

Clinical Trial Protocol

Iranian Registry of Clinical Trials

13 Jun 2026

Methylene Blue for the Treatment of COVID-19: A Randomized Clinical Trial

Protocol summary

Study aim

To evaluate the effect of intravenous methylene blue on the clinical course and outcomes of patients with COVID-19 infections

Design

This is a parallel design, single center, phase 3, concealed randomized clinical trial study which will be conducted on 260 patients. Patients will be randomized into two groups using an online program available from <https://www.sealedenvelope.com/simple-randomiser/v1/lists>.

Settings and conduct

This study will be conducted in the Shiraz Transplant Center, Abu Ali Sina Hospital, Shiraz, Iran. Patient will have 24-hour heart monitoring. In order to minimize any bias between groups as a general policy, all patients will only receive lopinavir/retonavir (Kaletra®) as their treatment regimen for COVID-19.

Participants/Inclusion and exclusion criteria

inclusion criteria: 1. >18 yrs old 2. PCR confirmation of COVID-19 3. Severe or critical diseases as: RR>30 breaths/second, SpO₂<94% on room air sea level, lung infiltration of >50%, PaO₂/FiO₂ <300 mmHg and/or any individual with respiratory failure, septic shock, and/or multiple organ dysfunction exclusion criteria: 1. Pregnancy 2. G6PD deficiency 3. Severe renal failure (defined as GFR<30 mL/min/1.3m²) 4. History of allergic reaction to drug 5. Patients on serotonergic psychiatric drugs (including SSRIs, SNRIs, TCAs, MAOIs), dapsone and different hydroxylamine 6. Organ transplantation recipients 7. Not consenting to enter study

Intervention groups

Intervention group: Kaletra and corticosteroid and methylene blue. Control group: Kaletra and corticosteroid.

Main outcome variables

Death; partial pressure of oxygen/Fraction of inspired oxygen ; Length of intensive care unit stay; In-hospital complications rates; white blood cell count/leukopenia;

C-reactive protein levels

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20090701002113N2**

Registration date: **2020-08-25, 1399/06/04**

Registration timing: **registered_while_recruiting**

Last update: **2020-08-25, 1399/06/04**

Update count: **0**

Registration date

2020-08-25, 1399/06/04

Registrant information

Name

Jamshid Roozbeh

Name of organization / entity

Shiraz university of medical sciences

Country

Iran (Islamic Republic of)

Phone

+98 71 1235 6400

Email address

roozbehj@sums.ac.ir

Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2020-08-15, 1399/05/25

Expected recruitment end date

2020-12-15, 1399/09/25

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

Methylene Blue for the Treatment of COVID-19: A
Randomized Clinical Trial

Public title

Methylene Blue in COVID-19

Purpose

Treatment

Inclusion/Exclusion criteria**Inclusion criteria:**

>18 yrs old PCR confirmation of COVID-19 Severe or critical diseases as: respiratory rate>30 breaths/second, oxygen saturation<94% on room air sea level, lung infiltration of >50%, partial pressure of oxygen/Fraction of inspired oxygen <300 mmHg and/or any individual with respiratory failure, septic shock, and/or multiple organ dysfunction

Exclusion criteria:

Pregnancy G6PD deficiency Severe renal failure (defined as glomerular filtration rate<15 mL/min/1.3m²) History of allergic reaction to drug Patients on serotonergic psychiatric drugs (including selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake Inhibitors, tricyclic antidepressants, monoamine oxidase inhibitors), dapson and different hydroxylamine Organ transplantation recipients Not consenting to enter study

Age

From **18 years** old

Gender

Both

Phase

3

Groups that have been masked

No information

Sample size

Target sample size: **260**

Randomization (investigator's opinion)

Randomized

Randomization description

Random allocation (case:control 1:1) will be done using the permuted block randomization method (block size of 4). The randomization sequence will be generated with an online program available from <https://www.sealedenvelope.com/simple-randomiser/v1/lists>. The generated random sequence will be inserted in an opaque envelop enumerated in sequence from 001 to 260, each of which will be used for consecutive study participants.

Blinding (investigator's opinion)

Not blinded

Blinding description**Placebo**

Not used

Assignment

Parallel

Other design features**Secondary Ids**

empty

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

Ethics Committee of Shiraz University of Medical Sciences

Street address

Zand Street

City

Shiraz

Province

Fars

Postal code

7134814336

Approval date

2020-04-05, 1399/01/17

Ethics committee reference number

IR.SUMS.REC.1399.016

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

COVID-19 infection

ICD-10 code

U07.1

ICD-10 code description

COVID-19, virus identified

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

Death

Timepoint

2 weeks after intervention

Method of measurement

follow-up visit

Secondary outcomes**1****Description**

partial pressure of oxygen/Fraction of inspired oxygen

Timepoint

first day of hospital admission, and 1, 3, and 5 days after administration

Method of measurement

By measuring arterial blood gas

2**Description**

Length of hospital stay
Timepoint
Daily until discharge
Method of measurement
Daily follow-up visitation

3

Description
ICU admission rate
Timepoint
Daily until the end of hospitalization
Method of measurement
Daily follow-up visitation

4

Description
In-hospital complications rates
Timepoint
Daily until the end of hospitalization
Method of measurement
Daily follow-up visitation

5

Description
White blood cell count/leukopenia
Timepoint
first day of hospital admission, and 1, 3, and 5 days after administration
Method of measurement
By blood test

6

Description
C-reactive protein levels
Timepoint
first day of hospital admission, and 1, 3, and 5 days after administration
Method of measurement
By blood test

Intervention groups

1

Description
Intervention group: In order to minimize any bias between groups as a general policy, all patients will only receive lopinavir/retonavir (Kaletra®) and corticosteroids as their treatment regimen for COVID-19. Antibiotic medications use will be limited as much as possible and will only be used in each specific case based on the diagnosis of the infectious specialist or intensivist when necessary. On the second day of hospital admission, the intervention group will initially receive a single intravenous bolus of 1 mg/kg (1% solution) of methylene blue administered over 20-60 minutes. The patients will then be given 0.25 mg/kg per hour dose of methylene blue for 24 hours. Methylene blue has a commercial name of METIBLO and generic name of Methylthionium

chloride . Each 1ml ampule contains 10 mg methylthionium chloride. It is made in Belgium by Oterop company.

Category
Treatment - Drugs

2

Description
Control group: These patients will only receive lopinavir/retonavir (Kaletra®) and corticosteroids as their treatment regimen for COVID-19. Antibiotic medications use will be limited as much as possible and will only be used in each specific case based on the diagnosis of the infectious disease specialist or emergency medicine specialist when necessary.
Category
Treatment - Drugs

Recruitment centers

1

Recruitment center
Name of recruitment center
Abu Ali Sina Hospital
Full name of responsible person
Siavash Gholami
Street address
Sadra street
City
Shiraz
Province
Fars
Postal code
71994-67985
Phone
+98 71 3334 4000
Fax
+98 71 3643 0038
Email
abualisinacharity@gmail.com
Web page address
<https://abualisina.net/%d8%aa%d9%85%d8%a7%d8%b3-%d8%a8%d8%a7-%d9%85%d8%a7/>

Sponsors / Funding sources

1

Sponsor
Name of organization / entity
Shiraz University of Medical Sciences
Full name of responsible person
Yunos Ghasemi
Street address
Zand street
City
Shiraz
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Postal code

71348-14336

Phone

+98 71 3230 5401

Email

info@sums.ac.ir

Grant name

Grant code / Reference number

Is the source of funding the same sponsor organization/entity?

No

Title of funding source

Shiraz 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

Shiraz University of Medical Sciences

Full name of responsible person

Jamshid Roozbeh

Position

Professor

Latest degree

Subspecialist

Other areas of specialty/work

Internal Medicine

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Person responsible for scientific inquiries

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Jamshid Roozbeh

Position

Professor

Latest degree

Subspecialist

Other areas of specialty/work

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Person responsible for updating data

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Full name of responsible person

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Position

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Latest degree

Subspecialist

Other areas of specialty/work

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Phone

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+98 71 1234 9336

Email

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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

Not applicable

Informed Consent Form

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

Clinical Study Report

Not applicable

Analytic Code
Not applicable

Data Dictionary
Not applicable