

Clinical Trial Protocol

Iranian Registry of Clinical Trials

10 Jun 2026

The effect of L-citrulline supplementation in ventilated intensive care unit patients: A double-blind randomized controlled trial

Protocol summary

Registration timing: **registered_while_recruiting**

Study aim

This study aims to evaluate the effects of citrulline on respiratory capacity, number of days spent in ventilator, mortality rate, number of hospital days and metabolic, oxidative and inflammatory status in critically ill patients admitted to the intensive care unit.

Last update: **2022-06-21, 1401/03/31**

Update count: **0**

Registration date

2022-06-21, 1401/03/31

Design

A randomized, double-blind clinical trial with two parallel groups, with a control group, on 60 patients. Random allocation software was used for randomization.

Registrant information

Name

Mohammadreza Askari

Name of organization / entity

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Settings and conduct

This study is a randomized clinical trial that will be conducted on patients admitted to the intensive care unit (ICU) of Imam Reza Hospital of Tehran affiliated with the AJA University of Medical Sciences in 2022.

Recruitment status

Recruitment complete

Funding source

Participants/Inclusion and exclusion criteria

Subjects will enroll if they require invasive ventilation via an intubation or tracheotomy tube for at least 72 hours after study entry. They will be expected to survive and remain in the ICU for at least 96 hours after its onset. Exclusion criteria are the age of fewer than 18 years, pregnancy, previous allergy to citrulline or arginine, a history of gastrointestinal disease, digestive tract surgery, intestinal obstruction, paralytic ileus, intestinal ischemia, septic patients, and hyperthyroidism.

Expected recruitment start date

2022-01-20, 1400/10/30

Expected recruitment end date

2022-07-21, 1401/04/30

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Intervention groups

Patients in placebo and Citrulline groups will receive 10 grams/day Microcrystalline cellulose and L-Citrulline powder respectively for 7 days.

Scientific title

The effect of L-citrulline supplementation in ventilated intensive care unit patients: A double-blind randomized controlled trial

Main outcome variables

Clinical outcomes, Blood sample collection

Public title

The effect of L-citrulline supplementation in ventilated intensive care unit patients

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20210920052530N1**

Registration date: **2022-06-21, 1401/03/31**

Purpose

Supportive

Inclusion/Exclusion criteria**Inclusion criteria:**

Required invasive ventilation via an intubation or tracheotomy tube for at least 72 hours after study entry
Expected to survive and remain in the ICU for at least 96 hours after its onset

Exclusion criteria:

The age of fewer than 18 years
Pregnancy
Previous allergy to citrulline or arginine
A history of gastrointestinal disease, digestive tract surgery, intestinal obstruction, paralytic ileus, intestinal ischemia, septic patients, and hyperthyroidism

Age

From **18 years** old

Gender

Both

Phase

3

Groups that have been masked

- Participant
- Care provider
- Investigator
- Outcome assessor
- Data analyser

Sample size

Target sample size: **30**

Randomization (investigator's opinion)

Randomized

Randomization description

Subjects will be randomly assigned for each group via a computer-generated assignment sequence in a centralized, blinded fashion. The randomization sequence is programmed in advance and generated by a statistician independent of the study. Physicians will be assigned the treatment after randomization, which are accessible through dedicated web-based software. Investigators, patients, and research staff were masked to the randomization list.

Blinding (investigator's opinion)

Double blinded

Blinding description

Except for the pharmacist who is in charge of preparing the supplements and the randomization sequence, Investigators, patients, and research staff were masked to the randomization list. This study is used to conceal the random allocation of coded cans. It will be hidden from participants and researchers until the end of the study. The degree of compliance of hospitalized people with the assigned intervention will be done by reviewing the drug card of the hospitalized ward.

Placebo

Used

Assignment

Other

Other design features**Secondary Ids**

empty

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

Research Ethics Committees of AJA University of Medical Sciences

Street address

AJA university of medical sciences, Etemad zadeh street, Fatemi-Gharbi Street, Tehran, Iran.

City

Tehran

Province

Tehran

Postal code

1416753955

Approval date

2022-01-12, 1400/10/22

Ethics committee reference number

IR.AJAUMS.REC.1400.269

Health conditions studied**1****Description of health condition studied**

Ventilated intensive care unit patients

ICD-10 code

J95.85

ICD-10 code description

Complication of respirator [ventilator]

Primary outcomes**1****Description**

Ventilator dependence

Timepoint

Count the number of ventilator dependence days up to 28 days after supplementation

Method of measurement

Count the number of ventilator dependence days

2**Description**

Mortality Rate

Timepoint

Number of deaths due to a specific disease divided by the total number of patients up to 28 days after supplementation

Method of measurement

Number of deaths due to a specific disease divided by the total number of patients

3

Description

Evaluate the severity of the disease

Timepoint

Before the intervention and on days 7 and 28 after starting the supplement

Method of measurement

Measurement of disease severity is calculated based on the parameters of blood pressure, blood gases and patient's consciousness.

4

Description

Evaluate the malfunction of multi-organ

Timepoint

Before the intervention and on days 7 and 28 after starting the supplement

Method of measurement

The Multi-Organ Dysfunction Questionnaire is calculated based on markers such as blood pressure, respiratory gases, respiratory support, bilirubin, platelets and creatinine, and the patient's urea.

5

Description

Clinical Pulmonary Infection Score (CPIS)

Timepoint

Before the intervention and on days 7 and 28 after starting the supplement

Method of measurement

Using the CPIS questionnaire

6

Description

Duration of hospitalization

Timepoint

The interval between the period of admission and the period of discharge from the hospital in terms of days

Method of measurement

The interval between the period of admission and the period of discharge from the hospital in terms of days

Secondary outcomes

1

Description

Blood indicators

Timepoint

Before the intervention and 7 days after starting the supplement

Method of measurement

CRP is measured by the method of agglutination of latex particles on the slide (ENISON Co kits). Albumin is assessed with a commercially available enzyme-linked immunosorbent assay (ELISA) kit (Abcam). Blood urea nitrogen (BUN) is determined using enzymatic methods. Alanine transaminase (ALT), aspartate transaminase (AST), and lactate dehydrogenase (LDH) are measured

based on the method recommended by the IFCC (International Federation of Clinical Chemistry).

Intervention groups

1

Description

Intervention group: Patients in the citrulline group will receive 10 grams of L-citrulline powder daily for 7 days.

Category

Treatment - Drugs

2

Description

Control group: Patients in the placebo group will receive 10 grams of microcrystalline cellulose per day for 7 days.

Category

Treatment - Drugs

Recruitment centers

1

Recruitment center

Name of recruitment center

Imam Reza (AJA) Hospital

Full name of responsible person

Saeid Hadi

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Etemad zadeh street, Fatemi-Gharbi Street, Tehran, Iran

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Sponsors / Funding sources

1

Sponsor

Name of organization / entity

Artesh University of Medical Sciences

Full name of responsible person

Saeid Hadi

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AJA university of medical sciences, Etemad zadeh street, Fatemi-Gharbi Street, Tehran, Iran.

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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

Artesh 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**

Artesh University of Medical Sciences

Full name of responsible person

Mohammad Reza Asgary

Position

University student

Latest degree

Master

Other areas of specialty/work

Nutrition

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Person responsible for scientific inquiries**Contact****Name of organization / entity**

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Full name of responsible person

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Position

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Person responsible for updating data**Contact****Name of organization / entity**

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

No - There is not a plan to make this available

Justification/reason for indecision/not sharing IPD

There is no more information

Study Protocol

Yes - There is 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

Yes - There is a plan to make this available

Clinical Study Report

Yes - There is 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

Title and more details about the data/document

Access to the data is possible only with the permission of the Army University of Medical Sciences.

When the data will become available and for how long

The access period starts 6 months after the results are published

To whom data/document is available

There is no more information

Under which criteria data/document could be used

There is no more information

From where data/document is obtainable

There is no more information

What processes are involved for a request to access data/document

There is no more information

Comments