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Drug interaction study with thyroid hormone and magnesium preparation in healthy volunteers

Submission date
16/10/2023

Recruitment status
No longer recruiting

Registration date
17/10/2023

Overall study status
Completed

Last Edited
17/10/2023

Condition category
Nutritional, Metabolic, Endocrine

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

Plain English summary of protocol

Background and study aims
Levothyroxine is a medication commonly taken with products that have certain types of minerals like calcium. When you take it with calcium, it can make your body absorb less of the levothyroxine. However, we don't have any information yet about how magnesium, which is also a similar kind of mineral, affects the absorption of levothyroxine. It's very possible that magnesium might also have an impact on how your body takes in levothyroxine. So, the aim of this study is to figure out how much magnesium affects the absorption of levothyroxine.

Who can participate?
Participants are healthy volunteers aged 18-65 years who have signed the informed consent form.

What does the study involve?
After giving initial information either in person or over the phone and signing the informed consent form, a comprehensive medical history is taken, along with a physical examination. Blood samples are collected to check certain factors that help determine if participants can participate in the study or not. If they meet all the requirements to join the study and don't have any factors that exclude them, they are randomly assigned to one of three groups: one that takes levothyroxine by itself, one that takes levothyroxine with Magnesium Citrate, and one that takes levothyroxine with Magnesium Aspartate.

During each of these administrations, we measure Thyroxin levels at a total of 6 different time points. This helps us calculate and compare the area under the curve (AUC) for Thyroxin. To make the process more comfortable and avoid multiple needle pricks during each visit, we use a catheter in the vein to draw blood. The duration of the visits can vary. The information session typically lasts 20-30 minutes, the screening phase takes about 30-60 minutes, and the following three visits each last around 6.5 hours.

All these visits need to happen within a 6-month period, and there should be at least 4 weeks between visits 3, 4, and 5 to ensure that any remaining medication from the previous visit doesn't affect the results

What are the possible benefits and risks of participating?
The participation has no direct advantage for the participants. Potential risks mainly concern the levothyroxine-sodium, since a higher dose than the one described in the prescription drug information is taken. Potential adverse effects of levothyroxine like insomnia, nervousness, diarrhea, tremor, diaphoresis, headache, tachycardia, dysrhythmias and angina pectoris cannot be excluded. But these are expected to be mild and transient in nature. Since there are only three doses of levothyroxine administered, the negative impact on the subjects is expected to be minimal. The administration of two standard doses in total of magnesium preparations are not likely to pose a significant risk to subjects, the potential adverse event of soft stool/diarrhea is unlikely after one dose and transient as well.

Where is the study run from?
University Hospital of Zurich (Switzerland)

When is the study starting and how long is it expected to run for?
March 2023 to December 2024

Who is funding the study?
University of Zurich (Switzerland)

Who is the main contact?
Dr Jérôme Bonzon, jerome.bonzon@usz.ch

Contact information

Type(s)
Public, Scientific, Principal investigator

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Additional identifiers

Protocol serial number
2.1

Study information

Scientific Title
Single Centre Drug-Drug Interaction study with Levothyroxine/Magnesium-Citrate and Levothyroxine/Magnesium-Aspartate in healthy subjects

Acronym
ThyroMag

Study objectives
The two treatments with a magnesium compound will reduce the AUC of thyroxine compared to levothyroxine alone, but no difference is expected between the combination of levothyroxine with magnesium-citrate vs. magnesium-aspartate.
The null hypothesis is that the three treatments do not differ regarding the AUC of thyroxine.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 06/10/2023, Kantonale Ethikkommission Zürich (Stampfenbachstrasse 121, Zürich, 8090, Switzerland; +41 43 259 79 69; admin.kek@kek.zh), ref: 2023-01493

Study design
Open-label drug-drug-interaction study with cross-over design

Primary study design
Interventional

Study type(s)
Safety

Health condition(s) or problem(s) studied
Hypothyroidism

Interventions
Cross-over study with three groups. Each of the three treatments is during only 360 minutes: The time required to take the blood samples. A wash-out phase of min. 4 weeks is planned between each treatment. No specific follow-up is planned.
Group 1: One dose of Magnesium-Aspartate (10 mmol) in powder form, taken orally along with levothyroxine 1 mg
Group 2: One dose of Magnesium-Citrate (300 mg) in powder form, taken orally along with levothyroxine 1 mg, compared to
Group 3: One dose of levothyroxine 1 mg alone

Randomization: Due to the cross-over design of the trial, subjects will receive all treatments. The subjects will be block-randomized to three different treatment sequences in a 1:1:1 fashion with a block size of 6. Treatment sequences are chosen to ensure that each treatment appears once in each position (1st, 2nd, 3rd), ABC, BCA and CAB, A being levothyroxine alone, B being levothyroxine + magnesium citrate and C being levothyroxine + magnesium aspartate. The randomization list is prepared in advance by the trial statistician, and allocation concealment will

be handled via sequentially numbered, opaque and sealed envelopes by a person at the study center that is not involved in the trial. Only after sealing, the envelopes are handed to the investigators. After inclusion of a participant, the four-digit-number assigned to the participant is written in wet ink on the envelope, before the seal is broken. The envelopes are opened according to their sequential number. Should a participant decide to terminate the study early, the sequences are re-used after all envelopes have been used up (for the 13th participant who replaces the participant that did not complete all visits).

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Euthyrox® (Levothyroxin-Natrium), Magnesiocard® (Magnesium-Aspartat) 10 mmol, Magnesium Diasporal® (Magnesium-Citrat) 300 mg

Primary outcome(s)
AUC of total thyroxin in the serum up to 6 hours after ingestion of levothyroxine, with measurements at 0 min, 30 min, 60 min, 120 min, 240 min and 360 min.

Key secondary outcome(s))
1. Cmax of total thyroxin in the serum during a 6-hour period after ingestion of levothyroxine
2. Tmax of total thyroxin in the serum during a 6-hour period after ingestion of levothyroxine

Completion date
31/12/2024

Eligibility

Key inclusion criteria
1. Age 18-65 years
2. Informed Consent as documented by signature

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
65 years

Sex
All

Key exclusion criteria
1. Contraindications to the drugs under study, e.g. known hypersensitivity or allergy
2. Need for any kind of drug therapy for the duration of the study
3. Women who are pregnant or breastfeeding
4. Intention to become pregnant during the course of the study
5. Lack of safe contraception, defined as: Female participants of childbearing potential, not using and not willing to continue using a medically reliable method of contraception for the entire study duration. Female participants who are surgically sterilised / hysterectomized or post-menopausal for longer than 2 years are not considered as being of child bearing potential.
6. Other clinically significant concomitant disease states (e.g., renal failure, thyroid dysfunction, cardiovascular disease, arterial hypertension, any other medical condition that could lead to an albumin deficiency such as anorexia etc.)
7. Abnormal findings in the screening tests (laboratory, ECG, physical examination).
8. Inability to follow the procedures of the study, e.g. due to language problems, psychological disorders, dementia, etc. of the participant
9. Participation in another study with investigational drug within the 30 days preceding and during the present study
10. Previous enrolment into the current study
11. Enrolment of the investigator, his/her family members, employees and other dependent persons

Date of first enrolment
01/12/2023

Date of final enrolment
30/06/2024

Locations

Countries of recruitment
Switzerland

Study participating centre
USZ
Klinik für Klinische Pharmakologie & Toxikologie
Rämistrasse 100
Zürich
Switzerland
8091

Sponsor information

Organisation

University Hospital of Zurich

ROR
https://ror.org/01462r250

Funder(s)

Funder type
University/education

Funder Name
Universität Zürich

Alternative Name(s)
University of Zurich, University of Zurich, Switzerland, UZH CH, UZH

Funding Body Type
Government organisation

Funding Body Subtype
Universities (academic only)

Location
Switzerland

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study will be published as a supplement to the results publication.

IPD sharing plan summary
Published as a supplement to the results publication