

Clinical Trial Protocol

Iranian Registry of Clinical Trials

11 Jun 2026

Study the effect of combination therapy with levothyroxine and liothyronine in comparison with levothyroxine on Well-Being, Quality of Life, or Cognitive Function in Patients with Primary Hypothyroidism

Protocol summary

Study aim

the present RCT will be conducted to evaluate the effect of combined LT4+LT3 therapy vs LT4 alone on the quality of life.

Design

A randomized, double-blind, parallel-group comparison trial in a 1:1 ratio including the baseline (April- Oct 2020) and the 6-months follow-up

Settings and conduct

Hypothyroid patients with levothyroxine monotherapy and normal TSH In this double blind study, patients divided in two groups Place of study: Sayad Shirazi Hospital Endocrinology Clinic, Gorgan

Participants/Inclusion and exclusion criteria

Inclusion Criteria Age over 16 years Being able to read and understand Persian Diagnosis of overt hypothyroidism at least 6 months before inclusion Stable and regular LT4 monotherapy for at least 3 months before inclusion Patient-reported signs and symptoms of hypothyroidism including fatigue, mood change, weight gain, lethargy, decreased psychomotor performance conative, depression, and disturbances despite normal thyroid hormone levels Exclusion criteria Pregnancy or planned pregnancy within the next 6 months Patients with drug or alcohol addiction Patients with Malignancy, cardiovascular disease ,renal, or hepatic disease, chronic liver disease ,depression, anxiety Patients with mental illness and had been on psychiatric medicine for 6 months before inclusion

Intervention groups

Patients will be randomized to continue receiving their usual dose of LT4 (100 µg/day) in the combination of placebo for 6 months (Group 1), or change their usual treatment to the combination therapy of LT4 50 µg and LT3 6.25 µg twice a day (Group 2) The placebo will be "liothyronine" and labeled "approved for research purposes only".

Main outcome variables

changes in quality of life between baseline and follow-up visits of the

General information

Reason for update

Change questionnaire

Acronym

IRCT registration information

IRCT registration number: **IRCT20200410047012N1**

Registration date: **2020-06-12, 1399/03/23**

Registration timing: **registered_while_recruiting**

Last update: **2022-08-07, 1401/05/16**

Update count: **4**

Registration date

2020-06-12, 1399/03/23

Registrant information

Name

Fatemeh Hajtalebi

Name of organization / entity

Country

Iran (Islamic Republic of)

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+98 17 3235 4068

Email address

fahajtalebi@yahoo.com

Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2020-03-19, 1398/12/29

Expected recruitment end date

2020-09-20, 1399/06/30

Actual recruitment start date

2020-03-19, 1398/12/29
Actual recruitment end date
2020-09-20, 1399/06/30
Trial completion date
2021-03-18, 1399/12/28

Scientific title

Study the effect of combination therapy with levothyroxine and leiothyronine in comparison with levothyroxine on Well-Being, Quality of Life, or Cognitive Function in Patients with Primary Hypothyroidism

Public title

effect of combination therapy of levothyroxine and levothyronine in comparison with levothyroxine in quality of life and cognitive function of patients with primary hypothyroidism

Purpose

Supportive

Inclusion/Exclusion criteria

Inclusion criteria:

Age over 16 years Being able to read and understand Persian Diagnosis of overt hypothyroidism at least 6 months before inclusion Stable and regular LT4 monotherapy for at least 3 months before Patient-reported signs and symptoms of hypothyroidism including fatigue, mood change, weight gain, lethargy, decreased psychomotor performance conative, depression, and disturbances despite normal thyroid hormone levels

Exclusion criteria:

Pregnancy or planned pregnancy within the next 6 months Patients with drug or alcohol addiction Patients with Malignancy Patients with cardiovascular disease Patients with renal, or hepatic disease Patients with chronic liver disease Patients with depression, anxiety Patients with mental illness and had been on psychiatric medicine for 6 months before inclusion

Age

From **16 years** old

Gender

Both

Phase

3

Groups that have been masked

- Participant
- Investigator

Sample size

Target sample size: **158**

Actual sample size reached: **151**

Randomization (investigator's opinion)

Randomized

Randomization description

We will design a randomized, double-blind (both patients and physicians), parallel-group comparison trial in a 1:1 ratio, and patients are randomly assign following procedures to LT4+placebo or LT4+LT3 treatment groups. The list of random allocation cards will be generated by an independent trained researcher using computer-generated random numbers. To avoid the confusion of coding A or B, the researcher will keeps the

original random allocation sequences in an inaccessible third place and works with a copy.

Blinding (investigator's opinion)

Double blinded

Blinding description

The placebo will be placed into envelopes according to the allocation orders by another independent nurse who was not aware of the study. The patient's ID, visit date, and other information will be recorded on each envelope. Neither the patients nor the physicians who will assess the patients are aware of the treatment. After 6 months, another independent researcher who is not aware of the treatment will assess the patient's health-related quality of life scores.

Placebo

Used

Assignment

Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Ethics committee of Gorgan University of Medical Sciences

Street address

Ethics Committee of the Vice Chancellor for Research and Technology, 3rd Floor, School of Dentistry, Golestan University of Medical Sciences, Shast Kola Road, Gorgan, Iran

City

Gorgan

Province

Golestan

Postal code

4915663158

Approval date

2020-04-12, 1399/01/24

Ethics committee reference number

IR.Goums.Rec.1399.016

Health conditions studied

1

Description of health condition studied

Hypothyroidism

ICD-10 code

E03

ICD-10 code description

Other hypothyroidism

Primary outcomes

1

Description

The quality of life changes between baseline and follow-up visits of the Physical component summary in SF-36V1

Timepoint

Before study (baseline) , follow-up visit (6 months later)

Method of measurement

The 36-item Short-Form Health Survey version 1 (SF-36V1) questionnaire

2

Description

The quality of life changes between baseline and follow-up visits of the Mental component summary in SF-36V1

Timepoint

Before study (baseline) , follow-up visit (6 months later)

Method of measurement

The 36-item Short-Form Health Survey version 1 (SF-36V1) questionnaire

Secondary outcomes

1

Description

changes between baseline and follow-up visits of the weight

Timepoint

Before the intervention and 6 months after taking the drug

Method of measurement

digital scale

2

Description

changes between baseline and follow-up visits of the Blood pressure

Timepoint

Before the intervention and 6 months after taking the drug

Method of measurement

manual auscultatory device

3

Description

changes between baseline and follow-up visits of the Serum TSH

Timepoint

Before the intervention and 6 months after taking the drug

Method of measurement

immunochemiluminometric assay

4

Description

changes between baseline and follow-up visits of the Serum total cholesterol

Timepoint

Before the intervention and 6 months after taking the drug

Method of measurement

enzymatic colorimetric methods

5

Description

changes between baseline and follow-up visits of the Serum triglyceride

Timepoint

Before the intervention and 6 months after taking the drug

Method of measurement

enzymatic colorimetric methods

6

Description

changes between baseline and follow-up visits of the Serum LDL cholesterol

Timepoint

Before the intervention and 6 months after taking the drug

Method of measurement

enzymatic colorimetric methods

7

Description

changes between baseline and follow-up visits of the Serum HDL cholesterol

Timepoint

Before the intervention and 6 months after taking the drug

Method of measurement

precipitation method

8

Description

changes between baseline and follow-up visits of the in physical activity

Timepoint

Before the intervention and 6 months after taking the drug

Method of measurement

International Physical Activity Questionnaire short form (IPAQ20)

9

Description

The quality of life changes between baseline and follow-up visits of the Physical functioning domain in SF-36V1

Timepoint

Before study (baseline) , follow-up visit (6 months later)

Method of measurement

The 36-item Short-Form Health Survey version 1 (SF-36V1) questionnaire

10

Description

The quality of life changes between baseline and follow-up visits of the Social functioning domain in SF-36V1

Timepoint

Before study (baseline) , follow-up visit (6 months later)

Method of measurement

The 36-item Short-Form Health Survey version 1 (SF-36V1) questionnaire

11

Description

The quality of life changes between baseline and follow-up visits of the Vitality domain in SF-36V1

Timepoint

Before study (baseline) , follow-up visit (6 months later)

Method of measurement

The 36-item Short-Form Health Survey version 1 (SF-36V1) questionnaire

12

Description

The quality of life changes between baseline and follow-up visits of the General mental health domain in SF-36V1

Timepoint

Before study (baseline) , follow-up visit (6 months later)

Method of measurement

The 36-item Short-Form Health Survey version 1 (SF-36V1) questionnaire

13

Description

The quality of life changes between baseline and follow-up visits of the Bodily pain domain in SF-36V1

Timepoint

Before study (baseline) , follow-up visit (6 months later)

Method of measurement

The 36-item Short-Form Health Survey version 1 (SF-36V1) questionnaire

14

Description

The quality of life changes between baseline and follow-up visits of the Limitations in physical activities domain in SF-36V1

Timepoint

Before study (baseline) , follow-up visit (6 months later)

Method of measurement

The 36-item Short-Form Health Survey version 1 (SF-36V1) questionnaire

15

Description

The quality of life changes between baseline and follow-up visits of the General health perceptions domain in SF-36V1

Timepoint

Before study (baseline) , follow-up visit (6 months later)

Method of measurement

The 36-item Short-Form Health Survey version 1 (SF-36V1) questionnaire

16

Description

The quality of life changes between baseline and follow-up visits of the Limitations due to emotional problems domain in SF-36V1

Timepoint

Before study (baseline) , follow-up visit (6 months later)

Method of measurement

The 36-item Short-Form Health Survey version 1 (SF-36V1) questionnaire

Intervention groups

1

Description

Patients are randomized to continue receiving their usual dose of LT4 (starting dose of an average of 100 µg/day) in the combination of placebo (liothyronine: to ensure blinding) for 6 months (Group 1)

Category

Treatment - Drugs

2

Description

the combination therapy of LT4 (LT4 dose at the time of inclusion-50 µg) and LT3 (6.25 µg twice a day) (Group 2).

Category

Treatment - Drugs

Recruitment centers

1

Recruitment center

Name of recruitment center

Shahid Sayad Shirazi Hospital in Gorgan

Full name of responsible person

Fateme Hajtalebi

Street address

Endocrinology and Metabolism Clinic, Ground Floor, Shahid Sayad Shirazi Hospital, Sayad Shirazi Blvd., Bahonar Square, Gorgan, Iran

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Email

fahajtalebi@yahoo.com

Sponsors / Funding sources

1

Sponsor

Name of organization / entity

Gorgan University of Medical Sciences

Full name of responsible person

Dr.Mahammad Reza Honarvar

Street address

Ethics Committee of the Vice Chancellor for Research and Technology, 3rd Floor, School of Dentistry, Golestan University of Medical Sciences, Shast Kola Road, Gorgan, Iran

City

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Grant name**Grant code / Reference number****Is the source of funding the same sponsor organization/entity?**

Yes

Title of funding source

Gorgan University of Medical Sciences

Proportion provided by this source

100

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**

Gorgan University of Medical Sciences

Full name of responsible person

Dr Hamide Akbari

Position

Assistant Professor

Latest degree

Subspecialist

Other areas of specialty/work

Internal Medicine

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Person responsible for scientific inquiries

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Full name of responsible person

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Position

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Latest degree

Medical doctor

Other areas of specialty/work

Internal Medicine

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Person responsible for updating data

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Phone

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Fax**Email**

Sharing plan

Deidentified Individual Participant Data Set (IPD)

Yes - There is a plan to make this available

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

Yes - There is 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

Title and more details about the data/document

All data in this study can be shared without identifying

individuals.

When the data will become available and for how long

Start access 3 months after printing the results

To whom data/document is available

Data from this study will only be available to researchers working at academic and research institutes and specialist physicians

Under which criteria data/document could be used

There are no restrictions on data analysis

From where data/document is obtainable

Dr. Fatemeh Talebi / Email: Fahajtalebi@yahoo.com/

Phone Number: 09151042897

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

The applicant will be able to access the document after submitting documents regarding the reason for requesting the data file and determining the identity of the person (specialist or researcher).

Comments