Clinical Trial Protocol
Iranian Registry of Clinical Trials

09 Nov 2026

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

Protocol summary

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.

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.

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.

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.

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

Main outcome variables
Clinical outcomes, Blood sample collection

General information

Reason for update

Acronym

IRCT registration information
IRCT registration number: **IRCT20210920052530N1**
Registration date: **2022-06-21, 1401/03/31**
Registration timing: **registered_while_recruiting**

Last update: **2022-06-21, 1401/03/31**
Update count: **0**

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

Registrant information
Name
Mohammadreza Askari
Name of organization / entity
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Recruitment status
Recruitment complete

Funding source

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

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

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

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
Street address
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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Phone
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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
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Position
University student
Latest degree
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Other areas of specialty/work
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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