Evening versus Morning Administration of Levothyroxine: a randomised controlled double-blind trial

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To study in a large randomised double-blind trial, if the administration of levothyroxine at bedtime significantly changes TSH and thyroid hormone levels compared to morning administration. Furthermore we want to evaluate the change of quality of...

Ethical review	Approved WMO
Status	Pending
Health condition type	Thyroid gland disorders
Study type	Interventional

Summary

ID

NL-OMON30653

Source
ToetsingOnline

Brief title
Evening versus morning administration levothyroxine

Condition

- Thyroid gland disorders

Synonym
Hypothyroidism, slow thyroid

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Centrum Rijnmond-Zuid
Source(s) of monetary or material Support: budget Interne Geneeskunde MCRZ

Intervention

Keyword: evening administration, hypothyroidism, levothyroxine

Outcome measures

Primary outcome

Primary endpoint will be a significant change in TSH and thyroid hormones FT4/T3 with a switch to the bedtime administration of levothyroxine compared to the morning administration.

Secondary outcome

Secundary endpoints will be a change in blood pressure, pulse, weight, other lab results (ferritin, albumin, lipids etc.), a change in quality of life and symptoms of hypo-or hyperthyroidism. Furthermore we will study if patients that were subclinically hypothyroid, and become euthyroid or (subclinically) hyperthyroid because of the different administration time of levothyroxine, have a change in quality of life.

Study description

Background summary

Primary hypothyroidism is a common disease, especially frequent among women, and usually has a large impact on quality of life. Untreated hypothyroidism can lead to serious symptoms, and needs to be treated with levothyroxine (synthetised T4). Subclinical hypothyroidism (elevated TSH with a normal T4) can also give symptoms of hypothyroidism, and there are contradictory trial results concerning the elevated risks of cardiovasculair incidents in sublinical hypothyroidism. This is why consensus concerning the need for treatment of subclinical hypothyroidism with levothyroxine still lacks. Especially a clear improvement of quality of life could be a reason to start treatment with levothyroxine.
Hypothyroid patients worldwide are advised to take levothyroxine tablets in the morning half an hour before breakfast. This is because a fiber-enriched diet

and ingestion of certain drugs have been shown to have an adverse effect on the intestinal absorption of L-thyroxine.
In a recent study we showed that TSH significantly decreased and T4 an T3 significantly increased after changing the administration time of levothyroxine from morning to the evening, at bedtime.

Study objective

To study in a large randomised double-blind trial, if the administration of levothyroxine at bedtime significantly changes TSH and thyroid hormone levels compared to morning administration. Furthermore we want to evaluate the change of quality of life in patients with significant thyroid hormone changes. In some patients the change in administration time of levothyroxine will cause them to become subclinical hypo- or hyperthyroid. Through quality of life questionairres we will evaluate if their quality of life changes because of this.

Study design

A randomised controlled double-blind cross-over studyamong patients with primary hypothyroidism. Patients will be asked to take a tablet in the morning as well as in the evening, with one of these tablets containing levothyroxine and the other tablet will be a placebo. The patient and his/her doctor will not know which tablet contains the actual levothyroxine. After 2 months the tablets will be switch, so that the tablet containing levothyroxine is taken at a different moment of the day. Every 4 weeks patients will return to the outpatient department for a check-up and bloodtests. At the start of the study and at 8 and 16 weeks Bij aanvang van de studie, en na 8 en 16 weken zal een uitgebreide QOL-vragenlijst worden afgenomen.

Intervention

During the study, patients will have to take 2 tablets a day (one in the morning and one at bedtime), instead of 1 tablet. During these 16 weeks they will return to the outpatient department five times for a check-up, and bloodsamples will be taken.

Study burden and risks

For the period of 16 weeks patients will need to take two tablets instead of one tablet. During this period they will visit the outpatient department 5 times, where blood samples will be taken.

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

Age > 18 years
At least 6 months on a stable regimen of levothyroxine, with TSH 0.4-4.0 mU/l

Exclusion criteria

Pregnancy
Disease of the stomach, jejunum or ileum
Use of medication known to interfer with the uptake of levothyroxine

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Crossover
Masking:	Double blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-01-2007
Enrollment:	100
Type:	Anticipated

Ethics review

Approved WMO Date:	28-02-2007
Application type:	First submission
Review commission:	TWOR: Toetsingscommissie Wetenschappelijk Onderzoek Rotterdam e.o. (Rotterdam)

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
CCMO	NL14445.101.06