The influence of metformin and a hypocaloric diet on thyroid radioactive iodide uptake in healthy volunteers: a pilot study.

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To assess the physiological effects of metformin and hypocaloric dieting on thyroid iodide uptake and thyroid function in healthy volunteers.

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

Summary

ID

NL-OMON43413

Source
ToetsingOnline

Brief title
The influence of metformin and a hypocaloric diet on thyroid iodide uptake

Condition

- Thyroid gland disorders
- Endocrine neoplasms malignant and unspecified

Synonym
fysiological Thyroid function

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: hypocaloric diet, iodide uptake, metformin, Thyroid

Outcome measures

Primary outcome

Primary endpoint is the change observed in 123I thyroid uptake measured by Radioactive iodide uptake testing (RAIU) before and after either metformin or hypocaloric dieting.

Secondary outcome

Secondary endpoints are the changes in serum levels of TSH, fT4 and T3 before and after intervention.

Study description

Background summary

Treatment with radioactive iodide (RAI) is a widely used and highly efficient treatment for benign and malignant thyroid diseases, such as differentiated thyroid cancer (TC). Specific thyroid iodide uptake is needed to assure effective RAI treatment in TC, which is facilitated by the expression of a sodium-iodide symporter (NIS) on the thyroid cell. Factors that influence either positively or negatively the NIS expression and function could affect the response to RAI treatment. We, and others have shown that that activation of AMP-activated-protein-kinase (AMPK) leads to decreased NIS expression and iodide uptake in in vitro studies and animal models. For this reason we will focus in this study on modulators of AMPK activity in relation to thyroid iodide uptake in humans. The first important modulator of AMPK is metformin, a well known drug in the treatment of type 2 diabetes mellitus (DM). Because there is evidence that thyroid disease and DM are closely linked and metformin is investigated as important adjunct in the treatment of TC, we estimate that there is a large group of patients that use metformin who undergo RAI treatment, making it interesting to investigate the effects of metfromin on thyroid iodide uptake. Secondly, we want to investigate the effects of a hypocaloric diet, since hypocaloric conditions also induce AMPK activation.

During RAI treatment for TC, patients undergo thyroid hormone withdrawal or administration of rhTSH to stimulated thyroid iodide uptake. Thyroid hormone withdrawal results in symptomatic hypothyroidism, leading to complaints such as weight gain and nausea, which could result in reduced food intake and thus hypocaloric conditions. Since this could influence AMPK activation and thus thyroid iodide uptake and RAI efficacy, it is relevant to investigate the effect of altered caloric intake on thyroid iodide uptake.

Study objective

To assess the physiological effects of metformin and hypocaloric dieting on thyroid iodide uptake and thyroid function in healthy volunteers.

Study design

This is an investigator initiated interventional pilot study.

Intervention

The first group of 7 subjects will follow a two week course of metformin according a specific dosing scheme. Group 2 with 7 subjects will follow a hypocaloric diet (40% caloric restriction, high fat, low carbohydrate content) for two weeks. There will be a control group of 3 subjects to assess the degree of intra-individual variation in thyroid iodide uptake.

Study burden and risks

Subjects will not benefit directly from this research but by participating they could have an important contribution to optimizing RAI treatment to improve efficacy and reduce adverse events. The risk of adverse effects is minimized by choosing a healthy study population who will be screened for health problems. We only use a short intervention period of twee weeks. The expected risk for both interventions and control group are considered very low and we do not expect any serious side effects from both interventions. All subjects will donate blood and urine at 3 different time points, including blood donation for health screening. Furthermore, subjects will undergo 123I uptake testing twice, which is not associated with any side effects and radiation dose will remain below recommend values.

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

* male
* No mental illness
* Informed consent
* Healthy, specifically no history of thyroid disease or renal insufficiency.
* Aged between 18-50 years
* Normal weight (BMI: 18.5-25.0 kg/m2)
* Maintained stable body weight for previous 6 months

Exclusion criteria

* Mentally incompetent
* Any thyroid condition: hypo- or hyperthyroidism, thyroid cancer, other thyroid conditions.
* Any chronic illness, including diabetes mellitus, acute or chronic infections, other disease requiring treatment.
* Use of any medication or homeopathic medications. Use of paracetamol is allowed.
* Smoking
* Previous radioactive iodide scanning or other imaging techniques with administration of

iodide containing contrast fluids within 6 months
* Use of supplements that contain large quantities of iodide
* Structural alcohol intake > 3 glasses/day
* Subjects who have taken part in any drug trial within 3 months prior start of this study.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	28-07-2016
Enrollment:	17
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Metformin
Generic name:	metformin
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	18-04-2016
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO

Date:	20-04-2016
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	31-08-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	05-09-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	20-03-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

ID: 28976
Source: NTR
Title:

In other registers

Register	ID
EudraCT	EUCTR2016-001455-42-NL
CCMO	NL56309.091.16
OMON	NL-OMON28976

Study results

Date completed:	14-07-2017
Actual enrolment:	20