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A randomised multiple centre trial of conservative versus liberal oxygenation targets in critically ill children (Oxy-PICU)

Submission date
06/01/2020

Recruitment status
No longer recruiting

Registration date
07/01/2020

Overall study status
Completed

Last Edited
20/12/2024

Condition category
Other

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

Plain English summary of protocol

Background and study aims
Around 20,000 children are admitted to paediatric intensive care units (PICU) each year in the UK. Around 75% of children admitted to PICU will receive additional oxygen, often in combination with a ventilator. Doctors and nurses adjust oxygen treatment based on how much oxygen their patient has in their blood, known as oxygen saturations. Whilst it is known that very low oxygen saturations are harmful, current research shows that very high saturations may also be dangerous for very ill people. Recent research in adults has shown that high oxygen saturations can lead to worse outcomes in emergencies like heart attacks and strokes. It is not known whether this harm is an effect of the oxygen level itself or a side-effect of the treatments given to keep oxygen levels high. Because of the differences in child and adult bodies, the results of this research cannot be applied to children. The aim of this study is to find out whether children in intensive care who are receiving oxygen while needing help from a ventilator should have their oxygen saturations kept at a lower level (88-92%, which is within recommended guidelines) or at the level currently used (95-100%).

Who can participate?
Children aged under 16 years from 15 NHS PICUs who are receiving oxygen while needing help from a ventilator

What does the study involve?
Participants are randomly allocated to the higher or lower oxygen saturation group which ensures that the two groups are as similar as possible. All other medical care is decided by the doctors and nurses. All participants are followed up after 90 days and one year to see how they are after leaving PICU.

What are the possible benefits and risks of participating?
The researchers cannot promise any benefit directly by participating in this study. The benefits and risks of maintaining lower blood oxygen levels are unclear at this time, which is why this

study is needed. Answering this question will help improve the future treatment of children in intensive care. If critically ill children on intensive care can be managed safely with slightly lower oxygen saturations, they might need less intensive treatment and may recover more quickly.

Where is the study run from?
Great Ormond Street Hospital for Children NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
August 2019 to September 2023

Who is funding the study?
National Institute for Health Research (NIHR) (UK)

Who is the main contact?
1. Paul Mouncey, oxypicu@icnarc.org
(updated 20/07/2020, previously: Mrs Daisy Wiley, daisy.wiley@icnarc.org)
2. Prof. Mark Peters, mark.peters@ucl.ac.uk

Study website
https://www.icnarc.org/Our-Research/Studies/Current-Studies/Oxy-Picu/About

Contact information

Type(s)
Public

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Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
272768

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 44070, IRAS 272768

Study information

Scientific Title
A randomised multiple centre trial of conservative versus liberal oxygenation targets in critically ill children (Oxy-PICU)

Acronym
Oxy-PICU RCT

Study objectives
Oxy-PICU is a multiple centre open, parallel-group, randomised control trial (RCT) with integrated economic analysis. An RCT design was chosen as this is the gold standard design for clinical trials.

Oxy-PICU aims to identify the best oxygen range to target in critically ill children to improve patient outcomes, with the hypothesis that a more conservative approach to oxygenation is superior to the more liberal approach often currently used.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 23/12/2019, East of England – Cambridge South (Tel: +44 (0)207 104 8134; Email: Nrescommitee.eastofengland-cambridgesouth@nhs.net), ref: 19/EE/0362

Study design
Randomized; Interventional; Design type: Treatment, Other

Primary study design

Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
See study outputs table

Health condition(s) or problem(s) studied
Critical care

Interventions
The researchers will recruit 2040 patients from 15 paediatric critical care units and their associated specialist retrieval services (teams of doctors and nurses that attend local hospitals to assist with the specialist care of critically ill children and their ambulance transportation to a regional, specialist paediatric intensive care unit).

The study will use a deferred consent model due to the emergency nature of the patient population. Eligible patients will be randomised by the PICU or the retrieval teams and their parents or legal guardians will be approached for consent to continue in the study at the earliest appropriate opportunity.

Whilst mortality is the most important outcome measure, it is challenging to adequately power a study on mortality alone within paediatrics. The researchers have therefore used information from qualitative work to inform a composite outcome. This work highlighted the child 'looking and feeling more like themselves' as the most important outcome measure for parents. The researchers will therefore use a combination of mortality (worst possible outcome) and days on organ support as the primary outcome.

Once recruitment is completed, an equal number of children will have been allocated to each treatment group:

Liberal group (greater than or equal to 95% blood oxygen)
Participants allocated to this group will receive supplement oxygen and ventilator settings at the discretion of the treating clinical team with the aim of peripheral oxygen saturations remaining at or above 95%. This will be continued until invasive mechanical ventilation is discontinued or PICU discharge, whichever is sooner.

Conservative group (88-92% blood oxygen)
Participants allocated to the conservative group will receive supplemental oxygen and ventilator settings at the discretion of the treating clinical team with the aim of peripheral oxygen saturations remaining 88-92% (inclusive). This will be continued until invasive mechanical ventilation is discontinued or PICU discharge, whichever is sooner. All other clinical care for patients in both treatment groups will be determined by the clinical team responsible for the patients care.

Data will be collected daily whilst in PICU to describe the intensity and duration of treatment, alongside routine data collection. Patients will be followed up after one year to ascertain their quality of life. One interim analysis will be undertaken.

An internal pilot will be conducted to assess key progression criteria in relation to site opening, recruitment and adherence to the protocol. The internal pilot will follow the same processes as the main trial and participants enrolled in the pilot will be included in the analysis of the main RCT. At the end of the internal pilot, the Trial Steering Committee will make a recommendation to the funder as to whether they feel the trial should continue. The funder will take the final decision.

Following the end of recruitment, analysis of the study data will take place and articles will be prepared for publication. It will not be possible to identify any participants in any publications.

Intervention Type
Other

Primary outcome measure
1. A composite of mortality and days of organ support at 30 days assessed through review of patient medical notes and/or data-linkage with nationally held death registrations (clinical effectiveness)
2. Incremental costs, quality-adjusted life years and net monetary benefit assessed using age-appropriate Pediatric Quality of Life Inventory (Peds-QL) and the Child Health Utility 9D (CHU-9D) at 12 months (cost effectiveness)

Secondary outcome measures
Current secondary outcome measures as of 09/11/2022:
1. Incremental costs calculated from patient-level resource data, length of stay in PICU/HDU and acute hospital for the index admission and any re-admission before 30 days after randomisation
2. Mortality assessed via patient medical notes and/or data linkage with nationally held death registrations at PICU discharge, 30 days, 90 days and 12 months
3. Time to liberation from mechanical ventilation, defined as the time the child was extubated and remained so for the remainder of their PICU stay
4. Duration of organ support during the child's PICU stay
5. Functional status at PICU discharge as assessed by a clinician using the Paediatric Cerebral Performance Category (PCPC) and Paediatric Overall Performance Category (POPC) scales using patient's notes
6. Duration of PICU and hospital stay assessed through review of patient medical notes at PICU discharge and hospital discharge
7. HrQoL at 12 months, measured by the child, self-or parent-proxy reported PedsQL-4.0 and the Child Heath Utility 9D (CHU-9D) at 12 months post randomisation

Previous secondary outcome measures:
1. Mortality assessed via patient medical notes and/or data linkage with nationally held death registrations at PICU discharge, 30 days, 90 days and 12 months
2. Time to liberation from mechanical ventilation defined as the time the child was extubated and remained so for the remainder of their PICU stay
3. Duration of organ support during the child's PICU stay
4. Duration of PICU and hospital stay assessed through review of patient medical notes at PICU discharge and hospital discharge

Overall study start date
01/08/2019

Completion date
30/09/2023

Eligibility

Key inclusion criteria
1. Age >38 weeks corrected gestational age and <16 years
2. Unplanned PICU referral
3. Commenced on invasive mechanical ventilation with supplemental oxygen
4. Within 6 hours of face-to-face contact with PICU staff or retrieval team

Participant type(s)
Patient

Age group
Child

Lower age limit
38 Weeks

Upper age limit
16 Years

Sex
Both

Target number of participants
Planned Sample Size: 2040; UK Sample Size: 2040

Total final enrolment
2040

Key exclusion criteria
1. Death perceived as imminent
2. Brain pathology/injury as primary reason for admission
3. Known pulmonary hypertension
4. Known or suspected uncorrected congenital cardiac disease
5. Known sickle cell disease
6. End-of-life care plan in place with limitation of resuscitation
7. Receiving long-term mechanical ventilation prior to this admission
8. Recruited to Oxy-PICU in a previous admission

Date of first enrolment
01/02/2020

Date of final enrolment
23/05/2022

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Great Ormond Street Hospital For Children NHS Foundation Trust
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Sponsor information

Organisation
Intensive Care National Audit and Research Centre (ICNARC)

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Sponsor type
Research organisation

ROR
https://ror.org/057b2ek35

Funder(s)

Funder type
Government

Funder Name

NIHR Evaluation, Trials and Studies Co-ordinating Centre (NETSCC); Grant Codes: NIHR127547

Funder Name
National Institute for Health Research (NIHR) (UK)

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
1. The protocol will be publicly available on the ICNARC and NIHR website
2. A protocol paper will be written and published (expected June 2020)
3. A statistical analysis plan paper will be written and publish (expected February 2021)
4. Peer-reviewed scientific journals
5. Conference presentation
6. Publication on website

Intention to publish date
31/01/2024

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from the Chief Investigator, Prof. Mark Peters (mark.peters@ucl.ac.uk). Application requests to access anonymised data for scientific research may be granted following review and approval by the Chief Investigator and the ICNARC CTU.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version v1.1	18/12/2019	07/01/2020	No	Yes
Other publications	Mechanistic substudy nested within the Oxy-PICU study	19/01/2023	01/03/2023	Yes	No

Protocol article	Protocol	01/09/2022	01/03/2023	Yes	No
Statistical Analysis Plan	version 1.2		01/03/2023	No	No
HRA research summary			20/09/2023	No	No
Results article		01/12/2023	05/12/2023	Yes	No
Results article		17/12/2024	20/12/2024	Yes	No