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Mechanistic evaluation of two approaches to oxygen therapy in critical care (MecROX)

Submission date
14/01/2023

Recruitment status
No longer recruiting

Registration date
27/03/2023

Overall study status
Completed

Last Edited
15/08/2024

Condition category
Surgery

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

Plain English summary of protocol

Background and study aims
Although oxygen is necessary, excess oxygen can be harmful, especially to those requiring artificial ventilation. Usually, lungs are kept open by a detergent-like material in the lungs called "surfactant" so they can work properly. However, too much oxygen can kill the cells that make surfactant or increase surfactant breakdown. This can cause the lung to become damaged and fill with fluid instead of air, causing unnecessary harm. Too much oxygen can also cause powerful chemical reactions (called oxidative stress) that can damage cells around the body, causing major organs to fail. This can lead to the worsening of a patient's condition.

Aims: Intensive Care Patients (ICU) are often given oxygen via artificial ventilation through a breathing machine. Giving too much oxygen is harmful and can damage the lungs. We want to improve patient outcomes by understanding how excess oxygen causes lung damage. In this study, we aim to determine whether using a lower oxygen target in patients on a breathing machine reduces lung damage.

What does the study involve?
A national research study (UK-ROX, https://www.isrctn.com/ISRCTN13384956) is looking to find out whether giving less oxygen to patients in ICU will improve their survival compared to standard care (more oxygen). UK-ROX trial will not be able to assess how exactly the excess oxygen may cause harm. Therefore, this study will run in parallel with UK-ROX to look in more detail at how excess oxygen might affect the lungs.
We will take blood and lung fluid samples from these participants three times during the study. We will take blood from a small catheter already in place as part of their standard ICU treatment. Lung fluid samples will be taken through a small suction tube attached to the breathing tube already in their windpipe.

Who can participate?
Anyone aged 18 years or above who requires mechanical ventilation (breathing machine) to support their breathing in an intensive care unit setting. We intend to recruit 100 patients from the UK-ROX trial and conduct this detailed sub-study to determine whether surfactant and

oxidative stress play a role in excess oxygen-induced lung damage. Half of the participants will be recruited from the low oxygen group of UK-ROX and the other half from the standard oxygen group.

What are the possible benefits and risks of participating?
No direct benefit will accrue for participants. However, this study will improve the understanding of how oxygen causes damage to the lungs and may lead to the development of treatments that benefit patients with similar diseases.

Where is the study run from?
The study is conducted in two NHS centres, University Hospital Southampton and University Hospital Plymouth (UK)

When is the study starting, and how long is it expected to run for?
December 2022 to July 2025

Who is funding the study?
The NIHR Efficacy and Mechanism Evaluation Programme (UK)

Who is the main contact?
MecROX study team (mecrox@soton.ac.uk)
Chief Investigator, Dr A Dushianthan (a.dushianthan@soton.ac.uk)

Contact information

Type(s)
Principal Investigator

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

320671

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
IRAS 320671, CPMS 54827

Study information

Scientific Title
Oxidative stress, redox status and surfactant metabolism in mechanically ventilated patients receiving different approaches to oxygen therapy

Acronym
MecROX

Study objectives
We hypothesise that both hyperoxia and hyperoxemia increase alveolar and systemic oxidative stress and adversely impact surfactant metabolism. Specifically, in mechanically ventilated patients: (i) Administration of high inspired oxygen concentrations will contribute to increased alveolar and systemic oxidative stress; (ii) increased alveolar and systemic oxidative stress will result in adverse changes in surfactant metabolism. We will characterise these metabolic phenotypes according to surfactant metabolism and alveolar and systemic oxidative stress.

This is a sub-study of the UK-ROX interventional randomised controlled trial. https://www.isrctn.com/ISRCTN13384956

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 19/12/2022, London-Bromley Ethics Committee (Temple Quay House 2 The Square Temple Quay Bristol BS1 6PN, UK; +44 207 104 8118; bromley.rec@hra.nhs.uk), ref: 22/LO/0877

Study design
Prospective observational 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 the contact details to request a patient information sheet.

Health condition(s) or problem(s) studied
Mechanically ventilated patients from hypoxic respiratory failure.

Interventions
Participants from UK-ROX will be enrolled. They will receive methyl-D9 choline infusion followed by endotracheal aspirate, and blood sampling will be done 0, 48 and 72 hours after the study initiation.

Intervention Type
Procedure/Surgery

Primary outcome measure
The difference of percentage of DPPC (PC32:0) in relation to total phosphatidylcholine composition (% of total PC in surfactant) at 48 hours between conservative and usual oxygen target groups.

Secondary outcome measures
1. Surfactant index: This is a composite PC surfactant molecular index calculated from surfactant specific PC molecules (PC32:0, PC32:1 and PC30:0) and unsaturated surfactant PC34:1. This index will give a composite measure of surfactant PC alterations, which will provide a measure of surfactant PC status for the two different targets after 48 hours of oxygen therapy. This outcome is a measure of surfactant specific PC composition. Surfactant index = {32:0+32:1+30:0} 34:1
2. Surfactant phosphatidylcholine concentration (urea corrected) at 48 hours. This outcome is a measure of endogenous surfactant level.
3. Systemic oxidative stress: Total free thiols, lipid peroxides and total surfactant oxidation products. This outcome will measure whole-body oxidative stress.

Secondary explanatory outcomes
1. Surfactant total phosphatidylcholine and PC32:0 methyl-D9choline enrichment at 48 hours. Measure of endogenous surfactant synthesis. This will measure the surfactant PC synthesis via the CDP-Choline pathway.
2. Surfactant total lysoPC and lysoPC16:0 concentrations, composition and methyl-D9 choline enrichment at 48 hours. This outcome is a measure of endogenous surfactant breakdown. This will help to assess dynamic surfactant PC breakdown through hydrolysis.
3. Surfactant oxidised PC composition and concentrations at 48 hours. Measure of endogenous surfactant breakdown. This will help to assess dynamic surfactant breakdown by oxidation.
4. Whole- body redox balance by quantifying stable products of ROS (e.g., isoprostanes), RNS (e. g., nitrite, nitrate, nitrosation products) and RSS (e.g., total free thiols, thiosulfate, low molecular weight thiols including sulfide) at 48 hours from tracheal aspirates and plasma. Measure of lung and systemic redox status.
5. Comparison of clinical outcomes (ICU mortality, hospital mortality, 90-day mortality, ICU, and hospital length of stay) in relation to surfactant abnormalities.
6. Comparison of clinical outcomes (ICU mortality, hospital mortality, 90-day mortality, ICU, and hospital length of stay) in relation to specific markers of oxidative stress.

Overall study start date

19/12/2022

Completion date
01/07/2025

Eligibility

Key inclusion criteria
1. Enrolled in UK-ROX study
2. Aged greater or equal to 18 years
3. Receiving invasive mechanical ventilation in the ICU for hypoxaemic respiratory failure
4. Receiving supplemental oxygen (fractional inspired concentration of oxygen (FiO2>0.21 at the time of enrolment)
5. Anticipated to be mechanically ventilated for a minimum of 72 hours

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
100

Key exclusion criteria
1. Currently receiving extra corporeal membrane oxygenation (ECMO)
2. The treating clinician considers that one UK-ROX trial intervention arm is either indicated or contraindicated

Date of first enrolment
01/02/2023

Date of final enrolment
01/08/2024

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University Hospital Southampton
Southampton University Hospital
Tremona Road
Southampton
United Kingdom
SO16 6YD

Study participating centre
University Hospitals Plymouth NHS Trust
Derriford Hospital
Derriford Road
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Sponsor information

Organisation
University Hospital Southampton NHS Foundation Trust

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Tremona Road
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+44 2381205664
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Sponsor type
Hospital/treatment centre

Website
http://www.uhs.nhs.uk/home.aspx

ROR
https://ror.org/0485axj58

Funder(s)

Funder type

Government

Funder Name
Efficacy and Mechanism Evaluation Programme

Alternative Name(s)
NIHR Efficacy and Mechanism Evaluation Programme, EME

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact journal

Intention to publish date
01/10/2025

Individual participant data (IPD) sharing plan
The datasets generated during and or analysed during the current study are/will be available upon request from Dr Ahilanandan Dushianthan (a.dushianthan@soton.ac.uk)

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		08/07/2024	15/08/2024	Yes	No