous-to-arterial CO_2 content difference and arterial-to-mixed venous O_2 content difference, and central veno-arterial carbon-dioxide tension difference p(cv-a) CO_2) measured sequentially after cardiac surgery will be able to identify children at risk of adverse outcomes assessed by composite time to complete organ failure resolution (CTCOFR score).

This study also aims to examine the presence of a relationship between absolute and delta (change) values of these novel and existing markers of tissue hypoxia (serum lactate and central venous saturations) with the absolute and delta values of the micro-circulation assessment captured simultaneously by IDFI.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 21/12/2018, London - Surrey Research Ethics Committee (Whitefriars, Level 3, Block B, Lewins Mead, Bristol, BS1 2NT, UK; +44 (0)207 1048058; surrey.rec@hra.nhs.uk), ref: 18/LO/1587

Study design
Observational prospective single-centre non-randomised observational cohort pilot study

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Other

Participant information sheet
Not available in web format, please use contact details to request a participant/parent information sheet.

Health condition(s) or problem(s) studied
Cardiac surgery involving cardiopulmonary bypass

Interventions
Alll participants will undergo the following tests/observations around the period of their cardiopulmonary bypass (CPB):

1. Incident Dark Field Microcirculation Imaging (IDFI) measurements using CytoCam IDF Imaging, at the time of admission to paediatric intensive care unit (PICU) and 6 and 24 hours afterwards (or, if patient is discharged before 24 hours, images will be acquired as close to the time of discharge as possible), along with pre and post induction of anaesthesia and once after the CPB where possible (depending on anaesthetic team availability, along with patients' clinical state and compliance)
2. Estimation of novel blood markers (markers of tissue hypoxia) post-anaesthesia, post-CPB and 0, 2, 4, 6, 8, 10, 12 and 24 post-admission to PICU:
2.1. The ratio between central venous-to-arterial CO_2 content difference and arterial-to-mixed venous O_2 content difference
2.2. Central veno-arterial CO_2 tension difference
2.3. Serum lactate
2.4. Central venous saturations
3. Information regarding respiratory and cardiovascular physiological parameters and support, including inotropes, NIRS, neurological status (including sedation and paralysis), urine output and blood gas analysis, recorded every 2 hours up to 12 hours after PICU admission, along with a final recording at 24 hours after admission or at the time of discharge (whichever is earlier)
4. Echocardiogram, at the time of admission to PICU and 24 hours after, in order to detect large residual shunts and assess ventricular function
5. Paediatric modified sequential organ failure assessment (p-mSOFA) 1 and 3 days after PICU admission or at time of discharge (whichever is earlier)
6. Composite time to complete organ failure resolution score (CTCOFR) and survival data, 30 days after PICU admission

Intervention Type
Device

Phase
Not Applicable

Primary outcome measure
The following will be measured at the point of PICU admission and 6 and 24 hours afterwards:
1. The relationship between the sequential central venous-to-arterial CO_2 content difference and arterial-to-mixed venous O_2 content difference ratio and composite time to complete organ failure resolution (CTCOFR) score, assessed using Spearman's Rho test and coefficient determination of R^2. Central venous-to-arterial CO_2 content difference and arterial-to-mixed venous O_2 content difference ratio will be calculated at the baseline (point of admission to PICU), and 6, 12 and 24 hours after admission. The CTCOFR score will be calculated 30 days after admission to PICU)
2. Practicability of sequential use of IDFI at beside, assessed using:
2.1. Recording ease of data capturing using a 1-3 scale (1 indicates "extremely difficult", 2 indicates "difficult" and 3 indicates "easy")
2.2. Quality of images, assessed by visual inspection on aspects such as illumination, focus, stability and pressure artefacts (randomly selected 8 sets from each time frame after PICU)
2.3. Patient compliance and concurrent use of anaesthetic agents
2.4. Reproducibility of CytoCam IDF imaging, assessed used the intraclass correlation efficient (ICC) by performing 2 subsequent measurement sets by 2 different trained operators within the same time frame

Secondary outcome measures

The agreement between the absolute and delta values of the following markers of tissue hypoxia (ratio between central venous-to-arterial CO_2 content difference and arterial-to-mixed venous O_2 content difference, mixed veno-arterial CO_2 tension difference, serum lactate and central venous saturations) and microcirculatory assays (total and perfused vessel density) at the baseline and 6 and 24 hours after PICU admission. This relationship will be determined using Spearman's Rho test and coefficient determination of R^2.

Overall study start date
11/01/2017

Completion date
31/12/2022

Reason abandoned (if study stopped)
Device malfunction

Eligibility

Key inclusion criteria
1. Aged up to 16 years
2. Requiring open heart surgery with cardio pulmonary bypass
3. Existing arterial and central venous catheters
4. Informed consent

Participant type(s)
Patient

Age group
Child

Upper age limit
16 Years

Sex
Both

Target number of participants
35

Total final enrolment
0

Key exclusion criteria
1. Large residual shunts,
2. Children with underlying lung disease requiring long term respiratory support or oxygen therapy (Persistent FiO_2 requirement of >30% and/or use of nasal continuous positive airway pressure (nCPAP) or positive pressure ventilation for more then 28 days immediately before the date of the surgery)

Date of first enrolment
01/01/2019

Date of final enrolment
31/12/2022

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University Hospital Bristol NHS Foundation Trust
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Sponsor information

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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/04nm1cv11

Funder(s)

Funder type
Not defined

Funder Name
David Telling Charitable Trust

Results and Publications

Publication and dissemination plan
It is intended that the results of the study will be reported and disseminated at international conferences and in peer-reviewed scientific journals. CI has also become a member of ESPNIC (European Society of Paediatric and Neonatal Intensive Care) haemodynamic group with an aim to collaborate with other national and international centres for future potential projects based upon the findings of this pilot.

Intention to publish date
31/03/2021

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
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No