The sensitivity of the pituitary thyrotrophs for ambient thyroid hormone levels.

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Ethical review	Approved WMO
Status	Pending
Health condition type	Thyroid gland disorders
Study type	Observational non invasive

Summary

ID

NL-OMON29857

Source
ToetsingOnline

Brief title
The sensitivity of the pituitary thyrotrophs.

Condition

- Thyroid gland disorders

Synonym
sensitivity of the pituitary

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: NWO

Intervention

Keyword: HPT, HPT-setpoint., hypothalamus-pituitary-thyroid axis, Thyroid (hormone)

Outcome measures

Primary outcome

The first outcome of this study is the relationship of TSH and FT4 for each individual presented in a graphical line. From that we can determine the sensitivity of the pituitary by the slope and baseline value of these lines, which are different for each individual.

Secondary outcome

The second outcome will be whether we can see inter- and intra-individual differences in sensitivity.

Study description

Background summary

The production of thyroid hormone is regulated by hypothalamic-pituitary-thyroid axis (HPT-axis). Small changes in serum levels (even within the physiological range) cause alterations in TSH response to TRH. This means that there is a HPT set-point, recognizing the ambient levels of circulating thyroid hormones. In the study of Spencer et. al. an inverse log-linear relationship was found between steady state serum TSH and FT4: the straight lines depicting the TSH-FT4 relationship of the individuals ran parallel to each other but their slopes were similar (5). This particular relationship in an individual can be seen as the set-point of the HPT-axis of that person (3). This means that this set-point can be genetically or environmentally determined. The study of Meikle et. al. found that genetical heritability was accounted for ~64% (95% CI: 57-70%) of the variation in serum TSH, FT4 and FT3 concentrations (8). Peeters et. al. identified in their study polymorphisms in the thyroid hormone pathways genes. They found these polymorphisms located in the coding sequences of the iodothyronine deiodinases and TSH receptor, which is associated with plasma thyroid hormone levels and TSH levels, respectively (9). This indicates that the pituitary has its own sensitivity which is different for each individual. It is important to

understand this since it indicates that there will be different reference ranges for each individual, which can differ from the population-based reference ranges. This can influence the diagnoses of (subclinical-) thyroid dysfunction. This study will give more information about this issue and help us in understanding the inter- and intra-individual reference ranges better.

Study objective

The aim of this pilot study is;
* To determine whether differences between individuals in the set-point of the HPT-axis can be determined by using this study-design,
* To examine whether this study design is practicable and tolerated by the healthy volunteers,
* To examine whether the subjects will have side effects caused by this study,
* To apply this study design in a population study (ERGO) if proven practicable and safe.

Study design

The study will be an observational, dose finding study. The study cohort will exist of 12 to 14 healthy volunteers in the age of 50 to 70 years.
Exclusion criteria:
* Subjects with thyroid disease and/or thyroid function-tests outside the reference range (TSH 0.4-4.0 mU/L, FT4 9-21 pmol/L).
* Subjects who have an active cardiovascular disease.
* Women that are pregnant or postpartum <6 months
* Women that use oestrogen (anti-conception)
* Subjects that have severe illness, or are drug addicts
* Subjects that use medication which interferes with thyroid hormone metabolism.

Intervention arms
The study cohort will be divided over 2 arms by randomisation. The subjects will receive in each arm placebo and then as determined by the doses order randomisation the low and high dose of either T3 or T4. A minimum of two weeks will be used between studies to allow serum TSH to return to basal control values. In total the individuals will have one placebo and two study doses of T4/T3. They have to give blood samples and will be additional examined each time before and after administration of thyroid hormone.

Study burden and risks

The volunteers will receive three pils of thyroid hormone, one of them will be placebo, which they have to take in the evening at 23.00 hours. Before and after each pil they receive they have to come in the morning to the departement for control (pulse rate, blood pressure, weight, height and blood sample will

be taken).

This means that they have to come in total 6 times to the departement, but between each set (2 mornings) there will be 2 weeks of rest.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

healthy volnteers in the age of 50 to 70 years.

Exclusion criteria

volunteers with a thyroid dysfunction and/or heart disease

Study design

Design

Study type:	Observational non invasive
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Placebo
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-09-2006
Enrollment:	14
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Cytomel
Generic name:	liothyronine
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Thyrax
Generic name:	levothyroxine
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Application type:	First submission

Review commission: METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2006-002373-42-NL
CCMO	NL13655.018.06