Clinical Trial Protocol
Iranian Registry of Clinical Trials

15 Nov 2026

“Efficacy of Manual Acupuncture, Thread Embedding and Laser Acupuncture Combined with Levothyroxine on Fatigue and Selected Inflammatory and Metabolic Parameters in Hypothyroid Patients”

Protocol summary

Study aim

To assess the effectiveness of different acupuncture methods (manual, laser, acupoint embedding) combined with standard medication in reducing fatigue and improving specific biochemical markers in hypothyroidism patients.

Design

This is a Phase III, four-arm, single-blinded(assessor and analyst) randomized clinical trial involving 100 patients. Randomization: Permuted block randomization (blocks of 4 and 6), with allocation concealment via SNOSE envelopes. Arms: Manual Acupuncture (MA) + Levothyroxine (LT4): 2 times/week for 6 weeks Acupoint Embedding (AET) + LT4: 1 session Laser Acupuncture (LA) + LT4: 2 times/week for 6 weeks Control: LT4 only.

Settings and conduct

Study Type: Phase III, randomized, four-arm clinical trial. Location: Acupuncture Clinic of Imam Reza Hospital, Mashhad, Iran. Patients: 100 patients with hypothyroidism. Randomization: Permuted block randomization method, SNOSE envelopes. Groups: MA, AET, LA, control (Levothyroxine only). Intervention Period: 6 weeks. Blinding: Assessors, laboratory personnel, statistical analysts blinded. Patients and practitioners not blinded.

Participants/Inclusion and exclusion criteria

Age 18-65, primary hypothyroidism, stable levothyroxine, normal TSH, severe fatigue (FSS≥4). Commitment to protocol and consent / Secondary/central hypothyroidism, history of thyroid cancer, pregnancy/lactation. Severe illnesses, specific medications (steroids, immunosuppressants...). Recent levothyroxine dose change, recent acupuncture/embedding/laser therapy. Coagulation/anticoagulation issues, skin problems, non-compliance.

Intervention groups

MA + Standard: 12 MA sessions over 6 weeks + Levothyroxine AET + Standard: 1 single AET session + Levothyroxine LA + Standard: 12 LA sessions over 6 weeks + Levothyroxine Control: Levothyroxine only

Main outcome variables

Primary : Mean change in FSS Secondary: TSH, T4, NLR, PLR, SII, lipid profile, TyG , FBS, QoL

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20121228011912N10**
Registration date: **2026-10-23, 1405/08/01**
Registration timing: **prospective**

Last update: **2026-10-23, 1405/08/01**
Update count: **0**

Registration date

2026-10-23, 1405/08/01

Registrant information

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Recruitment status

Not yet recruiting

Funding source

Expected recruitment start date

2027-02-20, 1405/12/01

Expected recruitment end date

2028-02-20, 1406/12/01

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

"Efficacy of Manual Acupuncture, Thread Embedding and Laser Acupuncture Combined with Levothyroxine on Fatigue and Selected Inflammatory and Metabolic Parameters in Hypothyroid Patients"

Public title

Effect of Manual Acupuncture, Embedding Acupuncture, and Laser Acupuncture on Improving Fatigue and Metabolic Status in Patients with Hypothyroidism

Purpose

Treatment

Inclusion/Exclusion criteria

Inclusion criteria:

Age range of 18 to 65 years. Diagnosis of primary hypothyroidism confirmed by medical history, patient records, or specialist assessment. Receiving standard levothyroxine therapy for at least 3 months prior to study enrollment. Stable dosage of levothyroxine for at least 6 to 8 weeks prior to enrollment. Documented euthyroid status with TSH levels within the normal range (0.35–3.5 mIU/L) in the past 3 months. Fatigue Severity Scale (FSS) score ≥ 4 (indicating significant clinical fatigue). Willingness and ability to attend scheduled treatment sessions and follow-up assessments. Agreement to refrain from initiating any new complementary or alternative therapies related to fatigue or thyroid condition during the study period. Ability to read, understand, and complete the Persian-language study questionnaires. Provision of written informed consent to participate in the research.

Exclusion criteria:

Secondary or central hypothyroidism (due to pituitary or hypothalamic disease). History of thyroid surgery due to thyroid cancer. Pregnancy or lactation. Severe acute or chronic medical conditions that could significantly affect fatigue levels or inflammatory markers, including: - Active systemic inflammatory diseases - Acute clinical infections - Clinically significant anemia - Active autoimmune disorders - Active malignancies - Severe cardiac, hepatic, or renal insufficiency - Uncontrolled psychiatric disorders (e.g., severe major depressive disorder or severe anxiety disorders) capable of causing significant fatigue. Concurrent use of medications that significantly influence fatigue, systemic inflammation, or metabolic rate, such as: - Systemic corticosteroids - Immunosuppressive agents - Central Nervous System (CNS) stimulants - New or recently initiated antidepressant medications. Any dosage adjustment of levothyroxine within the past 6 to 8 weeks prior to study enrollment. Pregnancy occurring during the study or planning to become pregnant during the follow-up period (for female participants of childbearing potential). Initiation of new medications affecting fatigue, inflammation, metabolism, or thyroid function (e.g., systemic corticosteroids, immunosuppressants, new antidepressants, weight-loss drugs, lipid-lowering agents, or drugs interfering with levothyroxine absorption/metabolism). Failure to complete the primary study questionnaires or scheduled laboratory evaluations at the designated time points. Serious protocol violation or persistent non-cooperation by the patient, at the discretion of the principal investigator.

Age

From **18 years** old to **65 years** old

Gender

Both

Phase

3

Groups that have been masked

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

Sample size

Target sample size: **100**

Randomization (investigator's opinion)

Randomized

Randomization description

The study is a randomized controlled trial with the unit of randomization being the individual participant. We will use a block randomization method with variable block sizes of 4 and 6 (allocation ratio 1:1:1:1). The randomization sequence will be generated using the Randomization.com website by an independent researcher not involved in recruitment or data collection. Stratified randomization is not applied in this study. To ensure allocation concealment, we will employ the Sequentially Numbered, Opaque, Sealed Envelopes (SNOSE) technique. Upon verifying eligibility criteria and obtaining informed consent, the researcher will open the envelopes in numerical order to reveal the assigned group.

Blinding (investigator's opinion)

Single blinded

Blinding description

Due to the nature of physical interventions and distinct procedural differences among study arms (manual acupuncture, catgut embedding, laser acupuncture, and standard pharmacotherapy), blinding of participants and the interventionists (acupuncturists) is not feasible. However, blinding is strictly implemented for outcome assessment and statistical analysis: Outcome Assessors: All follow-up evaluations and questionnaire assessments are conducted by an independent research assistant blinded to group allocation. Laboratory Personnel: Laboratory staff analyzing biochemical samples (thyroid profiles) are completely blinded to the allocated interventions, and samples are identified solely by unique alphanumeric codes. Data Analyst / Statistician: Statistical analysis is performed by an independent biostatistician with treatment arms coded as masked groups (e.g., Groups A, B, C, D), and unblinding will occur only after the final statistical analysis is finalized.

Placebo
Not used
Assignment
Parallel
Other design features
This is a 4-arm randomized controlled trial featuring a synergistic design that investigates the combined efficacy of Acupoint Embedding Therapy (AET) and Low-Level Laser Therapy (LLLT) in patients with hypothyroidism. The use of AET as a primary intervention—facilitating sustained stimulation of acupuncture points—serves as the distinctive feature of this protocol compared to conventional acupuncture trials. This multidimensional approach concurrently evaluates biochemical markers and patient-reported outcomes (PROs). While complete blinding of the practitioner and patient is not feasible due to the nature of the interventions, we employ a rigorous blinding protocol for outcome assessors, laboratory personnel, and data analysts to minimize bias. The study adheres to a strictly standardized protocol for point selection and laser dosimetry to ensure high reproducibility.

Secondary Ids

empty

Ethics committees

1

Ethics committee
Name of ethics committee
Imam Reza Hospital, Educational, Research, and Treatment Center - Mashhad University of Medical Scie
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Approval date
2026-10-19, 1405/07/27
Ethics committee reference number
IR.MUMS.IRH.REC.1405.148

Health conditions studied

1

Description of health condition studied
Hypothyroidism - Fatigue - Acupuncture - Acupoint Thread-Embedding - Laser Acupuncture
ICD-10 code
E03
ICD-10 code description
Other hypothyroidism

Primary outcomes

1

Description
Fatigue score measured by the FSS questionnaire
Timepoint
At baseline (before the intervention), at week 6 (end of the intervention), and 12 weeks after completion of the interventions.
Method of measurement
Measurement of fatigue score using the Fatigue Severity Scale questionnaire

Secondary outcomes

1

Description
Serum thyroid stimulating hormone level(TSH)
Timepoint
Before intervention, six weeks after the start of the intervention, and twelve weeks after the end of the intervention
Method of measurement
Blood test for measurement of serum thyroid stimulating hormone level

2

Description
Neutrophil to lymphocyte ratio(NLR)
Timepoint
Before intervention, six weeks after the start of the intervention, and twelve weeks after the end of the intervention
Method of measurement
Complete blood count and calculation of neutrophil to lymphocyte ratio

3

Description
Platelet to lymphocyte ratio(PLR)
Timepoint
Before intervention, six weeks after the start of the intervention, and twelve weeks after the end of the intervention
Method of measurement
Complete blood count and calculation of platelet to lymphocyte ratio

4

Description
Systemic immune inflammation index(SII)
Timepoint
Before intervention, six weeks after the start of the intervention, and twelve weeks after the end of the intervention
Method of measurement
Complete blood count and calculation of systemic

immune inflammation index

5

Description
Fasting blood sugar(FBS)
Timepoint
Before intervention, six weeks after the start of the intervention, and twelve weeks after the end of the intervention
Method of measurement
Fasting blood test for measurement of blood sugar level

6

Description
Blood lipid profile
Timepoint
Before intervention, six weeks after the start of the intervention, and twelve weeks after the end of the intervention
Method of measurement
Fasting blood test for measurement of total cholesterol, triglyceride, high density lipoprotein, and low density lipoprotein

7

Description
Triglyceride glucose index(TyG)
Timepoint
Before intervention, six weeks after the start of the intervention, and twelve weeks after the end of the intervention
Method of measurement
Calculation of triglyceride glucose index based on fasting blood sugar and triglyceride values

Intervention groups

1

Description
Intervention group 1: Patients in this group, in addition to receiving standard medical treatment with levothyroxine (1.7 mcg/kg/day), will undergo manual acupuncture. The intervention consists of 12 sessions (two sessions per week for 6 weeks). In each session, sterile disposable needles with dimensions of 0.25 by 40 mm (manufactured by SMC Acupuncture Needle Co.) will be inserted into selected acupuncture points and retained for 30 minutes.
Category
Treatment - Other

2

Description
Intervention group 2: Patients in this group, in addition to receiving standard medical treatment with levothyroxine (1.7 mcg/kg/day), will undergo thread embedding therapy. This intervention consists of a single session of embedding absorbable polydioxanone (PDO) surgical threads (size 0) into selected acupuncture points. The continuous stimulatory and therapeutic effect of these threads will persist in the targeted points for 4 to 6 weeks.
Category
Treatment - Other

3

Description
Intervention group 3: Patients in this group, in addition to receiving standard medical treatment with levothyroxine (1.7 mcg/kg/day), will receive laser acupuncture therapy. This intervention consists of 12 sessions (two sessions per week for 6 weeks). In each session, laser irradiation will be applied to the selected acupuncture points using a specific wavelength and a specialized laser probe.
Category
Treatment - Other

4

Description
Control group: Patients in this group will only receive standard medical treatment consisting of levothyroxine tablets (1.7 mcg/kg/day) adjusted to maintain thyroid-stimulating hormone levels within the normal range (0.35 to 3.5 mIU/L). The dosage is adjusted based on periodic laboratory tests, and no auxiliary interventions such as manual acupuncture, thread embedding, or laser acupuncture will be performed.
Category
Other

Recruitment centers

1

Recruitment center
Name of recruitment center
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Full name of responsible person
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Sponsors / Funding sources

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Grant name
Grant code / Reference number
Is the source of funding the same sponsor organization/entity?
No
Title of funding source
Mashhad 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

2

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Grant code / Reference number
Is the source of funding the same sponsor organization/entity?
Yes
Title of funding source
Mashhad 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

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Sharing plan

Deidentified Individual Participant Data Set (IPD)
Yes - There is a plan to make this available

Study Protocol
Yes - There is a plan to make this available

Statistical Analysis Plan
Yes - There is a plan to make this available

Informed Consent Form
Yes - There is a plan to make this available

Clinical Study Report
Yes - There is a plan to make this available

Analytic Code
Not applicable

Data Dictionary
Yes - There is a plan to make this available

Title and more details about the data/document
در مقاله ای که منتشر شود جزیات آماری داده ها ذکر می گردند.

When the data will become available and for how long
بعد از اتمام طرح

To whom data/document is available
تمام کسانی که به مقاله منتشره دسترسی یابند یا با مجوز نظارتی معاونت پژوهشی دانشگاه علوم پزشکی مشهد

Under which criteria data/document could be used
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بعد از چاپ مقاله به نویسنده مسئول و قبل از چاپ در صورت نیاز توسط مبادی ذیربط به محقق مسئول.

What processes are involved for a request to access data/document
از طریق معاونت پژوهشی دانشگاه

Comments