Clinical Trial Protocol
Iranian Registry of Clinical Trials

07 Nov 2026

The effect of the bromhexine-hydrochloride plus hydroxychloroquine on outcome of patients with COVID-19: A randomized, triple-blind, placebo-controlled trial

Protocol summary

Study aim
To find out the clinical efficacy of synergistic action of bromhexine hydrochloride and hydroxychloroquine or each drug alone in comparison to placebos on outcome of patients with COVID19 in a controlled and randomized clinical trial

Design
Triple blind randomized trial of two drugs in combination and each drug alone compared to placebo in four groups of COVID19 patients receiving, Bromhexine hydrochloride plus Hydroxychloroquine, either drug alone plus placebo of other drug, or two placebos.

Settings and conduct
EmamReza Hospital of Tabriz, Iran

Participants/Inclusion and exclusion criteria
CIVID19 patients of 18 years and older admitted to hospital fulfilling the enrolment criteria and free of specified exclusion criteria

Intervention groups
Four groups of COVID19 patients receiving: group 1) Bromhexine hydrochloride 16 mg q 8 h for 16 days + Hydroxychloroquine, bromhexine 200 mg tablets two tablets q 12 h first day and one tablets q 12 h day 2 to 5, group 2) bromhexine plus placebo of other drug, group 3) hydroxychloroquine + placebo of other drug, group 4) placebos for both of the drugs.

Main outcome variables
intensive care transfer, intubation and mechanical ventilation, and survival or death

General information

Reason for update

Acronym

IRCT registration information
IRCT registration number: **IRCT20200818048444N4**
Registration date: **2021-11-28, 1400/09/07**
Registration timing: **registered_while_recruiting**

Last update: **2021-11-28, 1400/09/07**
Update count: **0**

Registration date
2021-11-28, 1400/09/07

Registrant information

Name
Khalil Ansarin

Name of organization / entity

Country
Iran (Islamic Republic of)

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Email address
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Recruitment status
Recruitment complete

Funding source

Expected recruitment start date
2021-11-11, 1400/08/20

Expected recruitment end date
2022-05-01, 1401/02/11

Actual recruitment start date
empty

Actual recruitment end date
empty

Trial completion date
empty

Scientific title
The effect of the bromhexine-hydrochloride plus hydroxychloroquine on outcome of patients with COVID-19: A randomized, triple-blind, placebo-controlled trial

Public title

Efficacy of bromhexine-hydrochloride plus hydroxychloroquine on outcome of patients with COVID-19

Purpose

Treatment

Inclusion/Exclusion criteria

Inclusion criteria:

COVID19 diagnosis by a physician on the basis of history and physical examination and compatible imaging and PCR testing as: 1, Having symptoms of COVID19 disease: FEVER (measured or subjective), COUGH, DYSPNEA, DIFFICULTY BREATHING, SORE THROAT, NEW OLFACTORY OR TASTE DISORDERS, SEVERE LASSITUDE OR FATIGUE, MYALGIAS, HEADACH, GI SYMPTOMS plus having compatible imaging or positive PCR testing for SARS virus COVID19 2, Being free of chronic respiratory or other illnesses with symptoms confused with symptoms of COVID19 disease AND 3 , Signed consent form.

Exclusion criteria:

Major Exclusion Criteria: --1-1- Age: less than 18 years; justification: adult hospital with not enough young patients to compare and follow up 2- Pregnant or breast feeding woman: for fetal safety 3- Severe liver disease and severe renal failure: being confounding - 4- Serious eye disease with visual loss or cardiac conduction defects: as a confounder in side effects of drugs. 5- Subjects on immune modulating drugs for other diseases for: as confounding 6- Subjects already on bromhexine hydrochloride or hydroxychloroquine. 7- Subjects with history of allergy to bromhexine hydrochloride or hydroxychloroquine. 8- Subjects in other clinical trials for COVID-19 within 30 days before or after this trial: for being confounding. 9- Direct admission of patient to ICU at the the time of screening: because of the conflict with one of outcomes. 10- Having other subject characteristics (not thought to be related to underlying COVID-19) that portend a very poor prognosis (e.g, severe liver failure, severe renal failure, malignancies, and etc.) that may impact primary and other clinical endpoints. 11-Impending death at the time of admission on the judgement of physician. 12- Other uncontrolled disease, as judged by investigators influencing study endpoints.

Age

From **18 years** old

Gender

Both

Phase

3

Groups that have been masked

- Participant
- Care provider
- Investigator
- Outcome assessor
- Data analyser
- Data and Safety Monitoring Board

Sample size

Target sample size: **800**

Randomization (investigator's opinion)

Randomized

Randomization description

After the recruitment of the subject on the basis of the inclusion and exclusion criteria, centralized web-based randomization, through random allocation by balanced block method, individuals are divided into four groups of controls and experimental. Using Random Sequence Generator, groups are created and people are placed in one of these four groups based on the reference sequence.

Blinding (investigator's opinion)

Triple blinded

Blinding description

Using placebos and actual drugs blind to the investigator, patient, and care givers except for the person providing drug which is not associated with any of the three. This is a triple blinded study in which the investigator, the patient, and providers of the care all will be blind to the drug received by the patient. The drugs or placebos prepared in 4 similar packages with different codes will be delivered to patient by a member of the team as pharmacist and the data regarding the nature of the packages will not be will be revealed to providers.

Placebo

Used

Assignment

Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Regional Committee for Research Ethics(Human Subject Studies(91000001))

Street address

Third Floor, Tabriz University of Medical Sciences, Central Building Golgasht St.

City

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Province

East Azarbaijan

Postal code

5166614766

Approval date

2021-10-25, 1400/08/03

Ethics committee reference number

IR.TBZMED.REC.1400.656

Health conditions studied

1

Description of health condition studied

COVID19

ICD-10 code

U07.1

ICD-10 code description

SARS-associated coronavirus as the cause of diseases classified elsewhere CODE: U07.1

Primary outcomes

1

Description

ICU transfer

Timepoint

28 days after the start of the disease

Method of measurement

Patient hospital medical record

2

Description

Intubation and mechanical ventilation

Timepoint

28 days after the start of the disease

Method of measurement

Patient hospital medical record

3

Description

Survival or death of the patient

Timepoint

28 days after start of the disease

Method of measurement

Patient hospital medical record

Secondary outcomes

empty

Intervention groups

1

Description

After selection and enrolment and after obtaining and informed consent subjects will be assigned to one of four groups to to receive, in addition to the usual care as directed by national guideline, one of the four treatments. In GROUP1 the subject will receive bromhexine hydrochloride tablets16 mg every 8 hours for 14 days plus hydroxychloroquine tablets 400mg every 12 hours on day 1 and 200 mg every 12 hours on days 2 to five.

Category

Treatment - Drugs

2

Description

Intervention group 2: After selection and enrolment and after obtaining and informed consent subjects will be assigned to one of four groups to to receive, in addition to the usual care as directed by national guideline, one of 4 treatments. In GROUP 2 the subject will receive bromhexine hydrochloride tablets16 mg every 8 hours for 14 days plus placebo of hydroxychloroquine tablets for five days.

Category

Treatment - Drugs

3

Description

Intervention group 3: After selection and enrolment and after obtaining and informed consent subjects will be assigned to one of four groups to to receive, in addition to the usual care as directed by national guideline, one of the four treatments. In the group 3 the subject will receive hydroxychloroquine tablets 400mg every 12 hours at day one and 200 mg every 12 hours at days 2 to five + placebo of bromhexine for 14 days.

Category

Treatment - Drugs

4

Description

Control group: After selection and enrolment and after obtaining and informed consent subjects will be assigned to one of four groups to to receive, in addition to the usual care as directed by national guideline, one of the four treatments. In the control group (group 4) the individual will receive just placebo for bromhexine hydrochloride for 14 days and hydroxychloroquine for 5 days.

Category

Placebo

Recruitment centers

1

Recruitment center

Name of recruitment center

EmamReza Hospital, Tabriz University of Medical Sciences

Full name of responsible person

Khalil Ansarin, MD

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Sponsors / Funding sources

1

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Grant name
Donation
Grant code / Reference number
N/A
Is the source of funding the same sponsor organization/entity?
Yes
Title of funding source
Tabriz University of Medical Sciences
Proportion provided by this source
100
Public or private sector
Private
Domestic or foreign origin
Domestic
Category of foreign source of funding
empty
Country of origin
Type of organization providing the funding
Other

Person responsible for general inquiries

Contact
Name of organization / entity
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Position
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Latest degree
Subspecialist
Other areas of specialty/work
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Sharing plan

Deidentified Individual Participant Data Set (IPD)

Yes - There is a plan to make this available

Study Protocol

Yes - There is a plan to make this available

Statistical Analysis Plan

Yes - There is 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

Yes - There is a plan to make this available

Data Dictionary

Yes - There is a plan to make this available

Title and more details about the data/document

All data can be shared without names of participating subjects

When the data will become available and for how long

Summer of 2022

To whom data/document is available

Researchers can reach the data after their request and approval

Under which criteria data/document could be used

In order to use or control data the researchers should send their request of the data and the data will be delivered to them after approval of their request.

From where data/document is obtainable

Through the email of: or kansarin@tbxmed.ac.ir or dr.ansarin@gmail.com or the postal code: 5142954481

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

The researcher should send his/her request of data to our group and data will be sent as a Excel or SPSS file.

Comments