Clinical Trial Protocol
Iranian Registry of Clinical Trials

29 Oct 2026

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

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

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Fatemeh Hajtalebi

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

1

Sponsor
Name of organization / entity
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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
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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