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Can a nebulized medication reduce death rates in adults with severe lung failure on ventilators?

Submission date
20/03/2025

Recruitment status
Recruiting

Registration date
21/03/2025

Overall study status
Ongoing

Last Edited
23/04/2025

Condition category
Respiratory

[X] 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
Acute respiratory distress syndrome (ARDS) is a common and serious condition in intensive care units. It affects the lungs, making it difficult for patients to breathe normally, so they need mechanical ventilation to help them breathe. ARDS can be caused by various factors like infections, trauma, or smoke inhalation, and it has a high mortality rate because there is no single cause or definitive treatment. The main issue in ARDS is lung inflammation, and many anti-inflammatory medications have been tried. This study aims to see if nebulized furosemide, a drug usually used to increase urine production, can reduce death rates in ARDS patients on ventilators.

Who can participate?
Adults aged 18 years or older who have been on mechanical ventilation in the ICU for 7 days or less and are diagnosed with ARDS according to internationally accepted criteria can participate.

What does the study involve?
Participants will receive nebulized furosemide four times a day for up to 28 days. The study will monitor their health and progress during this period.

What are the possible benefits and risks of participating?
Possible benefits include reduced mortality, shorter duration on mechanical ventilation, and shorter ICU and hospital stays. While furosemide is generally safe, potential risks include allergic reactions, changes in blood element concentrations (especially potassium), increased urine output, and altered kidney functions.

Where is the study run from?
King Saud Medical City (Saudi Arabia)

When is the study starting and how long is it expected to run for?
The study will start recruiting patients on April 1, 2025, and is expected to complete by June 30, 2026.

Who is funding the study?
Investigator initiated and funded

Who is the main contact?
Dr Waleed Aletreby, waleedaletreby@gmail.com)

Contact information

Type(s)
Public, Scientific, Principal Investigator

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
researchregistry #10765

Study information

Scientific Title
Effect of Nebulized Furosemide on Mortality of Adult Mechanically Ventilated ARDS Patients. Protocol of a Randomized Clinical Trial (ENHALE Trial)

Acronym
ENHALE

Study objectives

Nebulized furosemide may be able to reduce 28 day ICU mortality of adult mechanically ventilated ARDS patients

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 29/08/2024, King Saud Medical City Institutional Review Board (Turki Bin Abdullah Street - Al Shemaisi, Riyadh, 12746, Saudi Arabia; +966118371777; irb@ksmc.med.sa), ref: H1RI-19-Aug24-01

Study design
Single center double blind placebo controlled parallel arm superiority randomized clinical trial

Primary study design
Interventional

Secondary study design
Randomised parallel trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
No participant information sheet available

Health condition(s) or problem(s) studied
Treatment of mechancally ventlated adults wiith Acute Respratory Distress Syndrome (ARDS)

Interventions
The intervention will be Nebulized Furosemide, in a dose of 40 mg furosemide in four ml of 0.9% saline, administered every six hours via the ventilator circuit over 30 minutes. The nebulization circuit used in our ICU is Aerogen ®. The intervention continues till extubation, death, or completion of 28 days

The control group receives placebo. They will receive the same regimen, but 0.9% Saline

Enrollment, randomization, and allocation concealment
Dedicated study team will round the ICU twice a day (8 AM and 8 PM) to identify patients who could be eligible for enrollment, once an eligible patient who fulfills inclusion criteria and has no exclusion criteria is identified, the patient or legal guardian will be approached for consenting in participation. Only after obtaining an informed consent, randomization will be obtained via phone call to an independent statistician who will provide a study code, without breaking the allocation concealment.
The independent statistician will prepare randomization sequences using variable size blocks (4, 6, 8) stratified by ARDS severity (Mild – Moderate – Severe), with unique study codes. Only the study code will be disclosed to the study team

Blinding
Furosemide and saline are identical in appearance, color, and solution characteristics. The investigational product will be prepared by an independent study pharmacist, put in identical vials, labelled only with study code and patient identifiers (name and MRN), and delivered to the clinical area. The independent study pharmacist will not have any contact with the clinical team, and will not participate in the clinical care, or any other study role.

Intervention Type
Drug

Pharmaceutical study type(s)
Dose response

Phase
Phase II

Drug/device/biological/vaccine name(s)
Furosemide

Primary outcome measure
28 day mortality measured using hospital records

Secondary outcome measures
1. All-cause hospital mortality is measured using hospital records at discharge
2. ICU length of stay (LOS) is measured using ICU records at discharge
3. Hospital length of stay (LOS) is measured using hospital records at discharge
4. Difference of P/F ratio is measured using arterial blood gas analysis at day one and day seven (not calculated for patients who are censored before seven days)
5. Ventilator-free days (VFD) is measured using ventilator records at 28 days
6. Successful extubation rate is measured using patient records at extubation
7. Hypersensitivity reactions of any magnitude are measured using patient reports and clinical assessments at any time during the study
8. Abnormal lab investigations, specifically electrolytes and renal function tests, are measured using blood tests at baseline and at regular intervals during the study
9. Volume of urine output is measured using urine output records at baseline and at regular intervals during the study

Overall study start date
12/01/2024

Completion date
30/06/2026

Eligibility

Key inclusion criteria
1. Adults (≥18 years).
2. ICU admission.
3. Mechanical ventilation for <7 days.
4. ARDS diagnosed within 24 hours per Berlin Definition, which includes:

4.1. Chest x-ray showing bilateral opacities, not fully explained by effusions, lobar/lung collapse, or nodules.
4.2. Respiratory failure not fully explained by cardiac failure or fluid overload, and exclusion of hydrostatic edema (by echocardiography).
4.3. Oxygenation and ventilator settings matching one of the three categories of ARDS: Mild: 200 mm Hg < PaO2/FIO2 ≤ 300 mm Hg with PEEP or CPAP ≥ 5 cm H2O. Moderate: 100 mm Hg < PaO2/FIO2 ≤ 200 mm Hg with PEEP ≥ 5 cm H2O. Severe: PaO2/FIO2 ≤ 100 mm Hg with PEEP ≥ 5 cm H2O.

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
784

Key exclusion criteria
1. Pregnant or lactating ladies.
2. Patients who are not expected to survive more than 48 hours, according to the treating team.
3. Mechanical ventilation is expected to continue for less than 48 hours (due to rapid recovery) according to the treating team.
4. Advanced directive of Do Not Resuscitate (DNR).
5. Refusal to participate in the trial by the patient, or official surrogate.
6. Known allergy to furosemide.
7. Previous enrollment in the trial (a patient can only be enrolled once).

Date of first enrolment
01/04/2025

Date of final enrolment
30/06/2026

Locations

Countries of recruitment
Saudi Arabia

Study participating centre
King Saud Medical City
Turki Bin Abdullah Street - Al Shemaisi
Rriyadh

Saudi Arabia
12746

Sponsor information

Organisation
King Saud Medical City

Sponsor details
Turki Bin Abdullah Street - Al Shemaisi
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Sponsor type
Hospital/treatment centre

Website
http://www.ksmc.med.sa/user_en/login_ar/index

ROR
https://ror.org/03aj9rj02

Funder(s)

Funder type
Other

Funder Name
Investigator initiated and funded

Results and Publications

Publication and dissemination plan
Once the study s coompleted, and a manuscript has been drafted and approved by all authors, we plan to publish the study in a peer reviewed journal.

Intention to publish date
01/01/2027

Individual participant data (IPD) sharing plan

The dataset generated during and/or analysed during the current study will be stored in a publicly available repository. We plan to store data in: https://www.kaggle.com/

IPD sharing plan summary

Stored in publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file			21/03/2025	No	No
Protocol article		22/03/2025	23/04/2025	Yes	No