

Clinical Trial Protocol

Iranian Registry of Clinical Trials

17 Sep 2026

evaluation of the effectiveness of L-citrulline plus nCPAP versus solitary nCPAP in improvement of endothelium dysfunction and decreasing the severity of obstructive sleep apnea in patients undergoing polysomnography in Baharloo hospital and are categorized as moderate to severe OSA

Protocol summary

Study aim

evaluation of the efficacy of L-citrulline plus CPAP on improving endothelial function

Design

Clinical trial with community-based and pragmatic control group, with parallel groups, double blind, randomization method: block randomization with stratification

Settings and conduct

If FMD>NMD, we can conclude that there is endothelial dysfunction and for ruling out arterial muscular dysfunction we use TNG and assess the artery by color doppler sonography. Then we randomly divide patients into 2 groups. For group no.1, we begin the cpap therapy for 1 month plus placebo and for group no.2, we use CPAP during the night and L-citrulline(Stimol Biocodex, which contains 1 gram of citrulline malate) as following: For the first 10 days, 3 times daily, and for the following 20 days, 2 times daily. After 1 month, we evaluate patients again for AHI and the ratio of FMD to NMD. As the AHI level can be extracted using CPAP memory, we calculate NMD and FMD levels by Brachial artery color doppler ultrasonography.

Participants/Inclusion and exclusion criteria

Inclusion criteria: 1. patients who are categorized as moderate to severe OSA (obstructive sleep apnea) on basis of AHI criteria and polysomnography 2. proving their endothelial dysfunction (FMD>NMD) by color doppler sonography 3. ruling out arterial muscular dysfunction by color doppler sonography Exclusion criteria: 1- if less than 40 days is passed from patient's treatment for OSA 2. History of CAD 3- Heart failure or MI 4- Smoking

Intervention groups

We randomize patients into 2 groups. Both groups receive CPAP for 4 hours every night during 1 month. For the intervention group we apply L-citrulline (Stimol-biocodex) with following prescription: for the first 10 days, 3 times daily and for the 20 following days, 2 times a day. for the control group we prescribe placebo with the same protocol.

Main outcome variables

Brachial artery diameter change

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20181126041757N1**

Registration date: **2019-04-18, 1398/01/29**

Registration timing: **prospective**

Last update: **2019-04-18, 1398/01/29**

Update count: **0**

Registration date

2019-04-18, 1398/01/29

Registrant information

Name

Saeed Nateghi

Name of organization / entity

Country

Iran (Islamic Republic of)

Phone

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snateghi@sina.tums.ac.ir

Recruitment status

Recruitment complete**Funding source****Expected recruitment start date**

2019-05-05, 1398/02/15

Expected recruitment end date

2020-05-04, 1399/02/15

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

evaluation of the effectiveness of L-citrulline plus nCPAP versus solitary nCPAP in improvement of endothelium dysfunction and decreasing the severity of obstructive sleep apnea in patients undergoing polysomnography in Baharloo hospital and are categorized as moderate to severe OSA

Public title

Evaluation of the effectiveness of L-citrulline plus nCPAP versus solitary nCPAP in improvement of endothelium dysfunction and decreasing the severity of obstructive sleep apnea

Purpose

Treatment

Inclusion/Exclusion criteria**Inclusion criteria:**

Patients who are categorized as moderate to severe according to AHI criteria by using polysomnography. The ones that clinical ultrasonography proves that the patient has endothelial dysfunction (FMD > NMD). Patients whose arterial muscular dysfunction has been ruled out.

Exclusion criteria:

If less than 40 days have been passed from patient's OSA treatment. History of coronary artery disease (>50% of arterial occlusion, or any background PCI or CABG). Ischemic heart disease. Smoking. Patients who do not have endothelial dysfunction (FMD ratio to normal vessel diameter is more than one). Receiving any medication that affects endothelial function unless 4 half-life of the drug has been passed since its last consume.

Age

No age limit

Gender

Both

Phase

3

Groups that have been masked

- Participant
- Care provider
- Outcome assessor

Sample size

Target sample size: 42

Randomization (investigator's opinion)

Randomized

Randomization description

We divide patients into two groups by permuted block

randomization. Since diabetes status of patients can be as an important covariate which affects the outcome, we control it by stratification approach. By using <https://www.sealedenvelope.com> we are going to make 2 randomized group in the basis of their diabetes status and only one person is going to be aware of our allocation concealment. The investigator gets in touch with that person each time that we have a new participant and ask which of the groups should the participant get involved with and for each drug box we have a number on it which is assigned randomly.

Blinding (investigator's opinion)

Double blinded

Blinding description

Usage of placebo for the patient and assign each patient with a code for radiologist blindness and allocating numbers to each box of drugs

Placebo

Used

Assignment

Parallel

Other design features**Secondary IDs**

empty

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

National Ethics Committee for Biomedical Research

Street address

Building of Tehran University of Medical Sciences, Qods St.

City

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Tehran

Postal code

1366736511

Approval date

2018-11-28, 1397/09/07

Ethics committee reference number

IR.TUMS.VCR.REC.1397.630

Health conditions studied**1****Description of health condition studied**

Obstructive sleep apnea/L-citrulline effect on artery

ICD-10 code

G47.33

ICD-10 code description

Obstructive sleep apnea (adult) (pediatric)

Primary outcomes

1

Description

Brachial artery diameter

Timepoint

The beginning and the end of the study

Method of measurement

colour doppler ultrasound

Secondary outcomes

1

Description

daily sleepiness

Timepoint

at the beginning and the end of the study

Method of measurement

Epworth sleepiness scale questionnaire

2

Description

Depression rate

Timepoint

The beginning and the end of the study

Method of measurement

patients health questionnaire-9

3

Description

Dislipidemia

Timepoint

The beginning and the end of the study

Method of measurement

Patient case

Intervention groups

1

Description

Intervention group: patients are divided into 2 groups by block randomization and by stratification protocol we try that the diabetes dispersion be the same in both groups. For our intervention group we prescribe stimol biocodex which contains 1gr citrulline malate with the following schedule: for the first 10 days,TDS and for the next 20 days, BD. During this 1 month, patients have to utilize CPAP for 4 hours each night. After this 1 month we assess patients from the point of AHI, FMD/NMD by using colour doppler ultrasonography and then we compare data from the beggining to end of our trial.

Category

Treatment - Drugs

2

Description

Control group: cpap therapy for 1 month, 4 hours each night and placebo which is prescribe TDS for the first 10 days and BD for the next 20 days

Category

Placebo

Recruitment centers

1

Recruitment center

Name of recruitment center

Baharlo Hospital

Full name of responsible person

Dr Saeed Nateghi

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Sponsors / Funding sources

1

Sponsor

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Grant name

Grant the first proposal submitted by the faculty

Grant code / Reference number

Is the source of funding the same sponsor organization/entity?

Yes

Title of funding source

Tehran University of Medical Sciences

Proportion provided by this source

90

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
Saeed Nateghi
Position
Associate professor
Latest degree
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Person responsible for updating data

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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