

# Clinical Trial Protocol

## Iranian Registry of Clinical Trials

27 Jun 2026

### Evaluation of the effect of melatonin on improving the symptoms of patients with COVID-19-double-blind randomized clinical trial

#### Protocol summary

##### Study aim

Determining the effect of melatonin on improving the symptoms of patients with COVID-19

##### Design

Clinical trial with control group, double-blind, randomized, phase 3 on 46 patients. In this study, individuals will be randomly assigned to two groups of intervention and control.

##### Settings and conduct

This clinical trial will be performed on 46 patients aged 18 to 75 years admitted to the intensive care unit of Vali-e-Asr Hospital of Birjand with a diagnosis of COVID-19. All of the steps will be covered by the patient, physician and evaluators.

##### Participants/Inclusion and exclusion criteria

Inclusion criteria: Age 18 to 75 years; Diagnosis of COVID-19 in the last 24 hours; One of the three following: respiratory rate more than 30 per minutes, O<sub>2</sub> saturation less than or equal to 93% at room temperature, PaO<sub>2</sub>/FiO<sub>2</sub> less than or equal to 300 Exclusion criteria: Patients with shock or hemodynamic instability (increase or decrease in blood pressure and irregular heartbeat); GFR less than 30 ml/minute; History of cirrhosis, hepatitis and severe liver diseases; History of hypertension, depression and epilepsy; Patients with a history of allergic reaction or allergy to melatonin; Patients receiving chemotherapy for cancer; Severe diseases of the immune system; Pregnant and lactating women; Use of alcohol and benzodiazepines

##### Intervention groups

Intervention group: Melatonin tablet 18 mg at night along with standard treatment for 14 days Control group: Melatonin placebo tablet 18 mg at night along with standard treatment for 14 days

##### Main outcome variables

One-month mortality; Duration of hospitalization in the ICU; Clinical symptoms according to the seven-category ordinal scale; Lymphocyte count; PaO<sub>2</sub>/FiO<sub>2</sub> ratio; ESR and CRP levels; AST, ALT and LDH levels

#### General information

##### Reason for update

##### Acronym

##### IRCT registration information

IRCT registration number: **IRCT20150724023315N2**

Registration date: **2021-07-18, 1400/04/27**

Registration timing: **prospective**

Last update: **2021-07-18, 1400/04/27**

Update count: **0**

##### Registration date

2021-07-18, 1400/04/27

##### Registrant information

##### Name

Mahmoud Ganjifard

##### Name of organization / entity

Birjand University of Medical Sciences

##### Country

Iran (Islamic Republic of)

##### Phone

+98 56 3238 1338

##### Email address

ganjim@bums.ac.ir

##### Recruitment status

**Recruitment complete**

##### Funding source

##### Expected recruitment start date

2021-07-23, 1400/05/01

##### Expected recruitment end date

2021-12-22, 1400/10/01

##### Actual recruitment start date

empty

##### Actual recruitment end date

empty

##### Trial completion date

empty

## Scientific title

Evaluation of the effect of melatonin on improving the symptoms of patients with COVID-19-double-blind randomized clinical trial

## Public title

Evaluation of the effect of melatonin in the treatment of patients with COVID-19

## Purpose

Treatment

## Inclusion/Exclusion criteria

### Inclusion criteria:

Age 18 to 75 years  
Diagnosis of COVID-19 in the last 24 hours  
One of the three following: respiratory rate more than 30 per minutes, o<sub>2</sub> saturation less than or equal to 93% at room temperature, PaO<sub>2</sub>/FiO<sub>2</sub> less than or equal to 300  
Female patients should not be pregnant and should not become pregnant until 30 days after the end of the study

### Exclusion criteria:

Patients with shock or hemodynamic instability (increase or decrease in blood pressure and irregular heartbeat)  
GFR less than 30 ml/minute  
History of cirrhosis, hepatitis and severe liver diseases  
History of hypertension, depression (taking fluvoxamine and other potent CYP1A2 inhibitors) and epilepsy  
Patients with a history of allergic reaction or allergy to melatonin  
Patients receiving chemotherapy for cancer  
Severe diseases of the immune system  
Pregnant and lactating women  
Use of alcohol and benzodiazepines

## Age

From **18 years** old to **75 years** old

## Gender

Both

## Phase

3

## Groups that have been masked

- Participant
- Care provider
- Investigator
- Outcome assessor

## Sample size

Target sample size: **46**

## Randomization (investigator's opinion)

Randomized

## Randomization description

Patients will be randomly divided into two groups of intervention and control using a random number table. First, we create a variable from 1 to 46 in Excel software. Then we create another variable in another column and generate 23 random numbers one and 23 random numbers two with the randomization command. The numbers of one and two are intervention and placebo groups, respectively.

## Blinding (investigator's opinion)

Double blinded

## Blinding description

All of the steps will be covered by the patient, physician and evaluators. Packaging of the drugs will be exactly identical in both arms of the study. Preparation, packaging, and labeling of the drugs will be performed

by the third person under the supervision of the senior manager of the project.

## Placebo

Used

## Assignment

Parallel

## Other design features

-

## Secondary Ids

empty

## Ethics committees

### 1

#### Ethics committee

##### Name of ethics committee

Ethics Committee of Birjand University of Medical Sciences

##### Street address

Birjand University of Medical Sciences , Ghaffari Street

##### City

Birjand

##### Province

South Khorasan

##### Postal code

9717853577

#### Approval date

2020-11-09, 1399/08/19

#### Ethics committee reference number

IR.BUMS.REC.1399.345

## Health conditions studied

### 1

#### Description of health condition studied

COVID-19

#### ICD-10 code

U07.1

#### ICD-10 code description

COVID-19, virus identified

## Primary outcomes

### 1

#### Description

One-month mortality

#### Timepoint

From baseline to end

#### Method of measurement

Questionnaire

### 2

#### Description

Time of death of patients

#### Timepoint

From baseline to end  
**Method of measurement**  
Questionnaire

### 3

**Description**  
Duration of hospitalization in the ICU  
**Timepoint**  
During hospitalization  
**Method of measurement**  
Questionnaire

### 4

**Description**  
Clinical symptoms according to the seven-category ordinal scale  
**Timepoint**  
Baseline and then on days 7 and 15  
**Method of measurement**  
Questionnaire

### 5

**Description**  
Lymphocyte count  
**Timepoint**  
Baseline and then on days 7 and 15  
**Method of measurement**  
Laboratory test

### 6

**Description**  
PaO<sub>2</sub>/FiO<sub>2</sub> ratio  
**Timepoint**  
Baseline and then on days 7 and 15  
**Method of measurement**  
Laboratory test

### 7

**Description**  
ESR and CRP levels  
**Timepoint**  
Baseline and then on days 7 and 15  
**Method of measurement**  
Laboratory test

### 8

**Description**  
AST, ALT and LDH levels  
**Timepoint**  
Baseline and then on days 7 and 15  
**Method of measurement**  
Laboratory test

## Secondary outcomes

### 1

**Description**  
Number of patients who need support through mechanical ventilation  
**Timepoint**  
From baseline to end  
**Method of measurement**  
Questionnaire

### 2

**Description**  
Discharge from the hospital  
**Timepoint**  
From baseline to end  
**Method of measurement**  
Questionnaire

### 3

**Description**  
Fever relief time in patients who had a fever above 37.5 at the time of admission  
**Timepoint**  
During hospitalization  
**Method of measurement**  
Questionnaire

### 4

**Description**  
Adverse effects  
**Timepoint**  
On the 15th day  
**Method of measurement**  
Common Terminology Criteria for Adverse Event (CTCAE) version 5.0

## Intervention groups

### 1

**Description**  
Intervention group: Six melatonin tablet 3 mg (Razak pharmaceutical company, Tehran, Iran) at night along with standard treatment for 14 days  
**Category**  
Treatment - Drugs

### 2

**Description**  
Control group: Six Melatonin placebo tablet 3 mg (Industrial Laboratory of Mashhad School of Pharmacy, Mashhad, Iran) at night along with standard treatment for 14 days  
**Category**  
Placebo

## Recruitment centers

## 1

### Recruitment center

**Name of recruitment center**

Vali-e-Asr Educational and Medical Center affiliated to  
Birjand University of Medical Sciences

**Full name of responsible person**

Mahmoud Ganjifard

**Street address**

Vali-e-Asr Hospital, Ghaffari Street

**City**

Birjand

**Province**

South Khorasan

**Postal code**

9717964151

**Phone**

+98 56 3162 2001

**Email**

ganjim@bums.ac.ir

### Sponsors / Funding sources

## 1

### Sponsor

**Name of organization / entity**

Birjand University of Medical Sciences

**Full name of responsible person**

Toba Kazemi

**Street address**

Birjand University of Medical Sciences, Ghaffari Street

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9717853577

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research@bums.ac.ir

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

Yes

**Title of funding source**

Birjand 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**

Birjand University of Medical Sciences

**Full name of responsible person**

Mahmoud Ganjifard

**Position**

Associate Professor

**Latest degree**

Specialist

**Other areas of specialty/work**

Anesthesiology

**Street address**

Vali-e-Asr Hospital, Ghaffari Street

**City**

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### Person responsible for scientific inquiries

**Contact****Name of organization / entity**

Birjand University of Medical Sciences

**Full name of responsible person**

Mahmoud Ganjifard

**Position**

Associate Professor

**Latest degree**

Specialist

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### Person responsible for updating data

**Contact****Name of organization / entity**

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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