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Levothyroxine and liothyronine combination therapy in patients with hypothyroidism and persistent symptoms

Submission date
22/08/2026

Recruitment status
No longer recruiting

Registration date
25/08/2026

Overall study status
Completed

Last Edited
25/08/2026

Condition category
Nutritional, Metabolic, Endocrine

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Primary hypothyroidism occurs when the thyroid gland does not produce enough thyroid hormones. The standard treatment is levothyroxine, a synthetic form of the thyroid hormone thyroxine. Although treatment usually restores thyroid hormone levels, some patients continue to experience symptoms such as tiredness, weight gain, and memory problems, or sleep disturbances. One possible treatment option for these patients is to combine levothyroxine with liothyronine, a synthetic form of the thyroid hormone triiodothyronine.

This study aims to evaluate changes in quality of life in patients with primary hypothyroidism and persistent symptoms who receive combined levothyroxine and liothyronine therapy. The study also evaluates clinical and biochemical changes during treatment and explores whether genetic differences may be associated with the response to therapy.

Who can participate?
Adults aged 18 to 60 years with primary hypothyroidism of benign origin who continue to experience symptoms despite treatment with levothyroxine can participate. Participants must meet the study eligibility criteria and provide written informed consent.

What does the study involve?
Participants receive combined treatment with levothyroxine and liothyronine and are followed over time. Quality of life is assessed using a questionnaire specifically developed for people with thyroid disease. Clinical and body measurements are recorded, and blood samples are collected to measure thyroid hormones and other laboratory parameters. Blood samples are also used to study selected genetic variants that may be related to thyroid hormone metabolism.

What are the possible benefits and risks of participating?
Participants may experience improvements in symptoms and quality of life with combined therapy, although improvement cannot be guaranteed. Liothyronine may cause symptoms related to excessive thyroid hormone exposure, such as palpitations, anxiety, tremor, sweating, or sleep disturbances. Participants are clinically monitored during follow-up.

Where is the study run from?
The study is conducted at Hospital Juárez de México, Mexico City, Mexico.

When does the study start, and how long is it expected to run?
April 2023 to November 2024.

Who is funding the study?
The study was supported by institutional resources from Hospital Juárez de México. Productos Medix, S.A. de C.V. provided in-kind support through the donation of study medication.

Who is the main contact?
Katy Alejandra Sánchez Pozos, PhD, Hospital Juárez de México, katy.sanchez@salud.gob.mx

Contact information

Type(s)
Principal investigator, Scientific, Public

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Additional identifiers

Study information

Scientific Title
Quality of life in adults with primary hypothyroidism and persistent symptoms receiving combined levothyroxine and liothyronine therapy compared with baseline over 12-months

Study objectives
The primary objective of this study was to evaluate changes in quality of life in adults with primary hypothyroidism and persistent symptoms receiving combined levothyroxine and liothyronine therapy. Secondary objectives were to evaluate changes in anthropometric, biochemical, and thyroid hormone parameters during treatment; assess treatment-related adverse events; and explore the association of DIO2 genetic variants with response to combination therapy.

Ethics approval required
Ethics approval required

Ethics approval(s)

Approved 02/03/2023, Research Ethics Committee of Hospital Juárez de México (Av Instituto Politécnico Nacional 5160, Magdalena de las Salinas, Gustavo A. Madero, Mexico City, 07760, Mexico; +52 55 5747 7560 ext. 7634; cei.hjm@gmail.com), ref: HJM 042/22-I

Primary study design
Interventional

Allocation
N/A: single arm study

Masking
Open (masking not used)

Control
Uncontrolled

Assignment
Single

Purpose
Treatment

Study type(s)

Health condition(s) or problem(s) studied
Primary hypothyroidism of benign etiology in patients with persistent symptoms despite levothyroxine monotherapy

Interventions
All participants receive combined levothyroxine and liothyronine therapy; there is no control group, and participants are not randomized. The liothyronine dose is calculated as one-third of the participant´s previous levothyroxine dose, based on the pharmacodynamic equivalence between levothyroxine and liothyronine. Levothyroxine is administered orally once daily, 30 minutes before breakfast, and liothyronine is administered orally three times daily, 30 minutes before meals. Participants undergo clinical and anthropometric assessments and provide fasting blood samples before the morning medication dose at baseline and during follow-up. Thyroid function and biochemical parameters are evaluated, and treatment adherence is assessed using the Morisky Medication Adherence Scale and pill counts. Quality of life is assessed using the validated Spanish version of the Thyroid-Related Quality of Life Patient-Reported Outcome questionnaire (ThyPROes). Participants are monitored for adverse events and followed for 12 months.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Levothyroxine, liothyronine

Primary outcome(s)

1. Thyroid-related quality of life measured using the validated Spanish version of the Thyroid-Related Quality of Life Patient-Reported Outcome questionnaire (ThyPROes) at baseline, 6 months, and 12 months

Key secondary outcome(s)

1. Fatigue presence or absence measured using the study symptom questionnaire at baseline, 3 months, 6 months, 12 months

2. Weight gain presence or absence measured using the study symptom questionnaire at baseline, 3 months, 6 months, 12 months

3. Memory complaints presence or absence measured using the study symptom questionnaire at baseline, 3 months, 6 months, 12 months

4. Insomnia presence or absence measured using the study symptom questionnaire at baseline, 3 months, 6 months, 12 months

5. Achilles tendon reflex measured using a clinical assessment by eliciting the Achilles tendon reflex and recording the response as present or absent at baseline, 3 months, 6 months, 12 months

6. Body weight measured using standard methods in kilograms at baseline, 3 months, 6 months, 12 months

7. Body mass index, calculated as body weight in kilograms divided by height in meters squared measured using standard methods at baseline, 3 months, 6 months, 12 months

8. Waist circumference measured using standard methods in centimeters at baseline, 3 months, 6 months, 12 months

9. Serum thyroid-stimulating hormone concentration measured using chemiluminescence immunoassay at baseline, 3 months, 6 months, 12 months

10. Serum free thyroxine concentration measured using chemiluminescence immunoassay at baseline, 3 months, 6 months, 12 months

11. Serum total triiodothyronine concentration measured using chemiluminescence immunoassay at baseline, 3 months, 6 months, 12 months

12. Serum cholesterol concentration measured using enzymatic chemistry method on the ADVIA system at baseline, 3 months, 6 months, 12 months

13. Serum sex hormone-binding globulin concentration measured using chemiluminescence immunoassay at baseline and 12 months

14. Cardiac arrhythmia (safety outcome) measured using a clinical assessment at 6 months, 12 months

15. Fragility fracture (safety outcome) measured using a clinical assessment at 6 months, 12 months

16. Bone mineral density (safety outcome) measured using bone densitometry at 6 months, 12 months

17. Association between DIO2 genetic variants (rs225014, rs225015, and rs12885300) measured using real-time polymerase chain reaction using TaqMan assays at baseline

18. Response to combination therapy changes in thyroid-related quality of life measured using the validated Spanish version of the Thyroid-Related Quality-of-Life Patient-Reported Outcome questionnaire (ThyPROes) at baseline, 6 months, and 12 months

Completion date
25/11/2024

Eligibility

Key inclusion criteria
1. Adults aged 18-60 years
2. Diagnosis of primary hypothyroidism of benign etiology
3. Persistent hypothyroid symptoms despite levothyroxine monotherapy
4. Serum thyroid-stimulating hormone levels within the reference range while receiving levothyroxine monotherapy
5. Ability and willingness to provide written informed consent and comply with study procedures and follow-up visits

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
60 Years

Sex
All

Total final enrolment
45

Key exclusion criteria
1. Pregnancy or breastfeeding
2. Endocrine disorders other than primary hypothyroidism
3. Chronic cardiac, renal, or hepatic disease
4. Use of hormonal therapy other than levothyroxine or liothyronine
5. Current treatment with antidepressants, antipsychotics, anxiolytics, or beta-blockers

Date of first enrolment

13/04/2023

Date of final enrolment
24/11/2023

Locations

Countries of recruitment
Mexico

Study participating centre
Hospital Juárez de México
Av Instituto Politécnico Nacional 5160, Magdalena de las Salinas, Gustavo A. Madero
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Sponsor information

Organisation
Hospital Juárez de México

ROR
https://ror.org/04cepy814

Funder(s)

Funder type

Funder Name
Hospital Juárez de México

Funder Name
Productos Medix, S.A. de C.V.

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not expected to be made available