

Clinical Trial Protocol

Iranian Registry of Clinical Trials

17 Sep 2026

Evaluation of effect of melatonin tablet administration or placebo on insomnia and daytime sleepiness in patients with obstructive sleep apnea and insomnia (COMISA) treated with continuous positive airway pressure: A randomized double-blind placebo-controlled trial

Protocol summary

Study aim

Evaluation of the effect of melatonin tablet administration on insomnia and daytime sleepiness in patients with COMISA

Design

A clinical trial with placebo control, parallel groups, double blind, randomized, phase 3 on 50 patients. randomization will be prepared with online randomization generator

Settings and conduct

This clinical trial will be performed as a single-center trial in Emam Khomeini sleep clinic in Tehran. Patients in the melatonin group will receive 10 mg of melatonin 30-60 minutes before sleep with CPAP. In the placebo group, patients will receive the placebo tablets similar to melatonin tablets with CPAP 30-60 minutes before sleep with CPAP at night for one month.

Participants/Inclusion and exclusion criteria

Age: 18-65 years old Moderate- severe OSA (AHI $\geq$ 15 times per hour) Using CPAP for at least one month PSQI questionnaire score $\geq$ 5 Severe pulmonary disease (life expectancy less than 6 months) Severe heart disease (life expectancy less than 6 months) Severe neurologic disease (example: dementia, Parkinson's disease) Major psychiatric disorder (drug users, bipolar disorder, psychiatric disease in 3 months ago Using drugs that interfere with sleeping and breathing Known allergic reactions to melatonin according to past allergic history Pregnancy or lactation Hypothyroidism Narcolepsy Restless leg syndrome Shift workers

Intervention groups

In the melatonin group, patients receive one 10 mg melatonin tablet, 30-60 minutes before sleep as long as using CPAP. In the control group, patients receive one placebo tablet before sleep for one month.

Main outcome variables

Change from baseline in PSQI; ESS; ISI; FOSQ-10 questionnaire in melatonin group in comparison with placebo

General information

Reason for update

Acronym

Comorbid Insomnia with Obstructive Sleep Apnea (COMISA)

IRCT registration information

IRCT registration number: **IRCT20220105053635N1**

Registration date: **2022-04-19, 1401/01/30**

Registration timing: **prospective**

Last update: **2022-04-19, 1401/01/30**

Update count: **0**

Registration date

2022-04-19, 1401/01/30

Registrant information

Name

Shahideh Amini

Name of organization / entity

Country

Iran (Islamic Republic of)

Phone

+98 21 6695 4709

Email address

aminishahideh@gmail.com

Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2022-04-21, 1401/02/01

Expected recruitment end date

2023-01-20, 1401/10/30

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

Evaluation of effect of melatonin tablet administration or placebo on insomnia and daytime sleepiness in patients with obstructive sleep apnea and insomnia (COMISA) treated with continuous positive airway pressure: A randomized double-blind placebo-controlled trial

Public title

Evaluation of melatonin on insomnia and daytime sleepiness associated with comisa

Purpose

Treatment

Inclusion/Exclusion criteria**Inclusion criteria:**

Age: 18-65 years old Moderate- severe OSA (apnea - hypopnea index ≥ 15 times per hours) Using CPAP for a minimum duration of one month PSQI questionnaire point should be ≥ 5 The patient declares his / her commitment to strictly follow the study instructions, participate in visits and take interventions.

Exclusion criteria:

Severe pulmonary disease (life expectancy less than 6 months) Severe heart disease (life expectancy less than 6 months) Severe neurologic disease (example: dementia, Parkinson disease) Major psychiatric disorder (drug users, bipolar disorder, psychiatric disease in 3 months ago Using drugs which interfere with sleeping and breathing Known allergic reactions to melatonin according to past allergic history Pregnancy or lactation Hypothyroidism Narcolepsy Restless leg syndrome Shift workers

Age

From **18 years** old to **65 years** old

Gender

Both

Phase

3

Groups that have been masked

- Participant
- Care provider
- Investigator
- Outcome assessor
- Data analyser

Sample size

Target sample size: **50**

Randomization (investigator's opinion)

Randomized

Randomization description

Eligible patients will enter one of the two rows of the trial in a one-to-one ratio (1: 1). Allocation will be done by permuted block randomization method. The size of 4 blocks will be selected. The allocation in each block will

be simple randomization. Randomization will be done centrally and before the start of the study by a person who has no direct role in the entry of participants with a random number table. People who include patients in the study will not know the order of assignment. The order of allocation will be hidden from the researchers by thick, tightly packed dark envelopes. The medicine is given to patients by researchers. The drugs and placebo are provided to the researchers in the form of packages containing the study drug and the placebo for one month. The drugs are provided to researchers in packages of the same shape and only after determining the order of treatment. There is an expiration date on the package. If the expiration date of the package is less than 5 months at the time of entry into the study, the package will be returned to the allocation officer and the package with the appropriate expiration date will be given to the researcher in the same way. In the event of a serious adverse event for the participant, unblinding will be performed immediately for both the participant and the researcher. In the event of a severe adverse event in more than 12.5% of participants (at least 7), unblinding will be performed for the researcher for all participants, and if the adverse event is due to melatonin use and is unexpected for melatonin, It will be done for all participants as well.

Blinding (investigator's opinion)

Double blinded

Blinding description

The study will be double-blind which means the patients and researchers who include patients in the study will not know the order of assignment. The order of allocation will be hidden from the researchers by thick, tightly packed dark envelopes

Placebo

Used

Assignment

Parallel

Other design features**Secondary Ids**

empty

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

Ethics committee of drug sciences of Tehran
University of Medical Sciences

Street address

Qods ave. Keshavarz Blvd.

City

Tehran

Province

Tehran

Postal code

۱۴۱۷۶۱۴۴۱۱

Approval date

2021-12-11, 1400/09/20

Ethics committee reference number
IR.TUMS.TIPS.REC.1400.177

Health conditions studied

1

Description of health condition studied

Comorbid insomnia and obstructive sleep apnea

ICD-10 code

G47.33

ICD-10 code description

Obstructive sleep apnea (adult) (pediatric)

Primary outcomes

1

Description

Change from baseline in PSQI questionnaire score in melatonin group in comparison with placebo group.

Timepoint

Measurement of PSQI questionnaire score at the baseline and one month after initiation of treatment

Method of measurement

PSQI questionnaire

2

Description

Change from baseline in ESS questionnaire score in melatonin group in comparison with placebo group.

Timepoint

Measurement of ESS questionnaire score at the baseline and one month after initiation of treatment

Method of measurement

ESS questionnaire

3

Description

Change from baseline in ISI questionnaire score in melatonin group in comparison with the placebo group.

Timepoint

Measurement of ISI questionnaire score at the baseline and one month after initiation of treatment

Method of measurement

ISI questionnaire

4

Description

Change from baseline in FOSQ-10 questionnaire score in melatonin group in comparison with the placebo group.

Timepoint

Measurement of FOSQ-10 questionnaire score at the baseline and one month after initiation of treatment

Method of measurement

FOSQ-10 questionnaire

Secondary outcomes

1

Description

change from baseline in CPAP uses duration in hours in melatonin group in comparison with placebo

Timepoint

CPAP uses duration in hours at the baseline and one month after intervention

Method of measurement

CPAP device information

2

Description

change from baseline in CPAP uses duration in number of nights in one month in melatonin group in comparison with placebo

Timepoint

change from baseline in CPAP uses duration in number of nights in melatonin group in comparison with placebo

Method of measurement

CPAP device information

Intervention groups

1

Description

Intervention group: 10 mg melatonin tablets, one tablet before sleep for 30 days. The tablets were supplied from the jalinus factory

Category

Treatment - Drugs

2

Description

Control group: placebo tablets, one tablet before sleep for 30 days. The tablets supplied from jalinus factory

Category

Placebo

Recruitment centers

1

Recruitment center

Name of recruitment center

Emam Khomeini hospital sleep clinic

Full name of responsible person

Tahereh Madani motlaq

Street address

Gharib street, Keshavarz street

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tmotlaq1994@yahoo.com

Sponsors / Funding sources

1

Sponsor

Name of organization / entity

Prescribing and rational use of medicine research center

Full name of responsible person

Dr. Kheirollah Gholami

Street address

North kheradmand avenue, Karimkhanzand street, Hafe tir Square

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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

Prescribing and rational use of medicine research center

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

Tehran University of Medical Sciences

Full name of responsible person

Dr. Shahideh Amini

Position

Associate Professor

Latest degree

Subspecialist

Other areas of specialty/work

Pharmacotherapy, ICU fellowship

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Person responsible for scientific inquiries

Contact

Name of organization / entity

Tehran University of Medical Sciences

Full name of responsible person

Dr. Shahideh Amini

Position

Associated Professor

Latest degree

Subspecialist

Other areas of specialty/work

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Person responsible for updating data

Contact

Name of organization / entity

Tehran University of Medical Sciences

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Latest degree

Specialist

Other areas of specialty/work

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Phone

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Email

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

No - There is not 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 of the individual participant data collected during the trial, after deidentification

When the data will become available and for how long

Immediately after publication. No end date.

To whom data/document is available

Anyone who wishes to access the data.

Under which criteria data/document could be used

Any purpose.

From where data/document is obtainable

Data are available indefinitely at (link to be included)

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

Data are available indefinitely at (link to be included)

Comments