Endokrynologia Polska/Polish Journal of Endocrinology
Tom/Volume 61; Numer/Number 5/2010
ISSN 0423–104X

Urinary iodine in patients with differentiated thyroid cancer (DTC) during L-thyroxine treatment

Analiza kliniczna wydalania jodu z moczem u chorych na zróżnicowane raki tarczycy w trakcie terapii L-tyroksyną

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Abstract

Introduction: Urinary iodine concentrations were analyzed in the morning urine samples of patients with differentiated thyroid cancer (DTC).

Material and methods: The analyzed group included 572 DTC patients who were treated with radioiodine or hospitalized for evaluation of radioiodine treatment effects in 2009 at the Institute of Oncology in Gliwice. Ioduria was analyzed by PAMM (Program Against Micronutrient Malnutrition) method before rhTSH administration. A total of 545 tests were performed during L-thyroxine treatment and 27 after L-thyroxine withdrawal.

Results: Median L-thyroxine dose was 150 μg/day. Median ioduria was 127.5 μg/L during L-thyroxine therapy and 134 μg/L after the L-thyroxine withdrawal. No distinct relation between ioduria and L-thyroxine dose was observed. Ioduria < 200 μg/L was observed in over 90% of patients and this cut-off was chosen for the reference range. Only 1.2% of patients showed a distinct stable iodine contamination (ioduria ≥ 300 μg/L).

Conclusions: Urinary iodine concentrations in differentiated thyroid cancer patients treated with L-thyroxine vary in a wide range and do not show a clear relation with L-thyroxine dose. **(Pol J Endocrinol 2010; 61 (5): 458–461)**

Key words: *thyroid cancer, ioduria, L-thyroxine treatment*

Streszczenie

Wstęp: W pracy przeanalizowano stężenie jodu w porannej próbce moczu u chorych na zróżnicowanego raka tarczycy (DTC, *differentiated thyroid cancer*).

Materiały i metody: Badano 572 chorych na DTC po operacji, którzy w 2009 roku byli hospitalizowani w celu leczenia jodem radioaktywnym lub oceny jego wyników. Stężenie jodu w moczu oznaczano metodą PAMM (*Program Against Micronutrient Malnutrition*). W trakcie leczenia L-tyroksyną wykonano 545 badań, 27 po przerwie w stosowaniu L-tyroksyny.

Wyniki: Mediana dawki L-tyroksyny wynosiła 150 μg/dzień. Mediana dobowego wydalania jodu z moczem wynosiła 127,5 μg/L, a po odstawieniu L-tyroksyny 134 μg/L. Nie obserwowano zależności stężenia jodu w moczu od stosowanej dawki tyroksyny. Jodurię < 200 μg/L obserwowano u ponad 90% chorych i ten zakres uznano za referencyjny. Kontaminację stabilnym jodem wykazano u 1,2% (joduria ≥ 300 μg/L).

Wnioski: Stężenia jodu w moczu u chorych na zróżnicowanego raka tarczycy, leczonych L-tyroksyną, wahają się w szerokim przedziale wartości i nie korelują z dawką L-tyroksyny. **(Endokrynol Pol 2010; 61 (5): 458–461)**

Słowa kluczowe: *rak tarczycy, joduria, terapia L-tyroksyną*

Introduction

Low iodine diet is not routinely administered in Polish patients with differentiated thyroid cancer (DTC), due to the moderate iodine deficiency in our country. Since iodine deficiency has been compensated for since the late nineties, the question of low iodine diet arises again.

The assessment of urinary iodine concentration is not routinely indicated in differentiated thyroid cancer (DTC) patients before planned radioiodine therapy or diagnostic radioiodine scan. However, its range should be known in every population of patients to define the indication for iodine diet preceding therapy and to avoid risk of interference with radioiodine therapy [1–5]. Also,

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the increasingly frequent use of rhTSH to support radioiodine therapy and diagnostics raises questions about ioduria during rhTSH-supported procedures.

The aim of the study was to analyze urinary iodine concentrations in DTC patients treated with radioiodine, or followed-up after radioiodine therapy during L-thyroxine treatment with the end of rhTSH, at the Institute of Oncology in Gliwice.

Material and methods

The analyzed group involved 572 DTC patients who were treated with radioiodine or followed up with ^{131}I scan after previous radioiodine therapy from April 17 to December 12 2009 at the Institute of Oncology in Gliwice.

The age range of patients was 10–87 years. Median age was 51 years. 545 tests were performed during L-thyroxine therapy under rhTSH administration and 27 after L-thyroxine withdrawal. The group of patients with L-thyroxine withdrawal stopped L-T4 intake 5 weeks before radioiodine treatment then used L-T3 for 3 weeks and after that used no thyroid hormone supplementation for 2 weeks. In the group under rhTSH administration, the recombinant TSH was injected two times in a 24-hour time interval and L-T4 therapy was given during the whole treatment process.

Median L-thyroxine dose was 150 μg/day (range 50-250 μg/day). Median TSH serum level in patents under rhTSH administration was: 0.039 mU/L before rhTSH administration, 176 mU/L on the next day after the second rhTSH administration, and in patents after L-thyroxine withdrawal it was 33 mU/L.

Iodine urine concentration was analyzed using the PAMM method (Program Against Micronutrient Malnutrition) based on measurement of the Sandell-Kolthoff reaction. This method is based on spectrophotometer analysis of the catalytic properties of iodine in reaction with Ce (IV) and As (III). As (III) reduces Ce (IV) to Ce (III) and iodine works as a catalyst of this reaction (the greater amount of iodine the quicker reaction is). The solution of cerium ions (IV) is orange and shows light absorption at 405 nm wavelength whereas the solution cerium (III) is colourless. It gives the opportunity to follow the reaction kinetics by the measurement of absorbance, and the reaction rate is a function of the iodine concentration. The colour change that occurs during the reaction can therefore be used to determine the iodine concentration in an unknown urine specimen, when compared to a set of known iodine standards. Due to possible interference coming from components of urine matrix, the pretreatment stage needs mineralization by the use of potassium chlorate (V).

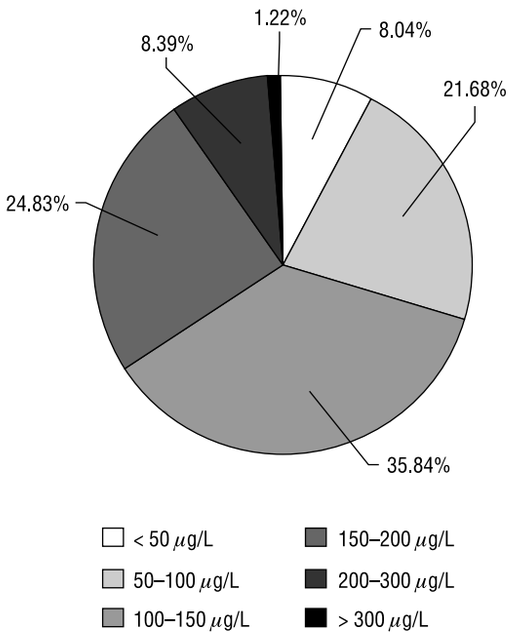

Figure 1. *The distribution of urinary iodine concentration in DTC patients*

Rycina 1. *Rozkład stężenia jodu w moczu u chorych na DTC*

Results

The median urinary iodine concentration was 127.5 μg/L and ranged from 10.1 to 395.2 μg/L. In patients investigated after the L-thyroxine withdrawal, median urinary iodine concentration was 134 μg/L and ranged from 10.1 to 345.1 μg/L. There were no differences between patients treated during and patients treated off L-T4 therapy. These results, ranked from the lowest to the highest, are shown in Figure 1.

Only a small fraction of patients exhibited iodine urinary concentrations > 200 μg/L and a few (1.2%) exceeded 300 μg/L (Fig. 2). Interestingly, no difference between L-thyroxine withdrawal patients and patients investigated during L-T4 therapy was noted. Although half of them are in the low range (< 100 μg/L), the other 50% are dispersed within the upper half of the range (Fig. 3).

No distinct relation between urinary iodine and L-thyroxine dose administered was observed (Fig. 4). There was also no relation between urinary iodine and TSH serum level.

Discussion

Our study is consistent with recently published Italian data showing no significant differences in iodine excretion between patients on or off L-T4. According to the authors'

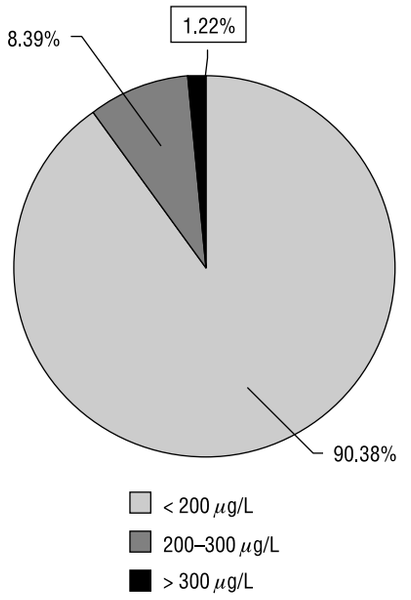

Figure 2. *The ratio of patients showing stable iodine contamination (urinary iodine was ≥ 300 μg/L)*

Rycina 2. *Tylko u 1,2% badanych stwierdzono kontaminację jodem stabilnym (joduria wynosiła ≥ 300 μg/l)*

opinion the body iodine content is not an important determinant of thyroid ablation when preparing patients with either L-T4 withdrawal or on rhTSH [1].

Our data show that iodine urinary concentrations in DTC patients treated with suppressive L-thyroxine doses are high and do not change depending on LT4 dose or L-T4 withdrawal. Similarly, Barbaro et al. demonstrated that L-T4 withdrawal was related to a slight reduction in urinary iodine level only, with no impact on the ^{131}I treatment effectiveness [2], while low iodine diet increased the sensitivity of radioiodine-avid foci detection [3–5].

Currently, in most of DTC patients, rhTSH is applied without the necessity of L-thyroxine (containing stable iodine) withdrawal. Thus, the question arises whether low iodine diet before radioiodine administration in order to increase ^{131}I uptake should be recommended. Our results showing no relation of urinary iodine with L-thyroxine doses do not support this assumption.

The majority of papers confirming the relevance of low iodine diet before radioiodine administration for diagnostic or therapeutic purposes have been published in the early eighties [3–10]. In many countries low iodine diet is a standard procedure applied to DTC patients before radioiodine administration. However, until recently, low iodine diet was not routinely recommended in Poland due to iodine deficiency and low iodine content in food. The introduction of this recommendation without evidence-based data supporting its use seems precautious.

In DTC patients on L-T4 suppressive treatment the reference urinary iodine concentration should not extend 200 μg/L [11, 12]. Published data suggest that contamination with stable iodine is present when iodine urinary level is > 300 μg/L [13]. This was stated only in the minority (1.2%) of our patients. However, iodine urinary excretion > 200 μg/L may also be related to higher risk of false negative whole body scintigraphy.

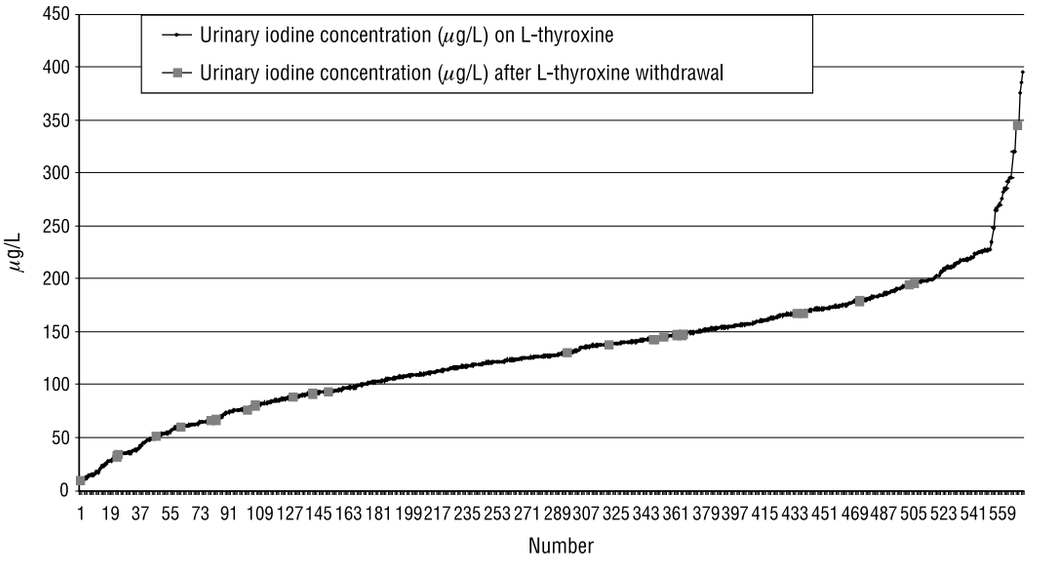

Figure 3. *Urinary iodine concentrations under rhTSH administration on L-T4 therapy and after L-T4 withdrawal. The dots represent urinary iodine values in patients after L-thyroxine withdrawal*

Rycina 3. *Stężenie jodu w moczu na stymulacji z użyciem rhTSH (w trakcie stosowania L-T4) i po odstawieniu L-tyroksyny (zaznaczone punktami)*

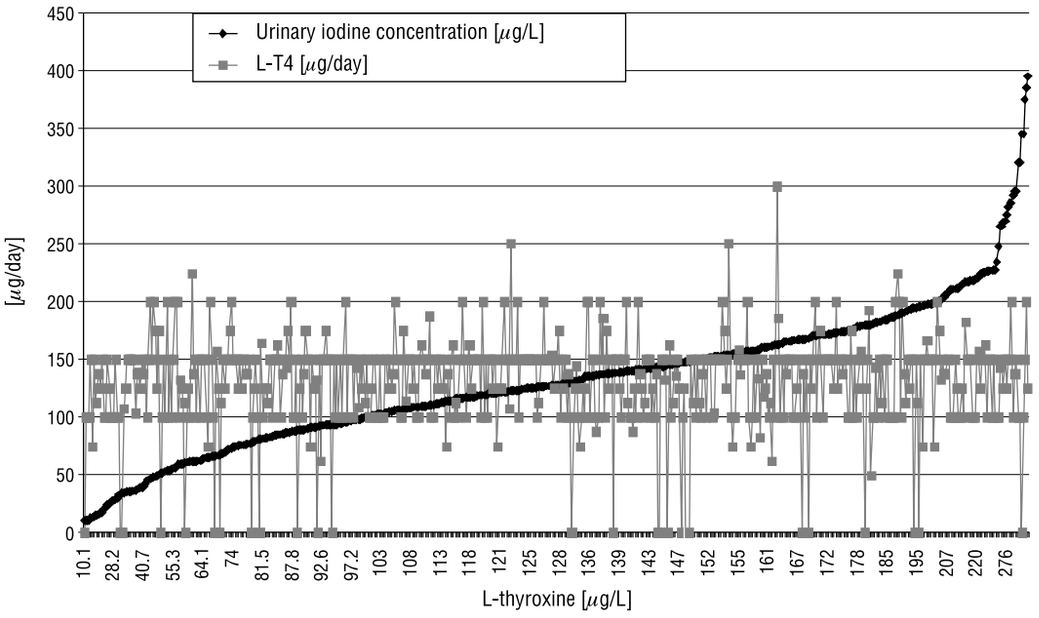

Figure 4. *Urinary iodine concentrations (μg/L) and corresponding L-thyroxine doses (μg/day) in DTC patients*
Rycina 4. *Wzrastające stężenia jodu w moczu (μg/l) i odpowiadające im dawki L-tyroksyny (μg/d.) u chorych na DTC*

Distant DTC metastases are currently rarely observed in Poland [14, 15]. The low incidence of stable iodine contamination (only 1.2% of DTC patients with urinary iodine concentration > 300 μg/L in our study) indicate that low iodine diet during rhTSH administration before radioiodine diagnostics and treatment may be considered non-obligatory. Nevertheless, because of higher iodine content in food, the recommendation of low iodine diet before radioiodine administration may be necessary in future.

Conclusions

1. In general, the iodine excretion by urine in DTC patients treated with thyroxine with the intention of TSH suppression is high and does not change with L-thyroxine dose or after L-thyroxine withdrawal. These observations suggest that a low iodine diet would not be effective either.
2. Urinary iodine concentrations > 200 μg/L, and particularly > 300 μg/L, may be connected with a risk of false negative radioiodine scan or ineffective radioiodine therapy, and in this group of patients low iodine diet before second treatment may be indicated.

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