

Clinical Trial Protocol

Iranian Registry of Clinical Trials

15 Jun 2026

Randomized control Clinical Trial to assess the efficacy of the three different combined preparations of levothyroxine plus slow-release liothyronine

Protocol summary

Study aim

To assess and compare the efficacy of treatment of hypothyroidism with LT4 monotherapy with three different combinations of LT4 plus SR-T3

Design

A parallel randomized, double-blind controlled clinical trial, phase 2, 120 samples

Settings and conduct

Patients will be recalled from a private clinic in Tehran to the Research Institute for Endocrine Sciences. The treatment will be allocated based on the pre-specified double-blinded random allocation while the researchers and patients are blinded to therapy. The drug will be continued for eight weeks. Participants will be evaluated for biochemical assessments and thyroid symptoms at baseline and the end of the study. TSQ will assess treatment satisfaction at the end of the study. Also, in the last visit, blood samples will be obtained six times during 24 hours to assess the pharmacokinetic of slow-release T3.

Participants/Inclusion and exclusion criteria

Patients ≥ 20 y with hypothyroidism who attain euthyroidism under LT4 monotherapy. Exclusion criteria: Pregnancy, chronic liver and kidney disease, heart failure, cancer, taking methimazole, PTU, Tamoxifen, estrogen, progesterone, and corticosteroids

Intervention groups

1. The group with a daily intake of 75 μ g LT4 plus 7.5 μ g SR-T3(ratio 1:10) 2. The group with a daily intake of 68.5 μ g LT4 plus 9 μ g SR-T3(ratio 1:8) 3. The group with a daily intake of 60 μ g LT4 plus 12 μ g SR-T3 (ratio 1:5) 4. The group with LT4 monotherapy (control group)

Main outcome variables

T3/T4 ratio, TSH, T4, T3, free T4. Clinical signs and symptoms of hypothyroidism(Thyroid symptom questionnaire), serum lipid profile, FBS, LDH, CK, insulin, Metabolomics, T3 Cmax, T3 Tmax ECG heart rate, BP,

Thyroid treatment satisfaction questionnaire(THY-TSQ)

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20100922004794N13**

Registration date: **2021-12-08, 1400/09/17**

Registration timing: **prospective**

Last update: **2021-12-08, 1400/09/17**

Update count: **0**

Registration date

2021-12-08, 1400/09/17

Registrant information

Name

Fereidoun Azizi

Name of organization / entity

Country

Iran (Islamic Republic of)

Phone

+98 21 2240 9309

Email address

azizi@endocrine.ac.ir

Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2022-02-20, 1400/12/01

Expected recruitment end date

2022-09-23, 1401/07/01

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

Randomized control Clinical Trial to assess the efficacy of the three different combined preparations of levothyroxine plus slow-release liothyronine

Public title

Improvement in treatment of hypothyroidism using slow-release Liothyronine

Purpose

Treatment

Inclusion/Exclusion criteria**Inclusion criteria:**

Hypothyroid patients over 20 yrs. due to radioactive iodine intake for treating Graves' Disease, who attained euthyroid status with LT4 monotherapy (TSH=0.5-5 mU/L is optimal).

Exclusion criteria:

Pregnancy, chronic kidney or liver disease, congestive heart failure, cancer, taking methimazole, PTU, Tamoxifen, estrogen, progesterone, and corticosteroids

Age

From **20 years** old

Gender

Both

Phase

2

Groups that have been masked

- Participant
- Investigator
- Outcome assessor
- Data analyser
- Data and Safety Monitoring Board

Sample size

Target sample size: **44**

Randomization (investigator's opinion)

Randomized

Randomization description

Patients will be allocated to three intervention groups and one control group using stratified randomization. Six stratifications will be made based on age and gender. At first, patients will be assigned to three age groups of $\leq 50y$, 51-70y, $> 70y$. Under each subgroup, patients will be assigned to male and female. Then under each sex subgroup, patients will be randomly assigned to four treatment groups using the random table.

Blinding (investigator's opinion)

Double blinded

Blinding description

After implementation of randomization and specific coding, the subjects will be assigned to the groups using allocation concealment, which helps to keep clinicians, participants, and investigators unaware of upcoming assignments. The standard methods of ensuring allocation concealment will be sequentially numbered or coded opaque containers. For single-center clinical trials such as the current trial, we will identify a staff member not involved with the trial who can keep the randomization list. This staff will be instructed to keep

the list private and only reveal a treatment allocation after receiving information demonstrating that the patient is eligible and has consented to the trial. The subjects and the investigators will be kept from knowing who will be assigned to which treatment (double-blind). Both groups will receive identical tablets in physical appearance, taste, and smell to fulfill this.

Placebo

Not used

Assignment

Parallel

Other design features

The drug will be continued in three intervention groups (three combinations of Levothyroxine plus Liothyronine) and one control group (Levothyroxine monotherapy) for eight weeks. Patients will be visited at four-week intervals to measure TSH and assess therapy adherence and adverse effects. Drug dosage would be adjusted to maintain serum TSH concentration within 0.5-3 mU/l. Participants will be evaluated at baseline and one consequent follow-up at eight weeks. At first and last visit at eight weeks, venous blood samples will be collected from all participants after a 12-hour fast for measurement of serum TSH, total T3, total T4, free T4, FBS, total cholesterol, HDL cholesterol and triglycerides, insulin, LDH and CK, and metabolomics. ECG, resting heart rate, and BP will be measured, and all questionnaires will be filled out at the first and last visits (TSF and TSQ). Also, in the last visit, after blood sampling and getting the specified treatment at 8 am, the blood sampling will be done at 9 am, 10 am, 12 MD, 2 pm, 4 pm and the next day at 8 am, and serum levels of T4, FREE T4, TSH, and T3 will be measured in all samples to calculate T3/T4 ratio, T3 CMAX, and T3 TMAX and AUC (0-24). To ensure compliance with drug therapy, the responsible person will check the drug package and count the number of pill intake by direct questioning in 2 weeks intervals by phone call and pill counting at the last visit.

Secondary Ids

empty

Ethics committees

1

Ethics committee**Name of ethics committee**

Ethics Human Research Review Committee of the Endocrine Research Center, Shahid Beheshti University

Street address

no 23, Erabi St, Velenjak

City

Tehran

Province

Tehran

Postal code

1985717413

Approval date

2021-07-11, 1400/04/20

Ethics committee reference number

IR.SBMU.ENDOCRINE.REC.1400.031

Health conditions studied

1

Description of health condition studied

Hypothyroidism

ICD-10 code

E03.9

ICD-10 code description

Hypothyroidism, unspecified

Primary outcomes

1

Description

T3/T4 ratio

Timepoint

8 weeks after intervention

Method of measurement

Serum Total tri-iodothyronine(TT3), total thyroxine (TT4) will be determined on -20°C stored serum samples by the electrochemiluminescence immunoassay (ECLIA) method, using Roche Diagnostics kits and Roche/Hitachi Cobas e-411 analyzer (GmbH, Mannheim, Germany).

Secondary outcomes

1

Description

Serum TSH and Free T4 concentrations

Timepoint

At the baseline and end of the study

Method of measurement

On -20°C stored serum samples by the electrochemiluminescence immunoassay (ECLIA) method, using Roche Diagnostics kits and Roche/Hitachi Cobas e-411 analyzer (GmbH, Mannheim, Germany)

2

Description

Serum Lipid Profile

Timepoint

At the baseline and end of the study

Method of measurement

Laboratory measurements with the related kits

3

Description

FBS, LDH, CK, ferritin

Timepoint

At the baseline and end of the study

Method of measurement

Laboratory measurements with the related kits

4

Description

metabolomics

Timepoint

At the baseline and end of the study

Method of measurement

Laboratory measurements with the related kits

5

Description

Cardiac parameters (ECG, resting heart rate, BP)

Timepoint

At the baseline and end of the study

Method of measurement

Laboratory measurements with the related kits

6

Description

Treatment satisfaction

Timepoint

At the first and last visits

Method of measurement

Treatment satisfaction questionnaire (THY-TSQ)

7

Description

Thyroid symptoms

Timepoint

At the first and last visits

Method of measurement

Thyroid symptom questionnaire

Intervention groups

1

Description

Intervention group 1: Taking 75µg LT4 Tab. plus 7.5µg SR-T3 Tab (ratio 1:10). Dorsa Pharmaceutical Company, Tavan Institute, will formulate these tablets. The patients will take medicine daily before breakfast for eight weeks. The treatment will be allocated based on the pre-specified random allocation.

Category

Treatment - Drugs

2

Description

Intervention group 2: Taking 68.5 µg LT4 Tab. plus 9 µg SR-T3 Tab (ratio 1:8). Dorsa Pharmaceutical Company, Tavan Institute, will formulate these tablets. The patients will take medicine daily before breakfast for eight weeks. The treatment will be allocated based on the pre-specified random allocation.

Category

Treatment - Drugs

3

Description

Intervention group 3: Taking 60 µg LT4 Tab. plus 12 µg SR-T3 Tab (ratio 1:5). Dorsa Pharmaceutical Company, Tavan Institute, will formulate these tablets. The patients will take medicine daily before breakfast for eight weeks. The treatment will be allocated based on the pre-specified random allocation.

Category

Treatment - Drugs

4

Description

Control group: Levothyroxine monotherapy Dorsa Pharmaceutical Company, Tavan Institute, will formulate these tablets. The patients will take medicine daily before breakfast for eight weeks. The treatment will be allocated based on the pre-specified random allocation.

Category

Treatment - Drugs

Recruitment centers

1

Recruitment center

Name of recruitment center

Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences

Full name of responsible person

Fereidoun Azizi

Street address

No.23, Erabi St, Yaman Ave., Velenjak

City

Tehran

Province

Tehran

Postal code

1985717413

Phone

+98 21 2243 2500

Fax

+98 21 2241 6264

Email

azizi@endocrine.ac.ir

Sponsors / Funding sources

1

Sponsor

Name of organization / entity

Dorsa Pharmaceutical Company

Full name of responsible person

Amir Esmail Saghafinia

Street address

No.1, Khajoo St, Rostamkhani St., Salehi Blvd., Tarasht

City

Tehran

Province

Tehran

Postal code

3188119978

Phone

+98 21 5461 2000

Email

info@dorsadarou.com

Grant name

Grant code / Reference number

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

Yes

Title of funding source

Dorsa Pharmaceutical Company

Proportion provided by this source

90

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

Industry

Person responsible for general inquiries

Contact

Name of organization / entity

Shahid Beheshti University of Medical Sciences

Full name of responsible person

Ladan Mehran

Position

Assistant Prof.

Latest degree

Ph.D.

Other areas of specialty/work

Internal Medicine

Street address

NO:23, Erabi St, Yaman St, Velenjak Ave

City

Tehran

Province

Tehran

Postal code

1985717413

Phone

+98 21 2243 2500

Email

lmehran@endocrine.ac.ir

Person responsible for scientific inquiries

Contact

Name of organization / entity

Research Institute for Endocrine Sciences

Full name of responsible person

Ladan Mehran

Position

Assistant Professor

Latest degree

Specialist

Other areas of specialty/work

Thyroid disorders

Street address

No. 23, Erabi St, Yaman Ave, Velenjak

City

Tehran

Province

Tehran

Postal code

1985717413

Phone

+98 21 2243 2500

Email

lmehran@endocrine.ac.ir

Person responsible for updating data

Contact

Name of organization / entity

Research Institute for Endocrine Sciences

Full name of responsible person

Ladan Mehran

Position

Assistant Professor

Latest degree

Specialist

Other areas of specialty/work

Thyroid disorders

Street address

No.23, Erabi St, Yaman Ave, Velenjak

City

Tehran

Province

Tehran

Postal code

1985717413

Phone

+98 21 2243 2500

Email

lmehran@endocrine.ac.ir

Sharing plan

Deidentified Individual Participant Data Set (IPD)

No - There is not a plan to make this available

Justification/reason for indecision/not sharing IPD

These data are belonged to Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran

Study Protocol

No - There is not a plan to make this available

Statistical Analysis Plan

No - There is not a plan to make this available

Informed Consent Form

No - There is not a plan to make this available

Clinical Study Report

No - There is not a plan to make this available

Analytic Code

No - There is not a plan to make this available

Data Dictionary

No - There is not a plan to make this available