Clinical Trial Protocol
Iranian Registry of Clinical Trials

07 Nov 2026

Evaluation of the effect of adding vitamin C supplementation to Levothyroxine compared with Levothyroxine alone on laboratory parameters and clinical symptoms in patients with primary hypothyroidism: A randomized, placebo-controlled pilot clinical trial

Protocol summary

Study aim
Investigating the effect of adding a Vitamin C supplement (60 mg) to levothyroxine, compared to levothyroxine alone, on laboratory parameters and clinical symptoms in patients with primary hypothyroidism

Design
This study is a Phase 3, randomized, double-blind, placebo-controlled clinical trial with a two-group parallel design, conducted on 40 patients. Randomization will be performed using fixed-size blocks of 2 and Excel software.

Settings and conduct
This study will be conducted at specialized endocrinology clinics affiliated with the Islamic Azad University of Medical Sciences, Tehran. After providing informed consent, eligible patients will be randomly assigned to either the Vitamin C group or the placebo group, and the intervention will continue for eight weeks. Clinical and laboratory assessments will be performed at the beginning and end of the study.

Participants/Inclusion and exclusion criteria
Inclusion criteria: Diagnosis of primary hypothyroidism by a specialist, based on elevated TSH accompanied by low or low-normal free T4 (FT4) levels. TSH levels exceeding the laboratory's upper limit of normal and above 4.5 mIU/L in a recent test, despite regular levothyroxine intake. Exclusion criteria: Chronic kidney disease (e.g., eGFR < 60 ml/min/1.73m² or CKD stage 3 or higher). History of recurrent calcium kidney stones. Known G6PD deficiency.

Intervention groups
Intervention group: Patients with primary hypothyroidism who receive 60 mg Vitamin C effervescent tablet daily for 8 weeks. Control group: Patients with primary hypothyroidism who receive placebo effervescent tablet daily for 8 weeks.

Main outcome variables
TSH level – Free T4 level – Zulewski questionnaire score

General information

Reason for update

Acronym

IRCT registration information
IRCT registration number: **IRCT20210519051348N5**
Registration date: **2026-09-29, 1405/07/07**
Registration timing: **registered_while_recruiting**

Last update: **2026-09-29, 1405/07/07**
Update count: **0**

Registration date
2026-09-29, 1405/07/07

Registrant information

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Name of organization / entity

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Iran (Islamic Republic of)

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Recruitment status
recruiting

Funding source

Expected recruitment start date
2026-09-23, 1405/07/01

Expected recruitment end date
2026-12-22, 1405/10/01

Actual recruitment start date
empty
Actual recruitment end date
empty
Trial completion date
empty

Scientific title
Evaluation of the effect of adding vitamin C supplementation to Levothyroxine compared with Levothyroxine alone on laboratory parameters and clinical symptoms in patients with primary hypothyroidism: A randomized, placebo-controlled pilot clinical trial

Public title
Evaluation of the effect of adding a Vitamin C supplement to levothyroxine compared to levothyroxine alone in patients with primary hypothyroidism
Purpose
Treatment
Inclusion/Exclusion criteria
Inclusion criteria:
Ages 18 to 65 The criteria include a diagnosis of primary hypothyroidism by a specialist, use of a fixed dose of levothyroxine for at least the past eight weeks, and suboptimal thyroid control—characterized by a TSH level exceeding the laboratory's upper limit of normal and 4.5 mIU/L—despite regular levothyroxine intake.
Exclusion criteria:
Patients with renal failure, a history of recurrent kidney stones, hyperoxaluria, iron overload disorders (such as hemochromatosis or thalassemia major), or G6PD deficiency. Pregnant or breastfeeding Regular consumers of high doses of vitamin C or other antioxidants.
Age
From **18 years** old to **65 years** old
Gender
Both

Phase
3
Groups that have been masked

- Participant
- Investigator

Sample size
Target sample size: **40**
Randomization (investigator's opinion)
Randomized
Randomization description
Participants will be randomly assigned to either the intervention group (Vitamin C) or the control group (placebo) in a 1:1 ratio. A fixed-block randomization method (block size of 2) will be employed to ensure an even distribution of participants across the treatment groups throughout the enrollment period. The randomization sequence will be generated by an independent third party—who is not involved in participant assessment or data collection—using randomization software (such as Sealedenvelope.com). The allocation sequence within each block will be fully randomized, and the list contents will remain concealed from the research team until the study concludes (allocation concealment). Following the acquisition of informed consent and confirmation of eligibility criteria, participants will be assigned to one of two groups based on their sequential number in a coded list, in the order of their enrollment. The person responsible for allocation—unaware of the contents of the subsequent block—will determine and announce the assigned group solely based on the participant's sequential number. This process enables the control of selection bias and the maintenance of statistical balance between the groups.
Blinding (investigator's opinion)
Double blinded
Blinding description
The patient, physician, researcher, and evaluator (student) will remain unaware of whether the patient has received the drug or the placebo (double-blinding). The drug (Vitamin C) and the placebo will be prepared as effervescent tablets that are identical in shape, color, size, taste, and method of administration, ensuring that participants cannot distinguish between them. The coding of the medication boxes will be performed by an independent third party not involved in the study, and the code will not be broken until the study concludes.
Placebo
Used
Assignment
Parallel
Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee
Name of ethics committee
REC of Islamic Azad Tehran Medical Sciences University-Pharmacy and Pharmaceutical Branches faculty
Street address
No 99, Yasaman Alley, Yakhchal St, Shariati Av
City
Tehran
Province
Tehran
Postal code
1941933111
Approval date
2026-06-09, 1405/03/19
Ethics committee reference number
IR.IAU.PS.REC.1405.014

Health conditions studied

1

Description of health condition studied
Effect of Adding Vitamin C Supplementation to

Levothyroxine Compared with Levothyroxine Alone

ICD-10 code

E03.9

ICD-10 code description

Hypothyroidism, unspecified

Primary outcomes

1

Description

TSH level

Timepoint

Beginning of the study and the end of week 8

Method of measurement

ELISA method

2

Description

Free T4 level

Timepoint

Beginning of the study and the end of week 8

Method of measurement

ELISA method

Secondary outcomes

1

Description

Clinical score for hypothyroidism based on the Zulewski questionnaire

Timepoint

Beginning of the study and the end of week 8

Method of measurement

Zulewski questionnaire

Intervention groups

1

Description

Intervention group: The pharmacological intervention consists of administering a 60 mg Vitamin C effervescent tablet daily. Participants in the intervention group will dissolve the tablet in a glass of water and consume it in the morning on an empty stomach, concurrently with their levothyroxine tablet. The 60 mg Vitamin C effervescent tablets will be produced in the university laboratory.

Category

Treatment - Drugs

2

Description

Control group: Participants in the control group will dissolve a placebo effervescent tablet (containing no Vitamin C) in a glass of water and consume it daily on an empty stomach in the morning, concurrently with their levothyroxine tablet. The placebo effervescent tablets will be produced in the university laboratory.

Category

Placebo

Recruitment centers

1

Recruitment center

Name of recruitment center

Booali Hospital

Full name of responsible person

Marjan Golabslekar

Street address

Booali Hospital, at the beginning of Damavand Street, Imam Hossein Square, Tehran, Iran

City

Tehran

Province

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Sponsors / Funding sources

1

Sponsor

Name of organization / entity

Islamic Azad University

Full name of responsible person

Masoud Parsania

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Tehran Medical Sciences, Islamic Azad University Central Building, Corner of Gol Yakh Alley, Ayeneh Boulevard, Pabarja Street, Qolhak Junction, Shariati Street

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Phone

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Email

masoud_parsania@yahoo.com

Grant name

Grant code / Reference number

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

Yes

Title of funding source

Islamic Azad University

Proportion provided by this source

1

Public or private sector

Private

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
Islamic Azad University
Full name of responsible person
Mobina Asasi
Position
Pharmacy student
Latest degree
Medical doctor
Other areas of specialty/work
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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
Yes - There is 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
Not applicable
Data Dictionary
Not applicable
Title and more details about the data/document
All study data will be available for sharing upon request after de-identification and anonymization of participant information, in accordance with confidentiality requirements.
When the data will become available and for how long
Just after the article's publication
To whom data/document is available
To whom data/document is available
Under which criteria data/document could be used
De-identified individual data will be available to qualified researchers upon written request and ethics committee approval after publication of the main results. Data may only be used for scientific purposes; commercial use is prohibited.
From where data/document is obtainable
For further information or to request access to the data, applicants may correspond via email with the Clinical

Department of the Islamic Azad University (Pharmaceutical Sciences Branch) and Dr. Hashemian. Email: farshadhashemian@gmail.com

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

Applicants may request access to the study data by contacting the relevant department through the provided email address or telephone number. Requests should include information regarding the applicant's academic background, institutional affiliation, and the intended purpose of data use. Applicants will also be required to acknowledge and appropriately cite the original study in any resulting scientific work. De-identified study data will be available beginning six months after publication of the study results. Following approval of the request by the principal investigator, the data files will be provided to eligible applicants via email within approximately one week.

Comments