Clinical Trial Protocol
Iranian Registry of Clinical Trials

09 Nov 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 categoriazed as moderate to serevere 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 artety 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-citruline(Stimul 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 critera and polysomnography 2. proving their endothelial dysfunction (FMD>NMD) by colordoppler sonography 3.ruling out arterial muscular dysfunction by colordoppler sonography Exclusion criteria: 1- if less than 40 days is passed from patine's treatment for OSA 2.History of CAD 3-Hear 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-citruline (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 diametre 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)

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+98 21 5517 6031

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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 categoriazed as moderate to serevere 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 the their arterial muscular dysfunction has been ruled out

Exclusion criteria:
If less than 40 days have been passed from patien's OSA treatment Hx of coronary artery disease (>50% of arterial occlusion, or any background PCI or CBAG) 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 diabet status and only one person is going to be aware of our allocation concealment . The investigator get 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 randomely.

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
Tehran

Province
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-citruline 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 sleepness 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 begginig 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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Ziaian Hospital,AbuZar Street
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Sponsors / Funding sources

1

Sponsor
Name of organization / entity
Tehran University of Medical Sciences
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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

Specialist

Other areas of specialty/work

Cardiology

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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