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Original

Biokinetics of ^{131}I after endogenous and exogenous stimulation of TSH in patients with DTC

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Abstract

BACKGROUND: The effective radioiodine treatment of patients with DTC is possible only after raising the TSH value over 30 μUI/ml. This effect might be obtained by either endogenous or exogenous stimulation. The aim of this study was to evaluate differences in ^{131}I biokinetics of selected regions of interest (ROIs) in cases of endogenous and exogenous stimulation.

MATERIAL AND METHODS: Two groups of 50 patients were enrolled in the study. All patients were treated with 3.7 GBq of ^{131}I; the first group after thyroid hormone withdrawal (THW), the second group after rhTSH administration (rhTSH). On the basis of post-treatment images, the uptake ratios over selected ROIs (thyroid remnants, mediastinum, liver, stomach, abdomen, and whole-body) were compared between groups.

RESULTS: In the case of uptake over the whole-body and the liver, statistically significant higher values were received for the THW group. For the remaining regions, the differences between groups were statistically insignificant, but uptake ratios in the rhTSH group were generally numerically lower compared to the THW group.

CONCLUSIONS: The revealed difference in radioiodine biokinetics after thyroid hormone withdrawal or administration of recombinant human TSH may influence many important aspects of patients with DTC treatment, such as the choice of proper therapeutic scheme, the cost of therapy, and the dose assessment.

Key words: endogenous stimulation, exogenous stimulation, thyroid hormone withdrawal, recombinant human TSH, radioiodine treatment, DTC

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Introduction

In patients with differentiated thyroid carcinoma (DTC), efficient treatment with radioiodine complementary to radical surgery is possible only on condition that the TSH value is over 30 μUI/ml. For many years, this effect was obtained by endogenous stimulation, which means that L-thyroxine (LT4) was withdrawn for at least four weeks before the planned treatment with ^{131}I. Recently, exogenous stimulation of TSH has become possible after intramuscular injection of recombinant human TSH, rhTSH (Thyrogen, Genzyme, Cambridge, MA) 24 h and 48 h before radioiodine treatment.

At first, recombinant human TSH was only approved for the stimulation of serum Tg and whole-body scintigraphy (WBS), to be performed during post-surgical follow-up and for patient staging. Next, many small clinical studies revealed that in low risk patients (pT1-2 N0M0) thyroid remnant ablation using rhTSH and thyroid hormone withdrawal (THW) methods had a similar rate of effective ablation. These findings were finally confirmed by a large multicentre controlled randomized study conducted in 2006 [1].

The aim of this study was to evaluate differences in the ^{131}I biokinetics of selected regions of interest (ROIs) in cases of endogenous and exogenous stimulation in patients from our Department.

Material and methods

A hundred patients were qualified for complementary treatment with ^{131}I in the Endocrinology Department of University Hos-

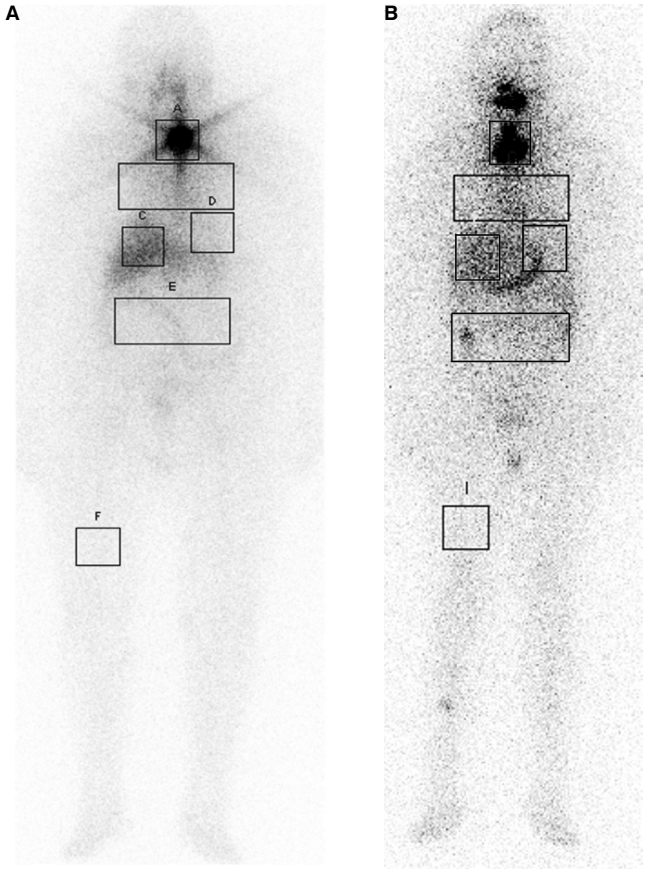

Figure 1. Localization of selected regions of interest. A. Endogenous stimulation, THW group; B. Exogenous stimulation, rhTSH group.

pital in Krakow because of DTC in the low stage of the disease (pT1aN0M0, pT1bN0M0, pT2N0M0). All patients received the same radioiodine activity, 3.7 GBq (100 mCi).

The THW group consisted of 50 patients (mean age 57 years, SD 13 years, min 29 years, max 79 years). Papillary thyroid carcinoma and follicular thyroid carcinoma were diagnosed in 83% and 17% of patients, respectively. In this group of patients, thyroid hormone treatment was withheld for 4–6 weeks before radioiodine therapy, until the patient's TSH was above the required level (mean TSH level 68 μIU/ml, SD 35 μIU/ml).

The rhTSH group also consisted of 50 patients (mean age 54 years, SD 16 years, min 19 years, max 77 years). Papillary thyroid carcinoma and follicular thyroid carcinoma were diagnosed in 86% and 14% of patients, respectively. In this group, the patients continued receiving L-thyroxine therapy after radical surgery of the thyroid. The Thyrogen was administered intramuscularly 48 h and 24 h before thyroid remnant ablation, in accordance with Polish standards [2].

Post-treatment whole-body imaging was performed in all patients seven days after ^{131}I administration. All images were acquired using a dual-head, large field of view E.CAM gamma camera (Siemens, 2000) with high-energy (HE) collimators. The camera settings were as follows: 1024 × 256 matrix, 8-cm/min scan speed, with autocontour, without scatter correction.

Between the groups, on the basis of AP scans, counts over selected regions of the body to counts over the background region ratios (uptake ratios) were compared. Such regions of interest (ROIs) as: region over the thyroid remnants (thyroid/backg), mediastinum (mediastinum/backg), liver (liver/backg), stomach (stomach/backg), abdomen (abdomen/backg), and whole-body (WB/backg), were chosen (Figure 1). The background was estimated from counts over the right thigh re-calculated on the same number of pixels as was assessed in the selected ROI.

Statistical analysis was performed by U Mann-Whitney test at a 95% confidence level.

Results

In the case of WB/backg ratios, statistically significant higher values were received for the THW group, 0.90 ± 0.69, compared with the rhTSH group, 0.52 ± 0.47 (Figure 2). Taking into consideration the thyroid/backg ratios, the difference between groups was statistically insignificant (THW group, 25.54 ± 36.21; rhTSH group, 27.64 ± 30.14).

For mediastinum and stomach, differences between the groups were statistically insignificant (mediastinum/backg — THW group, 3.01 ± 1.50; rhTHS group, 2.57 ± 0.86; stomach/backg — THW group, 4.70 ± 5.13; rhTSH group, 2.92 ± 1.02). For abdomen/backg ratios the same statistically insignificant results were observed (THW group, 0.84 ± 0.32; rhTSH group, 0.75 ± 0.19). In the case of liver/backg ratios, statistically significant higher values were also received for the THW group, 4.56 ± 1.66, compared with rhTSH group, 3.60 ± 0.89 (Figure 3).

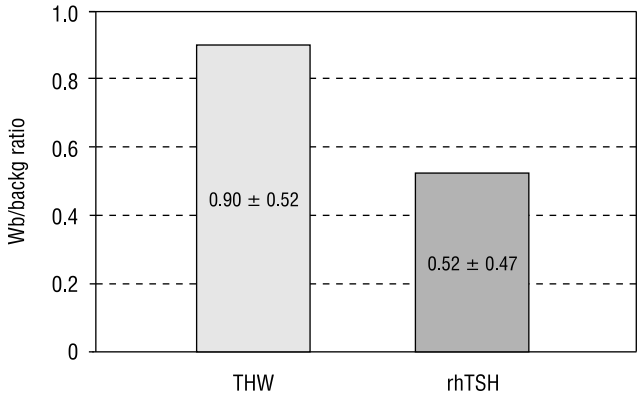

Figure 2. WB/backg ratios for both groups.

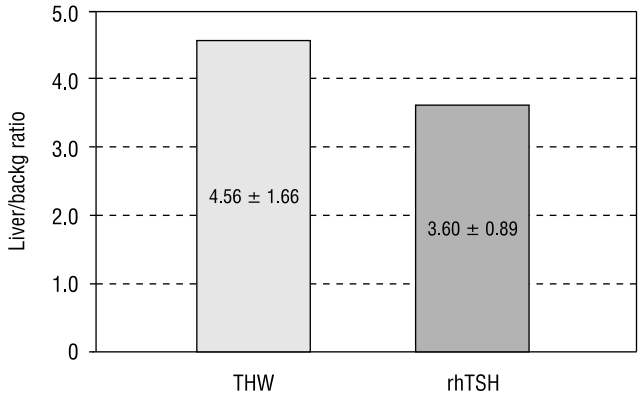

Figure 3. Liver/backg ratios for both groups.

Discussion

This present study is focused on an assessment of the differences in ^{131}I biokinetics in cases of endogenous and exogenous stimulation of patients with DTC.

In previous publications concerned with the evaluation of the biokinetics of radioiodine, mainly in thyroid remnant localizations and in the whole-body after the discussed DTC treatment schemes, different sophisticated procedures were used. In this paper, a new, simpler method for a number of different regions of interest was described. The result obtained for whole body region of interest is concordant with previous reports, finding that ^{131}I is excreted from the body significantly faster after an exogenous stimulation of thyroid stimulating hormone level. Furthermore, for the thyroid remnants region, the same level of tracer uptake was found for both therapeutic schemes [3, 4]. Despite the lack of statistically significant results for other regions (except the liver), uptake ratios in the rhTSH group were always numerically lower compared with the THW group. This might be interpreted such that after an rhTSH administration most human organs demonstrated faster radioiodine clearance because of the short-term influence of a factor which stimulated the high TSH level in patients without withdrawal of L-Tyroxine. So it is likely the patients' hyperthyroid state influenced the results. The only statistically significant difference between the groups was observed for the liver, which is an organ with a very high metabolism. This may perhaps be related to the fact that iodine contained in organic compounds undergoes deiodination mainly in this organ. On the other hand, in the THW group, after the withdrawal of L-Tyroxine, a slow rising of the TSH level is observed with simultaneous slow passing of all cells into a clinically manifested hypothyroid state.

Nowadays, the use of Thyrogen is only approved for patients with a low stage of the disease (pT1-2 N0M0). An observed faster removal of radioiodine after rhTSH administration might be a reason for delivering an insufficient radiation dose to metastases, which is crucial for their effective sterilization. So, taking into account patients with higher stages of DTC, this issue should be considered very carefully. Approval for exogenous stimulation should undeniably be confirmed by positive results from a multicentre controlled randomized study with a large group of patients.

Our results might be also considered in respect of the treatment cost. Faster elimination of radioiodine in the rhTSH group might permit patients a shorter stay in hospital and thus a reduction in the overall cost. Many factors might influence the profitability of the treatment. To confront two therapeutic schemes, building a Marcov model is a well-accepted statistical and economical technique for comparing cost-effectiveness. In the literature, only three manuscripts considered this problem, and they all showed a preferable overall cost for exogenous stimulation [5–7]. A simpler analysis, which was performed in a French hospital, is also mentioned. The parameter considered in order to discharge the patient from hospital was a level of body residual activity lower than 400 MBq [8]. It was clearly shown that exogenous stimulation reduced patients' average stay by one day. The cost of this therapeutic scheme is still higher than endogenous stimulation, but a shorter hospitalization allows for a 57% compensation of the Thyrogen cost for one patient. Preparing patients with rhTSH might be cost-effective in developed countries, but it should be stressed that this statement is only true in the case of proper estimation of the remaining treatment costs.

The next problem connected with our result is the potential difference in average absorbed dose for healthy organs, which is delivered by ^{131}I radiation during thyroid remnant ablation, after endogenous and exogenous stimulation of the TSH level. Currently just one paper has been published concerning a full estimate of the radiation dose for healthy organs only in the case of rhTSH stimulation [9]. However, this issue is very important from a radiation safety point of view and should be considered more carefully in future [10, 11].

Important information could be also obtained from compartment models for radionuclide kinetics, an element of patient dose estimates. The principle of utilizing compartment modelling is to find solutions for the differential equations and calculate the transfer coefficients between compartments. These constants describe the degree and rapidity of compartment interactions. They are estimated on the basis of each tracer biokinetic measurement. In connection with our results, the difference in values of estimated transfer coefficients might be observed for endogenous and exogenous therapeutic schemes. Hence it is crucial to know which therapeutic scheme the compartment model was set for.

Conclusions

The revealed difference in radioiodine biokinetics after thyroid hormone withdrawal or administration of recombinant human

TSH may influence many important aspects of treatment for patients with DTC.

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