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≥20y 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 75µg LT4 plus 7.5 µg SR-T3(ratio 1:10) 2. The group with a daily intake of 68.5µg LT4 plus 9 µg SR-T3(ratio 1:8) 3. The group with a daily intake of 60µg LT4 plus 12µg 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

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Iran (Islamic Republic of)

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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 ≤50y, 51-70y, >70 y. 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 -20ºC 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 -20ºC 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

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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

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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

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Person responsible for scientific inquiries

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Ladan Mehran

Position

Assistant Professor

Latest degree

Specialist

Other areas of specialty/work

Thyroid disorders

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Person responsible for updating data

Contact

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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