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Effect of omeprazole or resveratrol on iron status in thalassemia

Submission date
03/01/2025

Recruitment status
Recruiting

Registration date
08/01/2025

Overall study status
Ongoing

Last Edited
06/01/2025

Condition category
Haematological Disorders

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

Plain English summary of protocol

Background and study aims
Thalassemia is a common hereditary disorder affecting about 1% of the population in Thailand. It results from the defective production of globin chains, leading to symptoms like anemia, jaundice, and growth issues. There are two types: transfusion-dependent thalassemia (TDT) and non-transfusion-dependent thalassemia (NTDT). TDT patients often develop iron overload from regular blood transfusions, while NTDT patients absorb too much iron from their diet. This iron overload can cause various health problems. Current treatments include iron chelation therapy, but they have limitations. This study will investigate if using omeprazole (a proton pump inhibitor) and resveratrol (an antioxidant) can help reduce iron absorption and improve treatment for NTDT patients.

Who can participate?
NTDT patients at Maharaj Nakorn Chiang Mai Hospital in Thailand

What does the study involve?
Participants will be divided into three groups of 20, each receiving either a placebo (20 mg maltodextrin), 20 mg omeprazole, or 250 mg resveratrol, taken twice daily before meals for 6 months. All groups will continue with standard treatments like iron chelators, folic acid, vitamin D, calcium supplements, and lifestyle changes. Patients will have appointments at the start, 3 months, and 6 months to monitor clinical signs and blood parameters. Blood tests will measure various health indicators. The study compounds will be prepared in identical gelatin capsules and distributed in labeled bottles. Group 1 will take omeprazole, Group 2 will take resveratrol, and Group 3 will take a placebo, all twice daily for 6 months.

What are the possible benefits and risks of participating?
Possible benefits: Patients may not benefit from this study because the study drugs may not further decrease serum ferritin. However, the information from this study will be helpful for the treatment of thalassemia patients with iron overload in the future.

Risks of participants:
- Risk from blood drawing that may be pain, bruising, or a less common side-effect which is vasovagal syncope.

- Risk from study drugs: omeprazole may cause you to feel nausea, vomiting, diarrhea, abdominal pain, bloating, constipation, back pain or fewer side effects which are chest pain, myocardial infarction, intraabdominal infection, lower respiratory tract infection, pancreatitis, osteoporosis or other unexpected side effects.
- Risk from resveratrol is nausea, vomiting, diarrhea or fewer common side-effect is pancreatitis or other unexpected side effects.

Where is the study run from?
Adult thalassemia clinic, Maharaj Nakorn Chiang Mai Hospital, Division of Hematology, Department of Internal Medicine, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand

When is the study starting and how long is it expected to run for?
July 2024 to May 2026

Who is funding the study?
1. National Research Council of Thailand
2. Faculty of Medicine Fund, Chiang Mai University, Chiang Mai Thailand (under processing)

Who is the main contact?
Dr. Thanapong Chopetgool, M.D., Resident Hematologist, chopetgoolden@gmail.com

Contact information

Type(s)
Public, Scientific, Principal investigator

Contact name
Dr Thanapong Chopetgool

Contact details
Division of Hematology, Department of Internal Medicine, Chiang Mai University
Chiang Mai
Thailand
50200
+66 930748844
chopetgoolden@gmail.com

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Protocol serial number
National Research Council of Thailand Grant number: N42A670732

Study information

Scientific Title

Adjunct omeprazole or resveratrol in non-transfusion dependent thalassemia patients with secondary hemochromatosis: a randomized, double-blind, placebo-controlled trial

Study objectives
Adjunctive omeprazole or resveratrol in combination with iron chelators could reduce serum ferritin compared with placebo in thalassemia patients with iron overload.

The primary study objective:
To evaluate the efficacy of adjunct omeprazole or resveratrol in combination with iron chelators in reducing serum ferritin compared to placebo in non-transfusion-dependent thalassemia patients.

Secondary objectives are:
1. Evaluate the efficacy of adjunct omeprazole or resveratrol in combination with iron chelators in reducing labile plasma iron (LPI), non-transferrin bound iron (NTBI) and serum iron (SI) compared to placebo
2. Study the association between adjunct omeprazole or resveratrol in combination with iron chelators and the levels of ERFE and hepcidin (Hcd)
3. Study the association between resveratrol and changes in HbF levels
4. Assess the adverse effects of adjunct omeprazole or resveratrol with iron chelators

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 17/12/2024, Office of Research Ethics (Faculty of Medicine, Chiang Mai University, Chiang Mai, 50200, Thailand; +66 53936643; researchmed@cmu.ac.th), ref: 476/2024

Study design
Single-center interventional randomized placebo-controlled clinical trial

Primary study design
Interventional

Study type(s)
Efficacy

Health condition(s) or problem(s) studied
A decrease in serum iron levels in non-transfusion-dependent thalassemia patients

Interventions
The study will be conducted in non-transfusion-dependent thalassemia patients at the Out-patient department numbers 9 or 23 in Maharaj Nakorn Chiang Mai Hospital, Division of Hematology, Department of Internal Medicine, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand.

Using the stratified random sampling technique, sixty-three transfusion-dependent thalassemia (TDT) subjects were enrolled in the study, but three dropped out. The sample size was calculated using G*Power software version 3.1.9.7, allowing for comparison between the three groups. A repeated measures analysis of variance (ANOVA) F test was employed, incorporating within-

between interaction mode. The anticipated effect size for the new compound is 0.50, which is considered large. The statistical power is set at 95% with a significance level (α) of 0.05. Measurements were taken at three points: baseline (month 0), during the first intervention (month 3), and at the end of intervention (month 6). Consequently, the total sample size determined by G*Power is 60, with 20 participants allocated to each group.

The three groups involve taking 20 mg maltodextrin (placebo), 20 mg omeprazole capsule, and 250 mg resveratrol capsule orally twice daily before meals for 6 months. All groups will receive standard treatments including iron chelators, folic acid supplementation, vitamin D supplementation, calcium supplementation, and lifestyle modifications throughout the study. The patients will be appointed at the first visit, 3 months, and 6 months to evaluate clinical signs and blood parameters levels. Blood samples will be analyzed for complete blood count, hemoglobin types, serum levels of blood urea nitrogen (BUN), creatinine (Cr), electrolytes (e.g., Na+, K+, Ca2+, Mg2+ and phosphates), aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), soluble ferritin (sFt), iron (SI), total iron-binding capacity (TIBC), non-transferrin bound iron (NTBI), labile plasma iron (LPI), hepcidin (Hcd), and erythroferrone (ERFE).

The three study compounds, including omeprazole, resveratrol, and placebo, will be prepared and filled in gelatin capsules with the same appearance: 20 mg omeprazole capsule, 250 mg resveratrol capsule, and 20 mg maltodextrin. The capsules will be packed in a white plastic bottle (30 capsules each) and labeled with codes under the bottles. The patients in Group 1 will take an omeprazole capsule orally twice daily (total 40 mg/day) in the morning and evening before meals for 6 months. The patients in Group 2 will take a resveratrol capsule orally twice daily (total 500 mg/day) in the morning and evening before meals for 6 months. The patients in Group 3 will take a placebo capsule orally twice daily in the morning and evening before meals for 6 months.

Before the commencement of the trial, the results of genotyping and physical assessments were recorded. They documented participants' age, height, body weight (BW), body mass index (BMI), and the palpability of the liver and spleen. For 60 days, all participants consumed the product daily and were advised to avoid meals rich in polyphenolic components. Blood samples were taken on days 0, 30, and 60 after a 72-hour pause from their iron chelation therapy and just before their subsequent blood transfusion.

Intervention Type
Supplement

Primary outcome(s)
Changes in serum ferritin measured using an automated Biochemical Analyzer (immuno-chemiluminescence) at baseline, 3 and 6 months

Key secondary outcome(s))
The following secondary outcome measures are assessed at baseline, 3 and 6 months unless stated:
1. A CBC measured using an automated cell counter
2. Hemoglobin typing measured using cationic-exchange HPLC/DAD at baseline and 6 months.
3. Blood urea nitrogen measured using an automated biochemical analyzer
4. Creatinine measured using an automated biochemical analyzer
5. Electrolytes measured using an automated biochemical analyzer (ion selective method)
6. Aspartate aminotransferase measured using an automated biochemical analyzer (colorimetry)

7. Alanine aminotransferase measured using an automated biochemical analyzer (colorimetry)
8. Alkaline phosphatase measured using an automated biochemical analyzer (colorimetry)
9. Serum iron measured using an automated biochemical analyzer (ferrozine colorimetry)
10. Total iron-binding capacity measured using an automated biochemical analyzer (ferrozine colorimetry)
11. Labile plasma iron measured using Rhodamine B fluorochrome/spectrofluorometry
12. Non-transferrin bound iron measured using NTA/fluorescence chelator beads/flow cytometry a
13. Hepcidin measured using a sandwich enzyme-linked immunoassay
14. Erythroferrone measured using a sandwich enzyme-linked immunoassay
15. Vitamin B12 measured using reversed-phase HPLC/DAD
16. Vitamin D3 measured using a competitive enzyme-linked immunoassay

Completion date
05/05/2026

Eligibility

Key inclusion criteria
1. Aged 20-65 years old
2. Non-transfusion dependent thalassemia [alpha or beta] diagnosis by HPLC, PCR or gene mutation
3. Hemochromatosis with serum ferritin 300-1000 ng/mL or > 1000 ng/mL with a maximum iron chelator (DFP at 75 mg/kg/day or DFX at 20 mg/kg/day)
4. Concurrent iron chelators without changing dose during 3 months before enrollment and no tendency to adjust the dose of iron chelators between study
5. Inform consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
20 years

Upper age limit
65 years

Sex
All

Key exclusion criteria
Not meeting the participant inclusion criteria

Date of first enrolment

10/02/2025

Date of final enrolment
30/04/2026

Locations

Countries of recruitment
Thailand

Study participating centre
Out-patient department numbers 9 or 23 (Adult thalassemia clinic)
11th Floor, Sriphat Building, Maharaj Nakorn Chiang Mai Hospital, Division of Hematology, Department of Internal Medicine, Faculty of Medicine, Chiang Mai University
Chiang Mai
Thailand
50200

Sponsor information

Organisation
National Research Council of Thailand

ROR
https://ror.org/018wfhg78

Organisation
Chiang Mai University

ROR
https://ror.org/05m2fqn25

Funder(s)

Funder type
Research council

Funder Name
National Research Council of Thailand

Alternative Name(s)
NRCT

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Thailand

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analyzed during the current study will be available after the study finishes upon request from Dr. Thanapong Chopetgool, MD. from the Division of Hematology, Department of Internal Medicine, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand. Telephone numbers (Office) +66 53935482 and (Mobile): +66 930748844. Email: chopetgoolden@gmail.com

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet			03/01/2025	No	Yes
Protocol file			03/01/2025	No	No