

Clinical Trial Protocol

Iranian Registry of Clinical Trials

05 Dec 2023

Evaluation of the efficacy and safety of recombinant erythropoietin on the improvement of hospitalised COVID-19 patients

Protocol summary

Study aim

This study aims to investigate the effect of recombinant erythropoietin on the recovery process of COVID-19 patients.

Design

concealed, randomized, single blinded, phase 2 controlled clinical trial with two arm parallel group design of 20 patients, using the placebo in the control group.

Settings and conduct

This study will be performed at Shahid Mohammadi Hospital in Bandar Abbas. Patients enter the study after obtaining written consent, but will not know which group they belong to.

Participants/Inclusion and exclusion criteria

All positive COVID-19 patients who have $Hb \leq 9$ and at least one of the severe COVID-19 symptoms and are willing to cooperate in this project will be included in the study. Patients with a history of coronary heart disease, thrombosis, deep vein thrombosis, chronic lung disease, diabetes mellitus, weakened immune system, end stage renal disease, liver disease, and patients with a history of taking oral contraceptive pills, systolic blood pressure more than 160 mm Hg, diastolic blood pressure more than 90 mm Hg and age over 65 and erythropoietin above 500 are excluded.

Intervention groups

Patients are divided into two groups. In group A, the standard treatment for COVID-19 patients with recombinant erythropoietin is prescribed. In group B, patients receive standard COVID-19 treatment with the placebo.

Main outcome variables

Patient clinical symptoms, Laboratory examinations of patients and Hemoglobin

General information

Reason for update

The expected recruitment end date was on 2020/12/21

but since we had a wide and careful exclusion criteria because of the adverse reactions of the medication, the recruitment (for both cases and controls) was not so easy and did not finish on the expected date and we are still recruiting now. Recruitment began on 2020/8/17 and the updated expected recruitment end date is 2021/8/1.

Acronym

IRCT registration information

IRCT registration number: **IRCT20200509047364N1**

Registration date: **2020-08-09, 1399/05/19**

Registration timing: **registered_while_recruiting**

Last update: **2021-05-26, 1400/03/05**

Update count: **2**

Registration date

2020-08-09, 1399/05/19

Registrant information

Name

Dariush Hooshyar

Name of organization / entity

Country

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Email address

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Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2020-06-21, 1399/04/01

Expected recruitment end date

2021-08-01, 1400/05/10

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

Evaluation of the efficacy and safety of recombinant erythropoietin on the improvement of hospitalised COVID-19 patients

Public title

Effect of erythropoietin on COVID-19

Purpose

Treatment

Inclusion/Exclusion criteria

Inclusion criteria:

All definitively positive COVID-19 patients with Hb \leq 9. Having at least one of the severe symptoms of COVID-19, including tachypnea (breathing rate $>$ 30 beats per minute), hypoxemia (O₂ \leq 93 saturation, the partial pressure ratio of arterial oxygen $<$ 300), Lung infiltration ($>$ 50% of lung field within 24 to 48 hours), progressive lymphopenia, LDH $>$ 245 U/l, CRP $>$ 100

Exclusion criteria:

Patients with a history of coagulopathy Patients with a history of thrombosis Patients with a history of deep vein thrombosis Patients with a history of chronic lung disease Patients with a history of diabetes mellitus Patients with weakened immune systems Patients with a history of end stage renal disease Patients with liver disease Patients with a history of taking oral contraceptive pills (OCPs) Patients with systolic blood pressure greater than 160 mmHg Patients with diastolic blood pressure greater than 90 mmHg Patients over 65 years of age Patients with erythropoietin above 500 Patients with a history of myocardial infarction or unstable angina Patients with a history of malignancy

Age

To 65 years old

Gender

Both

Phase

2

Groups that have been masked

- Participant

Sample size

Target sample size: 20

Randomization (investigator's opinion)

Randomized

Randomization description

Before assigning groups to individuals eligible to participate in the study, informed consent is completed for grouping individuals. the person who has no role in admitting patients and assigning patients to random codes preparing random sequences using online tools (<https://www.sealedenvelope.com/>) and by permuted block randomization method. Individualized random allocation is done in blocks with sizes 2 and 4, and with stratification based on gender. eligibility criteria are monitored by the person responsible for admitting patients. Codes in a random sequence are assigned to patients by the treatment team without knowing that each code is in the intervention or placebo group. Patient codes are then matched to randomly generated

sequence information for interventions. (randomization concealment is done by the treatment team without informing the person responsible for admitting patients and the person who prepared the random sequence.)

Blinding (investigator's opinion)

Single blinded

Blinding description

In this study, all participants are aware of participating in this study and enter the study with their consent. All participants are unaware of which group of this study they are in and after grouping patients in the groups, Patients receive recombinant erythropoietin in the treatment group and receive a placebo in the control group. The lead researcher, health care personnel, data collection officials, and those who evaluate the outcome are aware of the grouping of patients. Those who prepare the draft of the article are unaware of the groupings if they do not cooperate in the above cases.

Placebo

Used

Assignment

Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Ethics committee of Hormozgan University of Medical Sciences

Street address

Deputy of Research and Technology, Hormozgan University of Medical Sciences, Shahid Chamran Boulevard, Bandar Abbas, Hormozgan, Iran

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bandar abbas

Province

Hormozgan

Postal code

7916613885

Approval date

2020-06-06, 1399/03/17

Ethics committee reference number

IR.HUMS.REC.1399.165

Health conditions studied

1

Description of health condition studied

Laboratory confirmed COVID-19

ICD-10 code

U07.1

ICD-10 code description

COVID-19, virus identified

Primary outcomes

1

Description

Respiratory rate

Timepoint

At the beginning of the study (before the intervention) and day 5 after the intervention

Method of measurement

Pulse oximeter

2

Description

Oxygen saturation state and arterial oxygen partial pressure ratio

Timepoint

At the beginning of the study (before the intervention) and day 5 after the intervention

Method of measurement

Pulse oximeter

3

Description

Lung infiltration status

Timepoint

At the beginning of the study (before the intervention) and day 5 after the intervention

Method of measurement

chest x-ray

4

Description

LDH level's

Timepoint

At the beginning of the study (before the intervention) and day 5 after the intervention

Method of measurement

pathobiology laboratory

5

Description

CRP level's

Timepoint

At the beginning of the study (before the intervention) and day 5 after the intervention

Method of measurement

pathobiology laboratory

6

Description

Lymphocyte count

Timepoint

At the beginning of the study (before the intervention) and day 5 after the intervention

Method of measurement

pathobiology laboratory

7

Description

Endogenous erythropoietin level's

Timepoint

Beginning of study (before intervention)

Method of measurement

Pathobiology laboratory

8

Description

Patients' blood pressure

Timepoint

At the beginning of the study (before the intervention), during the intervention (5-day erythropoietin administration)

Method of measurement

Sphygmomanometer

Secondary outcomes

1

Description

Patients' blood hemoglobin levels

Timepoint

Start of study (before the intervention), day 5 after the intervention and 2 to 4 weeks after the intervention

Method of measurement

Pathobiology laboratory

Intervention groups

1

Description

Intervention group: Group A.: The standard drug treatment is based on the treatment protocols of the National Committee of COVID-19 and erythropoietin recombinant (EPREX Manufactured by Johnson and Johnson Pharmaceutical Company) 300 units / Kg or 4000IU as subcutaneous injection five times a day for 5 days and simultaneously Enoxaparin 1mg / kg SQ daily is also taken to prevent thrombosis. Patients' blood pressure, along with other vital signs, is checked regularly and at regular intervals. Standard drug treatment according to the treatment protocols of the National Committee for COVID-19 includes Hydroxychloroquine / Chloroquine Phosphate: • Hydroxychloroquine sulfate tablets 200 mg or chloroquine phosphate tablets 250 mg (equivalent to 150 mg base dose) 2 tablets every 12 hours on the first day and then one tablet every 12 hours for at least 7 days and up to 14 days. One of the following medications at the discretion and diagnosis of the treating physician: • Caltrate tablets (Lopinavir / Ritonavir) 50/200 mg every 12 hours 2 pieces after meals for at least 7 days and a maximum of 14 days • Tablets (Atazanavir / Ritonavir) 300/100 One tablet daily with food or Atazanavir 400 mg daily for at least 7 days and up to 14 days

Category

2**Description**

Control group: Group B: The standard drug treatment is based on the treatment protocols of the National Committee for COVID-19 and the placebo (distilled water) is given as a subcutaneous injection five times a day for 5 days. Standard drug treatment according to the treatment protocols of the National Committee for COVID-19 includes Hydroxychloroquine / Chloroquine Phosphate: • Hydroxychloroquine sulfate tablets 200 mg or chloroquine phosphate tablets 250 mg (equivalent to 150 mg base dose) 2 tablets every 12 hours on the first day and then one tablet every 12 hours for at least 7 days and up to 14 days. One of the following medications at the discretion and diagnosis of the treating physician: • Caltrate tablets (Lopinavir / Ritonavir) 50/200 mg every 12 hours 2 pieces after meals for at least 7 days and a maximum of 14 days • Tablets (Atazanavir / Ritonavir) 300/100 One tablet daily with food or Atazanavir 400 mg daily for at least 7 days and up to 14 days

Category

Placebo

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

Shahid Mohammadi Hospital

Full name of responsible person

Dr. Mehdi Hassaniyazad

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Boulevard of the Islamic Republic of Iran, Bandar Abbas

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Full name of responsible person

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Web page address<https://resv.hums.ac.ir/>**Grant name****Grant code / Reference number****Is the source of funding the same sponsor organization/entity?**

Yes

Title of funding source

Bandare-abbas 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**

Bandare-abbas University of Medical Sciences

Full name of responsible person

Dariush Hooshyar

Position

Student of Medicine

Latest degree

Medical doctor

Other areas of specialty/work

General Practitioner

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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

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