Clinical Trial Protocol
Iranian Registry of Clinical Trials

08 Nov 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 SaO2/SPO2≤94% on room air or PaO2/FiO2 ratio <300mgHg 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 ≥ C, AST>5 times upper limit), pregnant or breastfeeding, or positive pregnancy test, patients with known severe renal impairment (estimated glomerular filtration rate ≤30 mL/min/1.73 m2) 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

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f_dastan@sbmu.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 SaO2/SPO2≤94% on room air or PaO2/FiO2 ratio <300mgHg ≤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 ≥ C, AST>5 times upper limit) Pregnant or breastfeeding, or positive pregnancy test Patients with known severe renal impairment (estimated glomerular filtration rate ≤30 mL/min/1.73 m2) 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
Age
From **18 years** old
Gender
Both

Phase
2-3
Groups that have been masked

- Participant
- Investigator

Sample size
Target 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 Committe 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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3rd floor, School of Medicine, Evin St, Shahid Chamran Highway

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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

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

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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

Zahra Mirshafiei Langari

Position

Hospital pharmacist

Latest degree

Medical doctor

Other areas of specialty/work

Medical Pharmacy

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z.mirshafei@gmail.com

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