

Clinical Trial Protocol

Iranian Registry of Clinical Trials

25 Jul 2026

Comparison the efficacy of adding levofloxacin and colistin inhalation form to basic regimen of colistin and meropenem in treatment of ventilator associated pneumonia (VAP) caused by multidrug resistant pathogens: a double-blind randomized clinical trial

Protocol summary

Study aim

Efficacy comparison of adding levofloxacin and colistin inhalation form to basic regimen of colistin and meropenem in treatment of ventilator associated pneumonia (VAP) caused by multi drug resistant pathogens (MDR)

Design

Parallel group randomized phase 3 on 46 patients trial with Random allocation software double blinded

Settings and conduct

46 patients of Imam Khomeini Hospital after consent form Drug prescription by doctors based on specific codes Registration: Demographic, duration of intubation before pneumonia, APACHE II: day1 WBC, ESR, CRP, BUN, SOFA, SCr, ABG, respiratory tract compliance and resistance: days 1, 3, 5 and 7 CPIS: days 1, 5 and 7 (or stop intervention day) Respiratory secretions sample: the last day PCT measurement: first and last day One pharmaceutical company produce vials with attempting to same appearance nurse preparation Blinding for clinical assistant and evaluator

Participants/Inclusion and exclusion criteria

Inclusion: 18-80 years Mechanical ventilation more than 48 hours Pneumonia diagnosis based on 2016 guidelines of IDSA CPIS score above 6 Positive MDR gram-negative bacteria sputum culture Exclusion: Pregnancy/lactation Allergy history and major interaction with intervention drugs Acute respiratory distress syndrome/Pulmonary tuberculosis under treatment/Cystic fibrosis Baseline creatinine clearance less than 15 mL/min Receiving effective antibiotics against MDR pathogens during hospitalization Pneumonia before intubation

Intervention groups

23 patients in each group Ultrasound nebulizer Inhaled Colistin 2 million units every 8 hours or levofloxacin 250 mg every 12 hours Both: infusion of meropenem 1 gram

every 8 hours and 9 million loading units of colistin and 4.5 million units every 12 hours up to 7 days Dose adjustment in renal failure

Main outcome variables

Average CPIS score reduction in two groups on days 1, 5, 7 (or stop intervention day)

General information

Reason for update

Limitation on the number of eligible patients and implementation facilities of the clinical trial

Acronym

IRCT registration information

IRCT registration number: **IRCT20100107003014N26**

Registration date: **2023-11-13, 1402/08/22**

Registration timing: **registered_while_recruiting**

Last update: **2024-10-17, 1403/07/26**

Update count: **1**

Registration date

2023-11-13, 1402/08/22

Registrant information

Name

Shahram Ala

Name of organization / entity

Mazandaran University of Medical Sciences

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Iran (Islamic Republic of)

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Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2023-10-23, 1402/08/01

Expected recruitment end date

2024-04-20, 1403/02/01

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

Comparison the efficacy of adding levofloxacin and colistin inhalation form to basic regimen of colistin and meropenem in treatment of ventilator associated pneumonia (VAP) caused by multidrug resistant pathogens: a double-blind randomized clinical trial

Public title

Efficacy of levofloxacin and colistin inhalation form in treatment of pneumonia

Purpose

Treatment

Inclusion/Exclusion criteria**Inclusion criteria:**

Age older than 18 years and less than 80 years
Mechanical ventilation for more than 48 hours
Pneumonia diagnosis based on the 2016 guidelines of the Infectious Diseases Society of America (IDSA) CPIS score above 6 Positive culture of sputum sample and growth of gram-negative bacteria resistant to treatment (MDR) (Acinetobacter baumannii, Pseudomonas aeruginosa, Enterobacteriaceae, etc.)

Exclusion criteria:

Pregnancy or breastfeeding History of allergy to any of the drugs Colistin, Levofloxacin and Meropenem Acute respiratory distress syndrome Pulmonary tuberculosis disease under treatment Cystic fibrosis disease Major interaction of other drugs used by the patient with levofloxacin, colistin or meropenem Baseline creatinine clearance less than 15 mL/min History of receiving antibiotics effective against MDR pathogens during hospitalization Presence of pneumonia before intubation

Age

From **18 years** old to **80 years** old

Gender

Both

Phase

1-2

Groups that have been masked

- Participant
- Investigator
- Outcome assessor
- Data analyser

Sample size

Target sample size: **46**

More than 1 sample in each individual

Number of samples in each individual: **23**

23 patients in the inhaled colistin group will receive this drug at a dose of 2 million units every 8 hours along with

meropenem infusion 1 gram every 8 hours for 3 hours and colistin infusion at a dose of 9 million units at first and then 4.5 million units every 12 hours for 1 hour up to 7 days. 35 patients in the inhaled levofloxacin group will receive an injection vial of this drug at a dose of 250 mg every 12 hours with an ultrasound nebulizer along with an infusion of meropenem 1 g every 8 hours for 3 hours and an infusion of colistin at a dose of 9 million units at first and then for 4.5 million units every 12 hours for 1 hour up to 7 days.

Randomization (investigator's opinion)

Randomized

Randomization description

After selecting patients with inclusion criteria, random allocation will be done by block method. Blocking process will be done with Random allocation software. With this software, the number of blocks and the size of each block will be determined. The samples are entered into the study based on the randomly generated numbers.

Blinding (investigator's opinion)

Double blinded

Blinding description

The diagnosis of VAP will be made by special care specialists (project partners). Consumable vials for use in the nebulizer device will be purchased from a pharmaceutical company, and the appearance of the vials will be similar. The ward nurse is in charge of preparing the device and prescribed inhaler for patients to use. Covering the therapeutic intervention is done for the clinical pharmacy assistant and the person who examines the study results.

Placebo

Not used

Assignment

Parallel

Other design features**Secondary Ids**

empty

Ethics committees**1****Ethics committee****Name of ethics committee**

Ethics department of Mazandaran University of Medical Sciences

Street address

Moallem square, Sari, Mazandaran, Iran

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Sari

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Mazandaran

Postal code

33971- 48157

Approval date

2023-09-23, 1402/07/01

Ethics committee reference number

IR.MAZUMS.REC.1402.423

Health conditions studied

1

Description of health condition studied

Ventilator associated pneumonia (VAP) caused by multidrug resistant pathogens

ICD-10 code

J95.851

ICD-10 code description

Ventilator associated pneumonia

Primary outcomes

1

Description

Average CPIS score reduction in two groups

Timepoint

days 1, 5, 7 (or stop intervention day)

Method of measurement

CPIS scoring table

Secondary outcomes

1

Description

The incidence of acute kidney injury (AKI) in patients of two groups during treatment according to the KDIGO definition, defined as increase in serum creatinine of 0.3 mg/dl or more within 48 hours or an increase in serum creatinine of ≥ 1.5 times

Timepoint

Days 1, 3, 5 and 7 of intervention

Method of measurement

Blood sample sent to the laboratory

2

Description

Registration of bronchospasm complication occurred during treatment in two groups of patients

Timepoint

During the intervention

Method of measurement

Airway resistance in the ventilator

3

Description

Improvement rate in compliance and resistance of the respiratory tract in patients of two groups

Timepoint

Days 1, 3, 5 and 7 of intervention

Method of measurement

Ventilator data and calculation according to the formula

4

Description

Mortality rate of patients in two groups until the duration

of hospitalization in ICU

Timepoint

During the intervention up to the duration of ICU stay

Method of measurement

Patient database

5

Description

The 28-day mortality rate of patients in two groups

Timepoint

28 days after pneumonia caused by mechanical ventilation

Method of measurement

Patient database

Intervention groups

1

Description

Intervention group: Inhaled colistin at a dose of 2 million units every 8 hours with ultrasound nebulizer along with meropenem infusion 1 gram every 8 hours for 3 hours and colistin infusion at a dose of 9 million units loading and then 4.5 million units every 12 hours for 1 hour up to 7 days

Category

Treatment - Drugs

2

Description

Intervention group: Inhaled levofloxacin vial with a dose of 250 mg every 12 hours with ultrasound nebulizer along with meropenem infusion 1 gram every 8 hours for 3 hours and colistin infusion at a dose of 9 million units loading and then 4.5 million units every 12 hours for 1 hour up to 7 days

Category

Treatment - Drugs

Recruitment centers

1

Recruitment center

Name of recruitment center

Imam Khomeini hospital

Full name of responsible person

Shahram Ala

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Razi street

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Sponsors / Funding sources

1

Sponsor

Name of organization / entity

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Full name of responsible person

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Grant name**Grant code / Reference number****Is the source of funding the same sponsor organization/entity?**

Yes

Title of funding source

Mazandaran University of Medical Sciences

Proportion provided by this source

100

Public or private sector

Public

Domestic or foreign origin

Domestic

Category of foreign source of funding

empty

Country of origin**Type of organization providing the funding**

Academic

Person responsible for general inquiries

Contact**Name of organization / entity**

Mazandaran University of Medical Sciences

Full name of responsible person

Shahram Ala

Position

Professor

Latest degree

Specialist

Other areas of specialty/work

Medical Pharmacy

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Sharing plan**Deidentified Individual Participant Data Set (IPD)**

Undecided - It is not yet known if there will be a plan to make this available

Study Protocol

Undecided - It is not yet known if there will be a plan to make this available

Statistical Analysis Plan

Undecided - It is not yet known if there will be a plan to make this available

Informed Consent Form

Undecided - It is not yet known if there will be a plan to make this available

Clinical Study Report

Undecided - It is not yet known if there will be a plan to make this available

Analytic Code

Undecided - It is not yet known if there will be a plan to make this available

Data Dictionary

Undecided - It is not yet known if there will be a plan to make this available