

Clinical Trial Protocol

Iranian Registry of Clinical Trials

11 Sep 2026

Evaluating the efficacy and safety of bromhexine in hospitalized COVID-19 patients

Protocol summary

Study aim

Evaluating the efficacy and safety of bromhexine as a treatment option for patients with COVID-19

Design

Prospective clinical trial with parallel randomized control and treatment, double blinded groups, phase 2 trial on 100 patients. Block randomization will be done using online website (www.sealedenvelope.com/simple-randomiser/v1/lists).

Settings and conduct

Masih Daneshvari Hospital. How to do the study: 100 patients with COVID-19, using block randomization will be divided in to intervention and control group (placebo). This is a double blind study. In this study patient and physician will be blinded. For blinding, treatment and placebo group will be named group A and B, respectively.

Participants/Inclusion and exclusion criteria

Patients who are ≥ 18 years old at time of signing Informed Consent Form with laboratory (RT-PCR) confirmed infection with COVID-19 and lung involvement confirmed with chest imaging will be included in the study. Furthermore, patients who are hospitalized with a $\text{SaO}_2/\text{SpO}_2 \leq 94\%$ on room air or $\text{PaO}_2/\text{FiO}_2$ ratio $< 300 \text{ mgHg}$ and it is ≤ 12 days since illness onset are included in the study. Study exclusion criteria is as follows: Severe liver disease (e.g. Child Pugh score $\geq C$, $\text{AST} > 5$ times upper limit), pregnant or breastfeeding, or positive pregnancy test, patients with known severe renal impairment (estimated glomerular filtration rate $\leq 30 \text{ mL/min/1.73 m}^2$) or receiving continuous renal replacement therapy, hemodialysis, peritoneal dialysis.

Intervention groups

Patients allocated to treatment group were given 8 mg bromhexine tablet (Tolid Daroo), four times a day, orally for 28 days in conjugation with supporting treatment. Furthermore, patients in the control group received placebo (Tolid Daroo) plus supportive treatment according to national guidelines.

Main outcome variables

Time to Clinical Improvement (TTCI), need for invasive mechanical ventilation, and death.

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20151227025726N24**

Registration date: **2020-11-25, 1399/09/05**

Registration timing: **retrospective**

Last update: **2020-11-25, 1399/09/05**

Update count: **0**

Registration date

2020-11-25, 1399/09/05

Registrant information

Name

Farzaneh Dastan

Name of organization / entity

Shahid Beheshti University of Medical Sciences

Country

Iran (Islamic Republic of)

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+98 912 270 5933

Email address

f_dastan@sbm.ac.ir

Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2020-07-10, 1399/04/20

Expected recruitment end date

2020-09-10, 1399/06/20

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

Evaluating the efficacy and safety of bromhexine in hospitalized COVID-19 patients

Public title

Evaluation of the efficacy and safety of bromhexine administration in COVID-19

Purpose

Treatment

Inclusion/Exclusion criteria**Inclusion criteria:**

Age ≥ 18 years at time of signing Informed Consent Form
Laboratory (RT-PCR) confirmed infection with COVID-19
Lung involvement confirmed with chest imaging
Hospitalized with a $\text{SaO}_2/\text{SpO}_2 \leq 94\%$ on room air or $\text{PaO}_2/\text{FiO}_2$ ratio $< 300 \text{ mmHg} \leq 12$ days since illness onset
Willingness of study participant to accept randomization to any assigned treatment arm
Must agree not to enroll in another study of an investigational agent prior to completion of Day 28 of study

Exclusion criteria:

Physician makes a decision that trial involvement is not in patients' best interest, or any condition that does not allow the protocol to be followed safely
Severe liver disease (e.g. Child Pugh score $\geq C$, $\text{AST} > 5$ times upper limit)
Pregnant or breastfeeding, or positive pregnancy test
Patients with known severe renal impairment (estimated glomerular filtration rate $\leq 30 \text{ mL/min/1.73 m}^2$) or receiving continuous renal replacement therapy, hemodialysis, peritoneal dialysis
Will be transferred to another hospital which is not the study site within 72 hours
Receipt of any experimental treatment for 2019-nCoV (off-label, or trial related) within the 30 days prior to the time of the screening evaluation
Allergic to the Bromhexine

AgeFrom **18 years** old**Gender**

Both

Phase

2-3

Groups that have been masked

- Participant
- Investigator

Sample sizeTarget sample size: **100****Randomization (investigator's opinion)**

Randomized

Randomization description

We randomize patients at a 1:1 ratio to receive either oral Bromhexine or placebo. Participants will be enrolled by the local principle investigators at site. Consecutively patients will receive a trial number by the principal investigator. Before the trial commences, each trial number will be randomized to a treatment arm by computer (randomization will be done using online

website

www.sealedenvelope.com/simple-randomiser/v1/lists)

The intervention assignment communicates to the principle investigators. The study is double blinded and the trial monitor throughout by the data monitoring committee. Trial recruitment stops after the target study population is reached and will close when all patients complete their follow-up.

Blinding (investigator's opinion)

Double blinded

Blinding description

In this double blind study, patients who received the drug or placebo and physician (researcher) are blinded to the study groups (drug or placebo). Similar labeling will be used for the drug and placebo and only the randomizer will be aware of the study groups.

Placebo

Used

Assignment

Parallel

Other design features**Secondary Ids**

empty

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

Ethics Committee of Shahid Beheshti University of Medical Sciences

Street address

3 rd floor, School of Medicine, Evin St, Shahid Chamran Highway

City

Tehran

Province

Tehran

Postal code

1983963113

Approval date

2020-06-30, 1399/04/10

Ethics committee reference number

IR.SBMU.NRITLD.REC.1399.142

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

COVID-19 pneumonia

ICD-10 code

U07.1

ICD-10 code description

COVID-19, virus identified

Primary outcomes

1

Description

Time to Clinical Improvement (TTCI)

Timepoint

Daily

Method of measurement

TTCI is defined as the time (in days) from initiation of the study treatment (active or placebo) until a decline of two categories from admission status occur. 1. Hospital discharge or meeting discharge criteria; 2. Non-ICU hospitalization, not requiring supplemental oxygen; 3. Non-ICU hospitalization, requiring supplemental oxygen (but not NIV/ HFNC); 4. ICU/non-ICU hospitalization, requiring NIV/ HFNC therapy; 5. ICU hospitalization, requiring IMV; 6. Death.

2

Description

Need for invasive mechanical ventilation

Timepoint

Daily

Method of measurement

Medical record

3

Description

Death

Timepoint

At the end of the study

Method of measurement

Medical record

Secondary outcomes

1

Description

Clinical status

Timepoint

Days 7, 14, 21, 28

Method of measurement

Medical record

2

Description

Time to hospital discharge

Timepoint

Daily

Method of measurement

Medical record

3

Description

All-cause mortality

Timepoint

Daily

Method of measurement

Medical record

4

Description

Duration of mechanical ventilation

Timepoint

Daily

Method of measurement

Medical record

5

Description

Duration of extracorporeal membrane oxygenation (ECMO)

Timepoint

Daily

Method of measurement

Medical record

6

Description

Duration of supplemental oxygen

Timepoint

Daily

Method of measurement

Medical record

7

Description

Duration of hospitalization

Timepoint

Daily

Method of measurement

Medical record

8

Description

Time to RT-PCR negativity in upper and lower respiratory tract specimen

Timepoint

Daily

Method of measurement

Medical record

9

Description

Change (reduction) in viral load in upper and lower respiratory tract specimen

Timepoint

Daily

Method of measurement

Medical record

Intervention groups

1

Description

Intervention group: Patients allocated to treatment group

were given 8 mg bromhexine tablet (Tolid Daroo), four times a day, orally for 28 days. Patients also received Supportive treatment includes interferon b1a (Resigen) 44 microgram every other day for 3 doses + Lopinavir/Ritonavir 200-50 mg (Hetero Labs Limited) 2 Tab twice daily for 7 days.

Category

Treatment - Drugs

2**Description**

Control group: Control group received placebo (Tolid Daroo), four times a day, orally for 28 days. Patients also received supportive treatment includes interferon b1a (Resigen) 44 microgram every other day for 3 doses + Lopinavir/Ritonavir 200-50 mg (Hetero Labs Limited) 2 Tab twice daily for 7 days.

Category

Treatment - Drugs

Recruitment centers**1****Recruitment center****Name of recruitment center**

Masih Daneshvari Hospital

Full name of responsible person

Payam Tabarsi

Street address

Daraabad, Shahid Bahonar St. (Niavaran), Masih Daneshvari Hospital

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Sponsors / Funding sources**1****Sponsor****Name of organization / entity**

Shahid Beheshti University of Medical Sciences

Full name of responsible person

Afshin Zarghi

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mpd@sbm.ac.ir

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

Yes

Title of funding source

Shahid Beheshti 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**

Shahid Beheshti University of Medical Sciences

Full name of responsible person

Payam Tabarsi

Position

Professor

Latest degree

Subspecialist

Other areas of specialty/work

Infectious diseases

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

Shahid Beheshti University of Medical Sciences

Full name of responsible person

Farzaneh Dastan

Position

Assistant professor

Latest degree

Specialist

Other areas of specialty/work

Medical Pharmacy

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Person responsible for updating data

Contact

Name of organization / entity

Shahid Beheshti University of Medical Sciences

Full name of responsible person

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Position

Hospital pharmacist

Latest degree

Medical doctor

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Sharing plan

Deidentified Individual Participant Data Set (IPD)

Yes - There is 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

Title and more details about the data/document

All potential data can be shared after blinding

When the data will become available and for how long

Six months after publishing the results

To whom data/document is available

Researchers working in academic institutions

Under which criteria data/document could be used

For research purposes and meta-analysis studies

From where data/document is obtainable

Dr. farzaneh Dastan, Dr. Masih Daneshvari Hospital, Daar-Abad, Niavaran

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

Official letter to the researchers through Email (fzh.dastan@gmail.com).

Comments