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A randomised controlled trial of high flow versus oxygen versus control in African children with severe pneumonia

Submission date
13/02/2016

Recruitment status
No longer recruiting

Registration date
20/02/2016

Overall study status
Completed

Last Edited
02/07/2025

Condition category
Infections and Infestations

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

Plain English summary of protocol

Background and study aims
Although giving oxygen is a basic element of hospital care, this treatment is costly and supplies are inadequate and erratic in African hospitals. The aim of this study is to identify which children would benefit from receiving oxygen and what would be the best delivery method.

Who can participate?
Children aged between 28 days and 12 years with a history of respiratory illness, hypoxia (lack of adequate oxygen supply) and signs of severe pneumonia (lung inflammation).

What does the study involve?
This study examines whether or not giving oxygen improves patient outcomes. For children with hypoxia, it is not certain what the best level to provide oxygen is and whether this results in a better outcome. The children with less severe hypoxia are randomly allocated to either receive oxygen or not. The children with more severe hypoxia all receive oxygen as we are more confident about the benefits of oxygen in this group. The children receiving oxygen are randomly allocated to receive oxygen either at a higher flow or at a lower flow (routine care). High flow oxygen provides extra pressure to the airways to prevent them from collapsing after every exhale. This helps reduce the effort of breathing, which is vital when lung infections can often lead to respiratory exhaustion and ultimately respiratory failure in critically sick children with limited access to relevant life support such as mechanical ventilation (the majority of hospitals in Africa).

What are the possible benefits and risks of participating?
The direct benefits to the child and/or family include:
1. Closer observation during the first 48 hours of admission, which, as a result, allows doctors and nurses to make important changes to the child’s treatment during in-hospital admission.
2. All routine non-trial medications required by the hospital to treat the child will be made available (when unavailable parents have to resort to sourcing these privately). All blood tests will be covered by the trial.
3. Reimbursement for transport cost after discharge and for follow up visits plus any treatment

costs required during the visits will be made. Snacks and drinks will be provided at each follow up visit.
High flow is an accepted strategy in the management of children with respiratory failure in a multitude of countries, with few reports that it is unacceptable, so the risks of harm from this strategy are known and are extremely low.

Where is the study run from?
1. Coast Provincial General Hospital, Mombasa (Kenya)
2. KEMRI Wellcome Trust Programme (Kenya)
3. Mulago Hospital (Uganda)
4. Mbale Regional Referral Hospital (Uganda)
5. Soroti Regional Referral Hospital (Uganda)

When is the study starting and how long is it expected to run for?
December 2016 to November 2019

Who is funding the study?
Joint Global Health Trials scheme (Medical Research Council, Department for International Development and Wellcome Trust)

Who is the main contact?
1. Prof. Kathryn Maitland (k.maitland@imperial.ac.uk)
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(updated 10/06/2020, previously: 2. Mr Ayub Mpoya (AMpoya@kemri-wellcome.org))

Contact information

Type(s)
Scientific

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Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
15IC3100, 203077/Z/16/Z

Study information

Scientific Title
Children's Oxygen Administration Strategies Trial (COAST): a randomised controlled trial of high flow versus oxygen versus control in African children with severe pneumonia

Acronym
COAST

Study objectives
1. To establish whether liberal oxygenation for SaO2 ≥80% will decrease mortality (at 48 hours and up to 28 days) compared with a strategy that includes permissive hypoxia (usual care)
2. To establish whether use of high flow oxygen delivery will decrease mortality (at 48 hours and up to 28 days) compared with low flow oxygen delivery (usual care)

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Imperial College, Research Ethics Committee, London, 18/08/2016, ref: 15IC3100
2. Faculty of Medicine, Research Ethics Committee Makerere University, Uganda, 29/02/2016, ref: 2016-030
3. KEMRI, Nairobi, Kenya, 31/10/2016, ref: KEMRI/RES/7/3/1

Study design
Open multicentre fractional factorial randomized 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 to request a patient information sheet

Health condition(s) or problem(s) studied
Severe pneumonia in African children

Interventions
The trial has two strata:
Stratum 1: severe hypoxia, SaO2 <80%); and Stratum 2: hypoxia SaO2 ≥80% and <92%).

Children in Stratum 1 (2-arm, 1:1 ratio) will all receive oxygen and randomisation will allocate participants to one of two methods of oxygen delivery:
1. High flow oxygen delivery
2. Low flow (usual practice) oxygen delivery

Children in Stratum 2 (3-arm, 2:1:1 ratio) will be allocated to:
1. Permissive hypoxia (no immediate oxygen): control
2. High flow oxygen delivery
3. Low flow oxygen delivery

The trial treatment period will last for a maximum of 48-hours post randomisation. After this time point, the participant will switch to usual care (standard clinical management). For children receiving oxygen delivered by high flow oxygen, at 48 hours, if oxygen is still required (i.e. failure to wean into room air) at this point, then the child will be switched to oxygen delivery by low flow (i.e. standard of care). During the 0-48 hour period, if a child is unable to tolerate high flow oxygen (indicated by a poor modified Comfort B (Behaviour) Scale score) and if oxygen is still required (i.e. failure to wean into room air), then the child will be switched to oxygen delivery by low flow (i.e. standard of care). If oxygen is discontinued before 48 hours e.g. hypoxia is resolved (SaO2 ≥92% measured continuously over 30 minutes) then they will switch to usual care (standard clinical management) following a successful trial of oxygen weaning.

All participants will be reassessed clinically at 1, 2, 4, 8, 12, 24 and 48 hours post-randomisation, and twice daily thereafter until discharged from hospital. All participants will then be seen at 4 weeks, and for those with suspected neurological sequelae an additional review will be done at 3 months post-randomisation. Any patient not returning for a study visit will be traced for vital status ascertainment (consent will be sought for this at recruitment).

Intervention Type
Mixed

Primary outcome measure
Mortality at 48 hours post-randomisation

Secondary outcome measures
1. Treatment failure at 48 hours
2. Survival to 28 days
3. Neurocognitive sequelae at 28 days
4. Disability-free survival to 28 days
5. Time to hypoxia (≥92%) resolution during initial hospital stay
6. Length of initial hospital stay
7. Re-admission to hospital by 28 days
8. Anthropometric status by 28 days
9. Resolution of neurocognitive sequelae at 90 days (for those with neurocognitive sequelae at 28 days)

Overall study start date
01/12/2016

Completion date
28/02/2020

Eligibility

Key inclusion criteria
1. Aged between 28 days to 12 years
2. History of respiratory illness (cough, upper respiratory tract symptom or any respiratory symptoms, e.g. rapid breathing or increase work of breathing)
3. Hypoxia (pulse oximetry reading of SaO2 <92% recorded in room air over 5 minutes)
4. Plus any one of the following signs of severe pneumonia (from 2013 WHO clinical definitions for pneumonia):
4.1. Sign of respiratory distress (any one of):
4.1.1. Severe lower chest wall in-drawing
4.1.2. Use of auxiliary muscles
4.1.3. Head nodding
4.1.4. Inability to feed because of respiratory problems
4.2. Suspected pneumonia
4.2.1. Fast breathing:
4.2.1.1. Age 2–11 months: ≥ 50/minute
4.2.1.2. Age 1–5 years: ≥ 40/minute
4.2.1.3. Age 5-12 years ≥ 30/minute
4.2.2. Chest auscultation signs:
4.2.2.1. Decreased breath sounds
4.2.2.2. Bronchial breath sounds
4.2.2.3. Crackles
4.2.2.4. Abnormal vocal resonance (decreased over a pleural effusion or empyema, increased over lobar consolidation)
4.2.2.5. Pleural rub
4.3. Signs of pneumonia with a general danger sign:

4.3.1. Inability to breastfeed or drink
4.3.2. Lethargy or unconscious
4.3.3. Convulsions

Participant type(s)
Patient

Age group
Child

Lower age limit
28 Days

Upper age limit
12 Years

Sex
Both

Target number of participants
4200

Total final enrolment
1852

Key exclusion criteria
1. Known uncorrected cyanotic heart disease
2. Assent/consent refusal by parent/carer
3. Previously recruited to COAST
4. Already received oxygen for this episode of illness

Date of first enrolment
01/12/2016

Date of final enrolment
28/02/2019

Locations

Countries of recruitment
Kenya

Uganda

Study participating centre
Coast Provincial General Hospital
Mombasa
Kenya
-

Study participating centre
KEMRI Wellcome Trust Programme
Kilifi District Hospital
PO Box 230
Kilifi
Kenya
-

Study participating centre
Mulago Hospital
Department of Paediatrics
Makerere University
PO Box 7072
Kampala
Uganda
-

Study participating centre
Mbale Regional Referral Hospital
Pallisa Road Zone
PO Box 921
Mbale
Uganda
-

Study participating centre
Soroti Regional Referral Hospital
PO Box 289
Soroti
Uganda
-

Study participating centre
Jinja Regional Referral Hospital
Uganda
-

Sponsor information

Organisation
Imperial College, London (UK)

Sponsor details
AHSC Joint Research Compliance Office
5th Floor Lab Block
Charing Cross Hospital
Fulham Palace Road
London
England
United Kingdom
W6 8RF

Sponsor type
University/education

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Research organisation

Funder Name
Joint Global Health Trials scheme (Medical Research Council, Department for International Development and Wellcome Trust)

Results and Publications

Publication and dissemination plan
All publications and presentations relating to the trial will be authorised by the Trial Management Group (TMG). The first publication of the trial results will be in the name of the TMG, if this does not conflict with the journal's policy. If there are named authors, these will include the chief investigator, Trial Statistician and Trial Manager. Members of the TMG, Trial Steering Committee (TSC) and Data Monitoring Committee (DMC) and other contributors will be cited by name, if this does not conflict with the journal's policy. Authorship of sub studies initiated outside of the TMG will be according to the individuals involved in the project but must acknowledge the contribution of the TMG. The TSC is the custodian of the data and specimens generated from the trial; trial data are not the property of individual participating investigators or health care facilities where the data were generated.

During the course and following completion of the trial there will be publications, including manuscripts and abstracts for presentations at national and international meetings, as well as

the preparation of manuscripts for peer-reviewed publication. In order to avoid disputes regarding authorship, a consensus approach will be established that will provide a framework for all publications derived in full or in part from this trial. Authorship criteria will be determined using the guidelines provided by The International Committee of Medical Journal Editors.

Dissemination plans
The trialists plan to communicate throughout the course of the trial with the following audience groups: national policymakers (Ministry of Health, child health services); international policymakers (WHO, UNICEF); healthcare workers, nursing and paediatric associations, and NGOs involved in providing treatment or advocacy for children with severe respiratory diseases; academics working in related fields; communities where the trial is taking place; and organisations who provide training to healthcare workers. Engaging with key audiences will be helped by the links the trial team already have with some key stakeholders.
The trial results will be made available in a number of different formats and fora, in order to be appropriate for and accessible to different audiences. There will be face-to-face meetings; workshops; open access peer-reviewed publication; policy briefs; presentation at international conferences; press releases; lay summaries; and websites. Depending on the results films and radio programmes may also be developed and distributed; and the trialists will consult with members of the intended audiences to assess what other opportunities and tools for communicating should be used.

Intention to publish date
30/08/2020

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	09/01/2018		Yes	No
Results article		01/05/2021	06/07/2021	Yes	No
Results article		01/07/2025	02/07/2025	Yes	No