Is it necessary to perform control diagnostic ^{131}I whole body scan after remnant ablation in differentiated thyroid carcinoma patients who have stimulated Tg levels under 2 ng/ml?

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Abstract

Background: The aim of this retrospective study is to evaluate whether diagnostic I-131 whole body scan (DWBS) performed 6-12 months after thyroid remnant ablation is necessary or not in differentiated thyroid carcinoma (DTC) patients with thyroglobulin (Tg) levels under 2 ng/ml and negative anti-Tg antibodies.

Methods: The study included 812 DTC patients undergoing the first control DWBS with Tg levels under 2 ng/ml and negative anti-Tg antibodies in the hypothyroid state, 6 months after postsurgical radioablation of residual thyroid tissue. Second DWBS was performed 18 months after ablative I-131 treatment (AIT) to 572 patients who had negative first control DWBS. These 572 patients had a stimulated Tg level under 2 ng/ml at 18th month control.

Results: The first control DWBS, 6 months after thyroid ablation, was negative in 789 (97.2%) patients and was positive for minimal residual uptake in the thyroid bed in 23 (2.8%) patients. Nine of the 23 patients with residual thyroid bed uptake, received a second dose of radioiodine therapy for complementary ablation of residual thyroid. Fourteen patients were not retreated. Second DWBS performed 18 months after AIT, was negative in all patients.

Conclusion: Our data suggest that in patients with stimulated Tg level under 2 ng/ml, DWBS performed 6 months after AIT, is informative only in minority of patients for residual uptake in the thyroid bed which is usually clinically not relevant. Therefore, we suggest that the DWBS may be avoided in patients with stimulated Tg level under 2 ng/ml.

Keywords: Diagnostic whole body ^{131}I scan, Thyroglobulin, ^{131}I ablation treatment, thyroid carcinoma

Introduction

Differentiated thyroid carcinoma (DTC) is a common malignancy with excellent survival rates [1]. Post surgical thyroid remnant ablation and suppression of thyroid-stimulating hormone (TSH) is a key element in treatment for DTC patients [2,3]. Life long follow-up of patients is important because recurrences may occur [4-6]. The follow-up of these patients mainly includes serum thyroglobulin (Tg) measurements and diagnostic ^{131}I whole-body scan (DWBS). Six months after thyroid ablation in the hypothyroid state, undetectable Tg levels with negative DWBS results are usually associated with complete remission, provided that anti-Tg antibodies are not present in the circulation, whereas detectable or elevated serum Tg levels correlate with persistent disease [7,8]. Serum Tg measurement is a more sensitive test than DWBS to detect residual functioning thyroid cells, benign or malignant [9-11]. Serum Tg levels during thyroid hormone withdrawal usually are correlated with the results of DWBS [12,13]. However, discordant results of Tg measurements and DWBS have been reported [6,14-16]. A positive Tg test and negative DWBS were found in almost all of these cases [6,14-16]. In patients with undetectable Tg levels, DWBS may add the information of minimal residual uptake in the thyroid bed in a

minority of cases which is usually clinically not relevant. Some studies have shown that the DWBS is almost no informative in patients with undetectable serum Tg and negative Tg antibodies [9,11]. On this basis, these researchers recommended to follow-up of DTC patients with serum Tg measurement alone and to abandon the routine use of DWBS.

The aim of this retrospective study is to evaluate whether DWBS performed 6 months after thyroid remnant ablation is necessary or not in DTC patients with Tg levels under 2 ng/ml and negative anti-Tg antibodies.

Methods

The study included 812 DTC patients (661 males, 151 females with mean age 45 ± 14) undergoing the first control DWBS with Tg levels under 2 ng/ml and negative anti-Tg antibodies in the hypothyroid state, 6 months after postsurgical radioablation of residual thyroid tissue, between January 2008 and January 2013. Firstly, a near-total or total thyroidectomy was performed to all patients. Within a few months after surgery, patients were given 75-100 mCi ^{131}I for remnant ablation after at least 3 week withdrawal of hormone therapy. A post treatment ^{131}I whole body scan (PWBS) was performed 5-10 days after

Table 1. PWBS, first control DWBS and second control DWBS results.

	Positive (%)	Negative (%)
PWBS	812 (100%)	--
First control DWBS	23 (2.8%)	789 (97.2%)
Second control DWBS	--	572 (100%)
Local or distant metastasis	--	812 (100%)

PWBS: posttreatment ¹³¹I whole body scan

DWBS: diagnostic ¹³¹I whole body scan

ablative ¹³¹I treatment (AIT) to all patients. To control the AIT efficacy, DWBS was planned approximately 6 months later while the patients were off hormonal therapy. Three weeks before undergoing DWBS, patients discontinued taking triiodothyronine, and followed a low-iodine diet during that period. Just before DWBS, Tg and anti-Tg antibodies levels were measured when TSH>30 IU/ml. Tg levels were measured using immunoradiometric analyzer that uses paramagnetic microparticles and chemiluminescent detection technology with a lower detection limit of 0.2 ng/ml. After TSH stimulation, 5 mCi (185 MBq) I-131 was given orally to the patients and 2-3 days later, DWBS was performed to all patients.

Second DWBS was performed 18 months after AIT to 572 patients who had negative first control DWBS. Tg and anti-Tg antibodies levels were measured before second DWBS when TSH>30 IU/ml.

During the follow-up, Tg and anti-Tg antibody levels were also measured in three months intervals while the patients on thyroid hormone replacement. Patients were followed up for the period of 6 months to 5 years. Statistical analysis and the calculations were performed using SPSS 11.0 for Windows. Differences were considered statistically significant at P<0.05.

Results

Soon after surgery, all patients underwent thyroid ablation with ¹³¹I, at doses ranging from 75–100 mCi, followed by PWBS. Thyroid remnants were present on PWBS in all patients and there was no foci of pathologic radioiodine uptake outside the thyroid bed. Six months later, all patients underwent the first control DWBS and serum Tg measurement in the hypothyroid state. Thyroglobulin levels of all patients were measured just before DWBS after a low-iodine diet without hormone therapy when TSH>30 IU/ml. At this time, all patients had a serum Tg level under 2 ng/ml. The control DWBS, 6 months after thyroid ablation, was negative in 789 (97.2%) patients and was positive for residual uptake at different levels in the thyroid bed in 23 (2.8%) patients. No patient had scintigraphic or clinical evidence of local or distant metastases.

Nine of the 23 patients with residual thyroid bed uptake, received a second dose of radioiodine therapy for complementary ablation of residual thyroid. Retreated 9 patients were scanned 6 months after second treatment with 5 mCi

¹³¹I and scan results were negative in all 9 patients. Fourteen patients were not retreated. A second DWBS was performed to these 14 patients approximately 1 year after first DWBS and second DWBS was negative in 3 patients and positive just like first DWBS in 11 patients. These 11 patients who had postablative thyroid remnant, were followed up 2-4 years and no signs for recurrence were detected. There was no statistically significant difference between Tg level and residual uptake in the thyroid bed on the first control DWBS (p=0.34), because Tg was undetectable (<0.2) in 16 patients and 0.8±0.5 ng/ml (range 0.3-1.6 ng/ml) in 7 patients.

Second DWBS performed 18 months after AIT, was negative in 572 (100%) patients and stimulated Tg levels of patients measured before second DWBS were under 2 ng/ml. PWBS, first control DWBS and second control DWBS results were given in [Table 1](#).

Discussion

The principal diagnostic tests used in the follow-up of patients with DTC are serum Tg measurements and DWBS after surgery and radioiodine ablation [3]. Also neck ultrasonography (US) is an important component of follow-up and ¹⁸F-fluorodeoxyglucose-positron emission tomography (FDG-PET) can be useful in patients who have positive Tg level and negative radioiodine whole body scan. The follow-up is mainly based on serum Tg measurement. Tg is a thyroid-specific protein with a diameter of 660 kDa which is the precursor element of thyroid hormone biosynthesis [17]. It is secreted from either normal thyroid tissue or functioning malign cells of thyroid cancer. Ablation of remnant thyroid tissue after surgery improves the accuracy of long-term patient monitoring with serum Tg measurements [18,19]. Serum Tg can be measured during thyroid hormone treatment or after withdrawal of thyroid hormone.

Six months after remnant ablation, a negative DWBS and stimulated Tg level under 2 ng/ml suggest that the thyroid tissue is totally ablated. Normally, there is a concordance between DWBS and Tg levels, but sometimes discordance is seen. Majority of this situation is a positive Tg test and negative DWBS. Negative results from DWBS may be caused by factors such as an insufficient increase in serum TSH or iodine contamination [20]. Another reason for negative DWBS is dedifferentiation of the tumor, leading to a loss of its ability to trap iodine. Finally, metastases may be too small to detect by DWBS. PWBS may detect new foci of tumor not seen on DWBS in up to 50% of patients [14,21]. Serum Tg measurement is superior to DWBS for detecting residual or metastatic lesions in patients with DTC.

Many researchers have found that in their study populations, DWBS added no diagnostic value to that provided by stimulated Tg measurement on the follow-up patients with DTC [9,11,22-27]. On this basis, these researchers suggested that the follow-up to DTC patients on serum Tg measurement alone and to abandon the routine use of DWBS. Routine

DWBS is advised for patients positive for anti-Tg antibody [19]. Because the presence of anti-Tg antibodies, levels of Tg can be mistakenly low.

Baudin et al., concluded that DWBS has a limited role for the follow-up of DTC patients and they suggested that follow up should rely on serum Tg level and prognostic parameters [27]. Siegrid et al., indicated that routine DWBS added no diagnostic value to stimulated Tg measurement in a large population of patients with high risk DTC [26]. Pacini et al., found that the combination of measurement of recombinant human thyrotropin stimulated serum Tg levels and neck US had highest sensitivity (96%) and negative predictive value (99%) for monitoring patients with DTC [28]. In a study Cailleux et al., including 210 patients with a Tg less than 1 ng/ml while they were hypothyroid, the control WBS was negative in the large majority of patients (195/210) and positive in the thyroid bed in a minority of patients (15/210) [9]. In another study Pacini et al., found that, with the exception of persistent thyroid bed uptake in a minority of cases, the control DWBS is not informative that could influence the follow-up therapeutic strategy [11]. They showed that the control DWBS, 6 months after thyroid ablation, was negative in 225 (71.4%) patients and was positive for residual uptake in the thyroid bed in 90 (28.6%) patients when stimulated Tg level under 3 ng/ml. In our study, first control DWBS performed 6 months after AIT, was negative in 789 patients and was positive for residual uptake in the thyroid bed in 23 (28.6%) patients when stimulated Tg level under 2 ng/ml. Second DWBS performed 18 months after AIT to 572 patients who had negative first control DWBS, was negative again in all patients when stimulated Tg level under 2 ng/ml. There was no statistically significant difference between first and second control DWBS after AIT ($p=0.31$).

The results reported by Robbins et al., seem to differ from the other and our studies. They found that using cut-off of 2 ng/ml, stimulated Tg measurement alone failed to detect 13% of metastatic patients [29]. The DWBS was informative in nearly half of these cases. Therefore, they concluded that Tg measurement alone is insufficient to detect all recurrences or metastases and the combination of DWBS and serum Tg measurement was superior to serum Tg measurement alone.

Conclusion

Our data suggest that in patients with stimulated Tg level under 2 ng/ml, DWBS performed 6 months after AIT, is informative only in minority of patients for minimal residual uptake in the thyroid bed which is usually clinically not relevant. Therefore, we suggest that the DWBS may be avoided in patients with stimulated Tg level under 2 ng/ml. The follow-up of these patients may be continued with periodic serum Tg measurements, neck US and clinical examination. If the clinician prefer to perform DWBS on the first control 6-12 months after remnant ablation, there is no need to perform DWBS for subsequent follow-up of these patients except in cases

with increased Tg levels. Diagnostic ^{131}I whole-body scan may be beneficial in patients with positive anti-Tg antibody. Also in patients with Tg levels higher than 2 ng/mL, DWBS is one of the methods that can be used to detect recurrent or metastatic disease.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

Authors' contributions	UE	EK	YC	HD	ES	MY
Research concept and design	✓	--	--	--	--	--
Collection and/or assembly of data	--	--	--	--	✓	✓
Data analysis and interpretation	--	✓	--	--	--	--
Writing the article	--	--	✓	--	--	--
Critical revision of the article	✓	--	--	--	--	--
Final approval of article	--	--	--	✓	--	--
Statistical analysis	--	--	--	--	--	✓

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