The uptake of radioactive iodine before and after a low iodine diet in patients with differentiated thyroid carcinoma

Published: 30-07-2019
Last updated: 28-09-2024

Primary objective: 1. To compare the difference in thyroid uptake of a low tracer dose radioactive iodine (10 MBq 123I or 37 MBq 123I) (1a), in DTC patients after thyroidectomy, before and after a LID of 7 days (1b).Primary objective described in...

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

Summary

ID

NL-OMON52405

Source
ToetsingOnline

Brief title
Iodine uptake after LID

Condition

- Thyroid gland disorders
- Endocrine neoplasms malignant and unspecified

Synonym
differentiated thyroid carcinoma (DTC), thyroid cancer

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Differentiated thyroid carcinoma (DTC), Low iodine diet (LID), Radioactive iodine, Thyroid uptake

Outcome measures

Primary outcome

Main study parameter/endpoint

The primary endpoint is the clinical relevant difference of a twofold uptake

increase, in the thyroid remnant after thyroidectomy in DTC patients, of 10 MBq

123I tracer dose before and after a LID of 7 days.

Secondary outcome

Secondary study parameters/endpoints

- Compliance to the LID will be evaluated by measuring the UIE before and after

the LID.

- Clinical cut-off values of SIE for sufficient, insufficient and, deficient,

iodine status will be determined based on UIE.

Study description

Background summary

Differentiated thyroid carcinoma (DTC) is the most common form of thyroid cancer. DTC develops from thyroid follicular cells and therefore has specific characteristics, e.g. the ability to take up iodine, and therefore also radioactive iodine (131I), and produce thyroglobulin (Tg). In 2015, in the Netherlands, 677 patients were diagnosed with thyroid cancer; 609 of them with DTC. The initial treatment of DTC consists of a total thyroidectomy followed by ablation therapy with 131I which destroys residual thyroid (cancer) tissue. The prognosis of DTC is very good, a 5-year survival over 90%.(1-3)
Before ablation and possible subsequent therapy with 131I, patients have to follow a low iodine diet (LID), reducing the iodine intake < 50 mcg per day.(2)
Depleting the overall iodine store in the body theoretically maximizes the

expression of the sodium-iodine symporter (NIS). This increased NIS expression results in an increase of the uptake of 131I in remaining thyroid (cancer) cells during 131I therapy and therefore should improve the ablation success rate.(4) All international guidelines recommend the LID, however, based on low quality evidence, with a duration that varies between 4 days and 2-3 weeks.1,2,5

Low iodine diet and ablation success

Several studies evaluated the effect of the LID on the ablation success. However, these studies show contradictionary data and are retrospective. In 1975, Goslings et al. studied 7 patients with metastatic follicular thyroid carcinoma and showed that the uptake of 131I was increased in the tumour with a factor 1.79 after 4 days of a LID, no significance level was given. The urine iodine excretion (UIE) in these 7 patients, who followed the LID for 4 days, decreased from 122 µg/day prior to the diet to 30 µg/day on the last day of the diet.(6)

Since then, there have been no prospective studies evaluating the effect of the LID on the ablation success. Only 6 retrospective studies, with the outcome ablation success, have compared patients with different iodine intake prior to 131I.(7-12)These studies differ in definition of ablation success, do not all report the UIE as a reflection of compliance of patient, differ in strictness and duration of the LID, and are, as already mentioned all retrospective, and therefore biased historically. Four out of these six studies showed no difference in ablation success between groups, two studies did show a difference. One of the studies that showed a difference, on which the recommendation of our Dutch guideline is based, is the study of Pluijmen et al. comparing a control group of 61 patients and a LID group of 59 patients. The LID was prescribed for 4 days aiming a maximum iodine excretion of 49,4 µg/day. The 24 hour 131I uptake in the thyroid region was significant higher in the LID group compared to the control group, 5.1% in the LID group compared to 3.1% in the control group. The number of patients who were successfully ablated (defined as absent of neck activity and Tg < 2 µg/l) was significantly higher in the LID group compared to the control group, 65% vs. 48%. A major limitation of this study is the exclusion of patients with UIE > 49,5 µg/dag after the LID, i.e. the analysis is not based on intention to treat. Furthermore, a group of before 1992 was compared to a group of after 1992, inducing a historical bias.(8)

Low iodine diet and uptake of 131I

As described, the underlying mechanism of a LID is to increase the uptake of 131I. As mentioned above, only Goslings and Pluijmen studied whether the LID increase the uptake of 131I, by evaluating the iodine uptake scan prior to the 131I treatment.(6,8)

Barriers and side effects of the low iodine diet

Several studies have investigated the knowledge and perceived barriers of thyroid cancer patients regarding the LID. The major conclusions are that most patients mistake the LID as a low salt diet, leading to a higher risk of

developing hyponatraemia, and have a low knowledge level about products containing iodine. Besides, patients experience the strict adherence to LID as stressful, distasteful and overwhelming, just after cancer diagnosis in their postsurgical period with complaints of hypothyroidism. In addition, minimizing iodine intake, complicates achieving a balanced diet, which is essential in cancer recovery.(7,13)

Determination of iodine status

Iodine status is usually determined by measuring iodine excretion. As iodine is primarily excreted in the urine, a 24-hour urine collection is considered the reference standard for measuring iodine status in an individual.(14) An iodine deficient status is defined as an UIE <50 µg/24 hours, which is also the target UIE value after a LID.(2) An iodine insufficient state is UIE values from 50-99 µg/24 hours and UIE values between 100-199 µg/24-hours are considered iodine sufficient. However, the collection of 24-hours urine is demanding and inconvenient resulting in undercollection and understatement of the actual iodine excretion.(14,15) Therefore, there is a clinical demand for a more convenient determination of iodine status. As salivary glands, like renal epithelial cells, express the NIS, iodine is excreted in saliva. Therefore, the salivary iodine excretion (SIE) might serve as an alternative to the 24-hours urine collection. Dekker et al. and Guo et al. showed a strong correlation between the 24-hours UIE and SIE.(16,17) Measuring SIE by saliva collection might be a more sanitary and convenient way of estimating iodine status, without the risk of undercollection. Reference values for SIE in different iodine statuses (deficiency, insufficiency, and sufficiency) are necessitated for clinical applicability of salivary collection. In the Netherlands, on a population basis, daily intake of iodine is optimal.(18,19) Therefore, the SIE reference values for iodine-deficiency and -insufficiency cannot be measured in healthy volunteers. As DTC patients follow the LID, their UIE will be somewhere in the range of an iodine insufficient to deficient status. Therefore it is possible to determine reference values for SIE in these patients: iodine sufficient before the LID, and iodine insufficient or deficient after the LID. We would therefore opt to perform a substudy in patients following the LID and aim to determine clinical cut-off values for SIE for iodine deficiency, insufficiency and sufficiency based on UIE values.

Aim of this study

In summary, data on the effect of the LID on ablation rates in DTC patients are limited and contradictionary, nevertheless, the diet is generally accepted and recommended before 131I . However, the LID is experienced as stressful and distasteful and patients are afraid to apply the LID inadequately, which complicates achieving a balanced diet, essential in cancer recovery. There is a clinical demand to confirm prospectively the necessity of the LID on preparation for 131I treatment. The aim of this study is to prospectively investigate whether the LID lead to a higher uptake of iodine in the remnant of the thyroid.

Aim of the substudy
Measuring salivary iodine excretion poses a promising solution to the burdensome 24-hours urine collection. For clinical applicability, we aim to determine clinical cut-off values for SIE.

Study objective

Primary objective:
1. To compare the difference in thyroid uptake of a low tracer dose radioactive iodine (10 MBq 123I or 37 MBq 123I) (1a), in DTC patients after thyroidectomy, before and after a LID of 7 days (1b).

Primary objective described in more detail:
1a. We expect a twofold increase in thyroid uptake after the LID compared to before, based on the study of Pluijmen et al.(8)
1b. Patients have to follow the diet for 7 days, supported by written dietary instructions with a sample menu, the link www.jodiumarm.nl with low iodine containing recipes and contact details of the dietician.

Secondary objective:
2. To determine cut-off values of SIE for iodine deficiency, insufficiency and sufficiency based on UIE (2a).

Secondary objective described in more detail:
2a. Cut-off values for iodine status based on 24-hours UIE are:
Deficient < 50
Insufficient 50-99
Sufficient 100-199
*

Study design

This study is a observational, single center study performed in the UMCG. Consecutive patients with DTC who will receive 131I ablation therapy and have to follow a LID according to the Dutch DTC guideline will be eligible for inclusion.

Duration of the study
Based on the numbers of patients with DTC, we expect that the inclusion of patients will be completed in September 2024.

Setting of the study
All patients who agree to participate will receive one additional (high risk patients, definition in figure 1) or two additional (low risk patients, definition in figure 1) 10 MBq 123I, on respectively one or two (separate) day(s), with consecutive thyroid uptake measurements and will collect their

urine for 24 hours twice, and collect saliva samples twice, on two separate days. On the day of the first administration of 10 MBq 123I, 1 blood sample (5 ml) will be collected for thyroid stimulating hormone (TSH) measurement. According to the Dutch DTC guideline, high risk patients receive one day before 131I ablation therapy, 37 MBq 123I to perform a pre-ablation scan. For this reason, these patients will receive one additional 10 MBq 123I in contrast with low risk patients, who will receive 10 MBq twice. On day 9, for standard care, blood will be collected for TSH measurement. The administration of 10 MBq 123I and the uptake measurements will be performed by the Department of Nuclear Medicine in the UMCG. The measurement of UIE and SIE will be determined by the Department of Clinical Pharmacy and Pharmacology of the UMCG. The standard treatment and follow-up of DTC patients is performed by the Departments of Endocrinology in cooperation with the departments of Surgical Oncology, Laboratory Medicine, Nuclear Medicine and Pathology.

Study burden and risks

Burden: low risk patients (according to the Dutch DTC guideline) will receive 10 MBq 123I twice, followed by a thyroid uptake measurement and will have to collect their urine for 24 hours twice and collect a salivary sample twice. High risk patients (according to the Dutch DTC guideline) will receive 10 MBq 123I once, followed by a thyroid uptake measurement and have to collect their urine for 24 hours twice and collect a salivary sample twice. On the day of the first administration of 10 MBq 123I, 1 blood sample (5 ml) will be collected. Low risk patients have to make three additional site visits to the UMCG, high risk patients two additional site visits.

Risks: The administration of two times 10 MBq will lead to an extra radiation exposure of 0,76 mSv for low risk patients and 0,38 mSv for high risk patients. Blood sampling carriers a negligible risk of a hematoma. The 24 hours urine collection and the salivary collections are is without additional risk for the patient or the lab technician.

Benefits: none, participants will participate based on altruistic motives.

Contacts

Public
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9713 GZ
NL

Scientific
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9713 GZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Patients, men and women above the age of 18 years, have to be diagnosed with DTC and have to follow a LID prior to the 131I therapy according to the Dutch DTC guideline
- Patients have to be fit to adhere to the study protocol
- Patients have to be able to read and understand the Dutch language

Exclusion criteria

- Age < 18 years
- Patients using amiodarone
- Patients receiving iodinated contrast < 3 months before the LID
- Pregnancy
- Patients prepared for ablation therapy with rhTSH
- R
enal impairment, EGFR <30ml/min/1,73m2

For the substudy, additional exclusion criteria are*:
- History of Sjogren*s disease, or other disease affecting the salivary gland

* If patients meet the exclusion criteria of the substudy, but not those of the

regular study, they are still asked to participate in the regular study.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	17-02-2023
Enrollment:	25
Type:	Actual

Ethics review

Approved WMO Date:	30-07-2019
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	13-04-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	19-04-2024
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	18-09-2024
Application type:	Amendment

Review commission: METC Universitair Medisch Centrum Groningen (Groningen)

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	NL65923.042.18