Radioiodine treatment (30mCi) for postsurgical remnant ablation in patients with differentiated thyroid carcinoma: Comparative analysis of patient preparation using conventional thyroid hormone (LT4/T3) withdrawal or recombinant human TSH

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Directed by Professor Woong Youn Chung

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Thyroid cancer is the fastest growing cancer in Korea, especially among women. Given the relative success we have had in its treatment, there is a need to capitalize on it by better understanding the factors that underpin this malignancy and exploring better strategies for treatment and follow-up. To do so, we must take full advantage of the revolution in modern therapeutics(including recombinant human TSH, allowing for better treatment outcomes and quality of life of well differentiated thyroid carcinoma and is imaging).

I hope that this paper may be one of the indispensable companion for endocrinologists (particularly those with an interest in thyroid cancer), thyroid surgeon, nuclear medicine physicians, clinical biochemists, and those in biotechnology intent on the innovation of better diagnosis and therapy of cancer.

Throughout this project I have been supported and advised by two wonderful specialists (Dr. W.Y. Chung; the untiring director, Dr. M.J. Yun; the grateful cooperator). Last but certainly not least, all my supervisors and colleagues (Dr. E.Y. Soh, Dr. W.T. Lee, Dr. C.G. Lee, Y.J. Oh, Dr. K.H. Nam, and Dr. C.S. Park). They are acknowledged for fruitful discussions, their collaboration and cooperation in the field and for their dedication to the well-being of our patients.

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<ABSTRACT>

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Purpose: Few reports have examined the use of recombinant human TSH(rhTSH) for ablation of postsurgical thyroid remnants after low dose RI (radioactive iodine) therapy, compared with conventional thyroid hormone withdrawal. The aim of the present study was to explore the effectiveness of each patient preparation method before RI ablation(30mCi) of the remnant thyroid in patients with differentiated thyroid carcinoma(DTC).

Methods: This study included three groups of patients, enrolled consecutively. From February 2006 to March 2007, 291 patients were enrolled and randomized, after total thyroidectomy, to a 4-week LT4 withdrawal group(Group, I, n=89), a 2-week T3 withdrawal group(Group II, n=133), and a rhTSH administration group(Group III, n=69). Quality-of-life(QoL) was determined at the time of ablation.

Results: Patients in the three groups did not differ significantly in baseline

characteristics or TNM staging. In all study groups, serum TSH levels showed very good stimulation(mean, 82.24±18.21 mU/L), without significant between-group differences($p=0.5213$). Follow-up examinations performed 12 months after ablation were satisfactory in all study patients, without significant between-preparation differences($p=0.2061$). QoL was better preserved in Group III than in Groups I and II($p<0.0001$). However, there was no QoL difference at the time of ablation between Groups I and II.

Conclusion: Our study indicates that use of rhTSH preserves QoL in patients undergoing RI ablation, and affords an ablation success rate comparable to that seen after thyroid hormone withdrawal. However, ablation preparation using withdrawal of LT3 for 2 weeks did not prevent development of profound hypothyroidism, as also occurred when LT4 alone was withdrawn for 4 weeks.

Key words : rhTSH, low dose radioiodine treatment, quality of life, T3

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I. INTRODUCTION

Initial treatment for differentiated thyroid carcinoma (DTC) is total or near-total thyroidectomy, which is often followed by [^{131}I] radioiodine (RI) ablation of remnant thyroid tissue after 4 weeks of LT4 (levothyroxine) withdrawal. Long-standing hypothyroidism has profound effects on many organs and systems, and causes cognitive impairment; emotional dysfunction; physical discomfort; and health risks in patients who are elderly, frail, or have concomitant illnesses. Withdrawal of thyroid hormone may also have a profound negative impact on patient quality-of-life (QoL) and ability to work in healthy young subjects [1-3].

The standard protocol of RI ablation involves withdrawal of thyroid

hormone to stimulate endogenous TSH, thereby inducing long-standing hypothyroidism. In the current protocol, remnant ablation after thyroid hormone withdrawal promotes RI uptake in residual thyroid cells. The consensus of the European Thyroid association and the guidelines of the American Thyroid Association for patients undergoing RI therapy or diagnostic scanning is that LT4 can be withdrawn for at least 3 weeks, or, alternatively, LT3 (Cytomel®; Theramed, Mississauga, Canada) can be administered for 2 weeks followed by LT3 withdrawal for 2 weeks [4,5].

In recent years, the development of more effective DTC treatment and the introduction of new follow-up modalities have led to modifications in patient management in order to improve QoL. Recombinant human TSH (rhTSH; TSHα; Thyrogen; Genzyme Corp., Cambridge, MA) has become available. The use of rhTSH has been invaluable in DTC management. Hypothyroidism is now avoidable at the time of RI ablation. The use of rhTSH permits maintenance of good QoL [3,4.6], without side-effects, and requires only minor whole-body irradiation [7-9]. rhTSH use has been approved by the European Medicine Agency (EMEA) and the United States Food and Drug Administration (FDA) for DTC patients treated with 3.7 GBq (100 mCi) RI. However, a postoperative low-dose (30 mCi) RI ablation of remnant thyroid tissue, after rhTSH patient preparation, remains controversial. To date, only four prospective studies have explored the efficacy of low-dose (30 mCi) RI ablation after such preparation [10-13],

because low RI doses have not been commonly used in medical centers [11-13]. The present study was designed to investigate whether patient preparation using rhTSH was comparable to conventional methods (T4/T3 withdrawal) with respect to efficacy of postsurgical remnant ablation, in low-risk patients receiving a fixed 30 mCi RI dose. In addition, a between-method comparison of peri-ablation QoL was performed.

II. MATERIALS AND METHODS

1. Inclusion Criteria

Patients with newly diagnosed DTC, more than 18 years old, who had recently undergone total or near-total thyroidectomy with central compartment neck dissection (CCND), were eligible for this study. Exclusion criteria were evidence of distant metastases (M1), lateral neck node metastases (N1b), and/or significant extrathyroidal invasion (T4) (TNM classifications) [14]. As individually assessed by the principal investigator at each site, included patients had no clinically significant abnormalities on routine hematological or blood chemistry tests, and serum creatinine concentrations were normal. No patient had any major concurrent medical disorder, including other malignancies, within the past 5 years, and no patient had recently been prescribed drugs affecting thyroid or renal function, including iodine-containing medications or radiocontrast agents. The study was approved by our Institutional Review Board and written informed consent was obtained from each patient.

2. Study design

The study was a prospective, randomized, controlled, open-label, single center study. The study was designed to compare the efficacies of various patient preparation methods prior to postsurgical remnant ablation using

low-dose (30 mCi) RI, and to explore QoL in patients undergoing RI treatment.

All patients underwent total thyroidectomy with CCND. After operation, all patients began treatment with a TSH-suppressing dose of LT4 (2ug/kg). After at least 30 days of LT4 supplementation, patients were randomized into three groups by RI preparation protocol. In Group I, patients discontinued LT4 for 4 weeks; in Group II, patients converted to LT3 for 2 weeks and then discontinued LT3 for 2 weeks; and in Group III, patients received rhTSH with a short stoppage(4 days) of LT4 from the day before rhTSH until iodine administration to emphasize the interference of iodine content of LT4 on the effectiveness of radiometabolic treatment.

RI treatment was performed on all patients after 2 weeks on a low-iodine diet. Measurements of circulating thyroid hormone, TSH, thyroglobulin (Tg), and anti-Tg antibodies (TgAbs) were performed at ablation, and before and after thyroid hormone withdrawal.

In the rhTSH injection group, rhTSH was administered to ambulatory patients as two 0.9 mg IM injections on 2 consecutive days, followed by the RI therapeutic dose 24 hours after the last injection, and a whole body scan was performed 48 hours after RI treatment. Serum TSH, free T4(fT4), T3, Tg, and TgAbs were measured on the day before the first administration of rhTSH and the day after the second rhTSH administration. Serum samples for Tg and TgAbs assessment were taken 3 days after the second rhTSH

injection. Serum TSH and fT4 were measured by chemiluminescence immunoassay(Centaur; Bayer Health Care, Mannheim,Germany), as was T3 (E-170 assay kit; Roche Diagnostics, Mannheim, Germany). Serum Tg was measured by immunoradiometric assay (Dynotest TgS, Brahms, Berline, Germany), as was TgAbs (Anti-Tgn RIA, Brahms, Berline, Germany). The Tg assay had a sensitivity of 0.2 ng/mL. TgAbs status was considered negative when readings were less than 20 IU/mL. Patients with potentially interfering levels of TgAbs were excluded from statistical analysis of serum Tg changes. To eliminate contamination by stable iodine, urinary iodine excretion over 24 hours was measured in all patients before RI administration and at follow-up assessment. Iodine measurements were performed in a central laboratory (the SCL facility of the Asan Medical Center; Seoul, Korea); an iodine-selective colorimetric method was employed.

To measure remnant thyroid activity, a tracer dose (7.4MBq) of RI was given orally to all patients the day before therapeutic RI administration. Images were obtained 2 hours and 24 hours later using a single-head gamma camera (KOROID, Seyong, Korea) featuring a 3/8-inch-thick crystal and a pinhole collimator. Residual thyroid bed uptake was evaluated both qualitatively (positive or negative) and quantitatively. Post-therapy whole body scans (WBSs) were acquired 48 hours after RI treatment.

3. Measurement of quality- of- life

We aimed to determine clinical QoL. We designed a seven-item written, anonymous questionnaire exploring hypothyroidism consequences for daily living during thyroid hormone withdrawal. The survey items focused on physical symptoms, signs, problem duration, impact on social life, mood changes, and medical resource utilization. Our psychometric study was a modified version of the self-rating Kellner Symptoms Questionnaire (KSQ), the Hamilton depression scale (HDS), and Luster's 13-item scale for measurement of hypothyroidism [2,15]. The minimum possible score is 0 and the maximum score is 31. At the time of RI ablation, our questionnaires was utilized, in a double-blinded fashion, to assess the hypothyroidism status of the patients. The same observer, blinded to the patient's clinical state, administered the questionnaires at all time. Both the observer and the patients were blinded to the treatment group being assigned Appendix 1 contains an English translation of the questionnaire.

4. Assessment of ablation success

In all patients, serum TSH, fT4, T3, Tg, and Tg Abs levels were periodically measured. After 12-18 months, ablation outcomes were assessed in each group by follow-up WBS, serum Tg measurement after TSH stimulation, and neck ultrasonography (US). To image thyroid remnants, a tracer dose of 150 MBq RI was administered to all patients. Neck US was performed by a radiologist specializing in head-and-neck evaluation using a Philips-ATL

HDI 5000 instrument equipped with a 12 MHz linear transducer.

5. Statistical anlaysis.

All data were expressed as means ± standard deviations (SDs), proportions, or absolute numbers. The Mann-Whitney U test and Kruskal-Wallis assessment were used to analyze between-group differences, and the Wilcoxon rank sum test was used for paired analysis within a group. The t-test was employed to explore the significance of differences between unpaired data. The $\chi 2$ test was used to compare between-group clinical and pathological features. A p value <0.05 was considered significant. SPSS for Windows version 12.0 (SPSS Inc., Chicago, IL) was used for all analyses.

III. RESULTS

1. Patient characteristics

Between February 2006 and March 2007, 291 patients were randomized, after total thyroidectomy, to conventional 4-week withdrawal of T4 (Group I, n=89), 2-week withdrawal of T3 (Group II, n=133), and rhTSH injection (Group III, n=69). The three groups did not differ in clinical characteristics or TNM classifications. Urinary iodine concentration before RI ablation was not significantly different between groups. <Table1>.

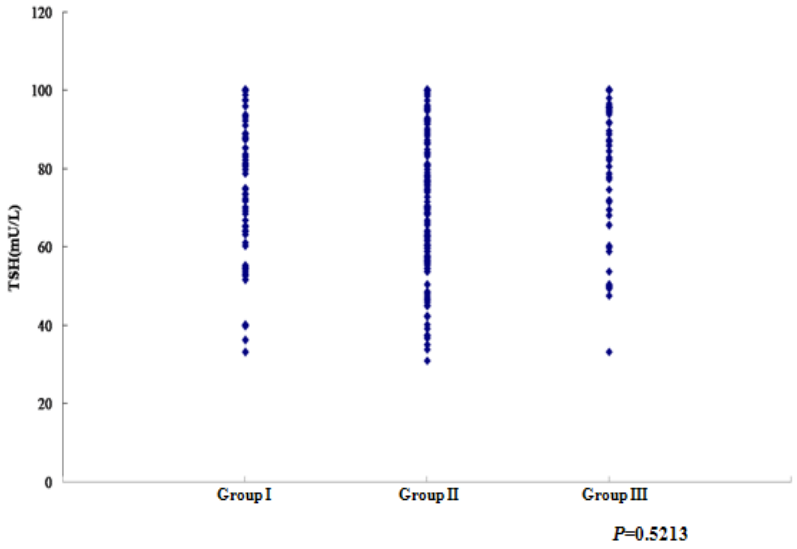
Table 1. Epidemiological and clinical characteristics of study patients.

	Group I	Group II	Group III	p-value
Age (years)				
	50.1±6.8	49.0±10.2	46.7±9.8	0.2151
Gender (female/male)				
	83/6	118/15	64/5	0.1583
Body mass index (kg/m^2)				
	23.4±4.68	21.9±5.63	22.8±5.41	0.2572
Papillary/follicular carcinoma				
	88/1	131/2	68/1	0.8551
TNM staging				
T1	48 (53.9%)	61 (45.9%)	28 (40.6%)	
T2	2 (2.2%)	12 (9.0.0%)	1 (1.4%)	
T3	39 (43.9%)	60 (45.1%)	40 (58.0%)	0.7541
N0	51 (57.3%)	78 (58.6%)	45 (65.2%)	
N1a	38 (42.7%)	55 (41.4%)	24 (34.8%)	0.1425
Urinary iodine concentration(ug/dL, 24hrs)				
	12.3±8.3	17.6±12.5	13.8±6.1	0.5214

2. Stimulated serum TSH and RI uptake

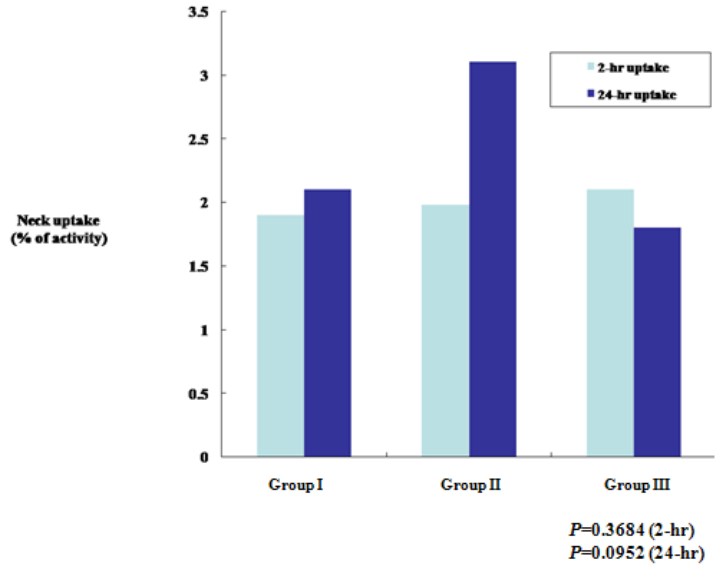
As shown in Fig. 1, serum TSH was elevated in Group I (mean, 81.2±19.0 mU/L; range, 33.1~100.0 mU/L), Group II (mean, 73.6±19.4 mU/L; range, 30.1~100.0), and Group III (mean, 86.6±17.6 mU/L; range 33.1~100.0 mU/L), without significant between-group differences (p=0.5213). <Fig.1>

Fig. 1. Stimulated serum TSH levels in the three Groups after preparation.



The basal 2-hour and 24-hour thyroid bed uptakes (% values) after administration of tracer RI were 1.9±1.1% (range, 0.2~10.7%) and 2.2±1.4% (range ,0.1~9.8%) in Group I; 2.0±1.9% (range, 0.2~10.7%), and 3.1±2.5% (range, 0.2~19.5%) in Group II; and 2.1±3.0% (range, 0.1~10.1%) and 1.8±1.6% (range, 0.1~13.4%) in Group III. Thyroid bed RI uptake after 2 hours showed no statistically significant between-group difference. Thyroid RI uptake after 24 hours tended to be lower in Group III than in Groups I or II, although the differences were not statistically significant (p=0.3684 vs. 0.0952, respectively). <Fig.2>

Fig. 2. Two-hour and 24-hour thyroid bed uptakes in each Groups.

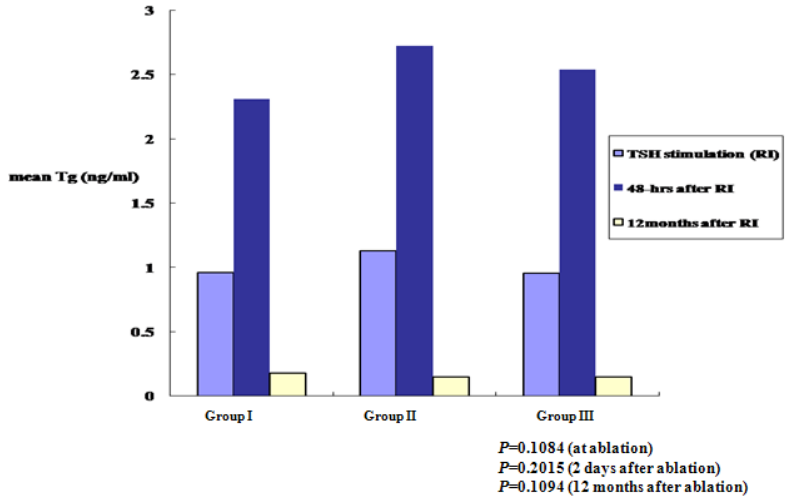


3. Serum Tg response to TSH stimulation

At the time of RI ablation, mean serum TSH was comparable in the three groups. Serum Tg level was 0.95±1.16 ng/mL (range, 0.1~4.7 ng/mL) in Group I, 1.12±1.22 ng/mL (range, 0.1~5.1 ng/mL) in Group II, and 0.95±1.63 ng/mL (range, 0.1~9.0 ng/mL) in Group III, with no significant between-group differences (p=0.1084). Three days after RI ablation, serum Tg was 2.30±2.46 ng/mL (range, 0.2~13.3 ng/mL) in Group I, 2.72±2.45 ng/mL (range, 0.1~10.4 ng/mL) in Group II, and 2.53±2.92 ng/mL (range, 0.1~11.1 ng/mL) in Group III, again with no statistically significant between-group differences (p=0.2015). After 12-18 months of follow-up,

mean serum Tg levels after TSH stimulation were 0.18±0.14 ng/mL (range, 0.1~2.9 ng/mL) in Group I, 0.14±0.19 ng/mL (range, 0.1~3.2 ng/mL) in Group II, and 0.14±0.05 ng/mL (range, 0.1~0.2 ng/mL) in Group III, once again with no significant differences between groups (p=0.1094). <Fig. 3>

Fig. 3. Serum Tg levels in the three Groups at ablation, 2 days after ablation, and 12 months after ablation.



4. Ablation outcomes (correlation between neck RI scans, stimulated Tg levels, and neck US data)

To assess the effectiveness of each preparation method, each patient underwent a WBS using a tracer RI dose, and neck US, 12-18 months after ablation. Stimulated Tg measurement after 4-week LT4 withdrawal was scheduled for each patient. The successful ablation rates are shown in Table

2. When correlating ablation outcomes with patient preparation methods before RI ablation, we found that rhTSH injection offered an ablation success rate equivalent to that achieved by thyroid hormone withdrawal.

Table 2. Ablation success rate 12 months after RI treatment.

	Group I	Group II	Group III	*p*-value
No visle uptake or uptake<0.1% with US- negative	84/89 (94.4%)	125/133 (94.0%)	63/69 (91.3%)	
Serum Tg ≤1.0ng/mL	81/89 (91.0%)	122/133 (91.7%)	64/69 (92.7%)	
Total ablation success rate (%)	91.0%	91.7%	91.3%	0.2061

5. Quality- of- life

Table 3 compares scores reflecting physical signs, social activities, mood changes, and use of medical resources, between the three groups. There was a highly significant difference in QoL status between the thyroid hormone withdrawal groups (Groups I and II) and the rhTSH injection group (Group III). However, there was no difference in QoL during preparation for RI between patients in Groups I and II.

Table 3. Comparison of QoL scores between Groups.

	Group I	Group II	Group III	*p*-value
Symptoms and signs(0-4)				
	2.9±0.7	3.0±0.7	0.7±0.4	<0.001
Duration of symptoms (0-3)				
	1.8±1.2	1.9±1.0	0.2±0.1	<0.001
Daily life (0-3)				
	1.3 ±0.7	1.1±1.0	0.1±0.0	0.002
Social life (0-3)				
	2.1±1.1	2.0±0.9	0.1±0.0	<0.001
Mood change and cognitive dysfunction (0-9)				
	3.5±1.9	3.7±1.7	1.8±0.9	0.004
Genital symptoms (0-3)				
	1.8±1.0	1.5±1.1	0.8±0.3	0.015
Medical resource utilization (0-6)				
	1.5±0.4	1.9±0.8	0.7±0.5	0.453
Total (0-31)				
	15.1±3.1	15.8±4.1	4.2±1.9	<0.001

IV. DISCUSSION

DTC is on the increase worldwide, although the figures may reflect enhanced detection of small incidentalomas rather than an actual increase in DTC levels [16,17]. Although proper management of small-sized DTC remains controversial, there is general agreement that total thyroidectomy and/or thyroid remnant ablation using RI are required. The optimal RI dose necessary for successful ablation in patients with low-risk DTC remains contentious. Some authors have employed dosimetric and kinetic methodology to define effective ablative doses, but most centers prefer to administer standard doses, varying with institutional preferences [10,18,19]. Generally, the larger the dose the better the remnant ablation. However, higher activity of radioiodine was associated with more nausea and taste disturbances, and a longer stay in a radioprotected isolation unit. Some studies have shown that a standard dose of 30 mCi may be effective in low-risk DTC patients [20,21]. The present work showed that a RI dose of 30 mCi ablated most, if not all, thyroid remnants, in patients prepared either by thyroid hormone withdrawal or rhTSH injection.

Remnant thyroid follicles can trap iodine and synthesize Tg, offering assistance in postoperative management of DTC. RI trapping and retention allows ablation of remnant thyroid tissue, and affords improved scan sensitivity for residual tissue detection postoperatively. RI ablation is

performed after thyroid hormone withdrawal, which increases endogenous TSH release to enhance, in turn, RI uptake by remnant tissue. Furthermore, serum Tg measurement after TSH stimulation is useful both to estimate ablation success and to detect recurrent disease [11,22]. Hormone withdrawal for TSH stimulation is associated with negative physiological impacts on QoL [1,23]. The use of rhTSH is a promising alternative for RI ablation preparation in DTC patients. However, the efficacy of rhTSH when low-dose (30 mCi) RI treatment is planned is still controversial.

Indisputable advantages of rhTSH use in patient preparation for thyroid remnant ablation after total thyroidectomy are the improved QoL and the need for less whole body irradiation [3,4,6-9]. Previous reports on rhTSH use to these ends found that the procedure was efficacious in most patients given high doses (over 100 mCi) of RI [2,4,7-9]. However, few reports have addressed rhTSH use in patients receiving low-dose (30 mCi) RI. One pilot study suggested that rhTSH use was less effective than LT4 withdrawal when the RI dose was 30 mCi [6]. However, several other reports have shown that rhTSH patient preparation in low-dose RI patients compared favorably with preparation using thyroid hormone withdrawal [11-13]. Our results suggest that rhTSH use is at least as effective as thyroid hormone withdrawal in preparation of low-risk patients for 30 mCi RI treatment. Considering about interference of iodine during ablation, this study was designed that the short interuppion of LT4 and 2 weeks iodine restriction diet could decrease the

size of iodine pool and that stimulation of rhTSH in this condition allows a rate of ablation that is at least the same as in the hypothyroid state. To avoid, at least partially, iodine interference coming from T4 metabolism, we choosed the modified rhTSH injection protocol with a short staoppage of LT4 from the day before rhTSH until iodine administration [11]. In fact, urinary iodine excretion could measure stable iodine intake before RI treatment. Our study also shows that median urinary iodine levels were below the conventional 20 g/dL threshold in all study patients and showed no significant between-group differences.

RI uptake (24-hour values) tended to be lower (1.8±1.6%) after rhTSH preparation than in the LT4 withdrawal Group (2.2±1.4%) or the LT3 withdrawal Group (3.1±2.5%), although the differences were not statistically significant. If RI treatment is not delayed, we suggest that RI uptake is comparable in patients prepared either by rhTSH administration or LT4/T3 withdrawal. The 12-month follow-up scans assessing ablation were performed after LT4 withdrawal, based on previous evidence that postablation RI scan and follow-up neck US data were not significantly different between the three groups. In the absence of circulating anti-TgAbs, TSH-stimulated serum Tg level is certainly the most sensitive marker of residual thyroid tissue, indicating incomplete ablation [24,25]. Consequently, we considered that TSH-stimulated serum Tg levels of less than 1 ng/mL at 12 months postoperatively indicated successful ablation. By this measure,

the successful ablation rates did not differ significantly between the three groups (p=0.2061). Indeed, serum Tg measurement under TSH stimulation combined with neck US examination has been reported by several research groups to be the best indicator of complete remission in follow-up after initial treatment [24,25].

The biokinetics of thyroid remnant RI ablation are both important and controversial [23,26,27]. When rhTSH is used to prepare patients for RI treatment, biokinetics are complex and depend on the amount of RI taken up and stored in thyroid cells. A detailed theoretical and methodological study is beyond the scope of this paper. However, additional studies on the kinetics and dosimetry of RI treatment are required to understand both RI uptake and clearance. An unresolved issue in the present work is whether patient preparation using rhTSH impacts on long-term outcomes, compared with thyroid hormone withdrawal. This question can be answered only by patient follow-up in future years.

Recently, the well-being of DTC patients has assumed greater importance, and several studies have reported impaired QoL associated with RI [1-3,6,23]. It is important to reduce both the duration and extent of hypothyroidism caused by LT4 withdrawal. The use of rhTSH has greatly assisted in avoiding hypothyroidism. Another alternative, used empirically, is substitution of LT4 withdrawal by temporary cessation of LT3 therapy. LT3 has a shorter half-life than LT4 and may be withdrawn for a shorter period

of time. Even though LT3 withdrawal should reduce hypothyroidism duration, this has never been clearly established. Few reports have addressed the topic. Leboeuf (2007) first explored QoL after LT3 withdrawal, compared with conventional LT4 withdrawal [28], and found (perhaps unexpectedly) that patients receiving additional LT3 after LT4 withdrawal showed a rate of hypothyroidism similar to that of patients in whom LT4 was withdrawn [28]. The cited authors sought to explain the data by claiming that thyroid hormone levels in the brain are controlled mainly by local transformation of T4 to T3, with little contribution from exogenous T3 [29]. Another explanation was that thyroid hormone receptors were not evenly distributed across all areas of the central nervous system, causing thyroid hormone effects to be variable in different brain regions [30]. This might explain why we found no differences in hypothyroidism status between Group I and II. As expected, the symptoms and signs of hypothyroidism, and subjective QoL perceptions, were significantly better in rhTSH patients than in the thyroid hormone withdrawal groups. However, we also found that LT3 substitution after LT4 withdrawal in DTC patients did not prevent development of profound hypothyroidism, as measured by a modified Korean QoL questionnaire.

V. CONCLUSION

rhTSH safely and effectively stimulated RI uptake by thyroid remnants in low-risk DTC patients, and was associated with clear clinical benefits in a substantial proportion of patients.

In patients with low-risk DTC, the use of rhTSH prior to post-surgical thyroid remnant ablation with 30 mCi RI appears to represent the best treatment option. LT3 substitution after LT4 withdrawal did not prevent development of profound hypothyroidism

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Appendix 1. Modified Pilot Questions for Determining Effects of Hypothyroidism (English version)

1) Hypothyroidism symptoms and signs

: Which types of symptoms disturbed you during the preparation period (Choose all that apply)?

Fatigue ( ):0.5

Weight gain ( ): 0.5

Edema of extremities ( ):0.5

Facial edema ( ):0.5

Insomnia ( ):0.5

Dry skin ( ):0.5

Bowel habit change ( ):0.5

Cold intolerance ( ):0.5

Total ( ) (0 – 4)

2) Duration of symptoms

: For how long did you experience symptoms?

Never (0)

Less than 1 week (1)

1-2 weeks (2)

More than 2 weeks (3)

Total ( ) (0 – 3)

3) Daily life

: During the preparation for RI treatment, were there any restrictions on your daily life, or were you unable to perform your daily activities as usual?

Never (0)

At intervals (1)

Sometimes (2)

Always (3)

Total ( ) (0 – 3)

4) Social life

: During the preparation for 131RI treatment, did you have any problems in your social life or at work?

Never (0)

At intervals (1)

Sometimes (2)

Always (3)

Total ( ) (0 – 3)

5) Mood changes & cognitive dysfunction

: During the preparation for 131RI treatment, have you experienced any of the following feelings?

5-1) Depression

(Gloomy attitude, pessimism about the future, feeling of sadness, tendency to weep, low morale misery, discouragement, hopelessness, emptiness, unhappiness, distress, pessimism)

Never (0)

At intervals (1)

Sometimes (2)

Always (3)

5-2) Anxiety

(Subjective tension and irritability, loss of concentration, worrying about minor matters, apprehension, fears expressed without questioning, feelings of panic, feeling jumpy)

Never (0)

At intervals (1)

Sometimes (2)

Always (3)

5-3) Retardation

(slowness of thought or speech, impaired concentration, decreased motor activity)

Never (0)

At intervals (1)

Sometimes (2)

Always (3)

Total ( ) (0 – 9)

6) Genital symptoms

(loss of libido, impaired sexual performance, menstrual disturbances)

Not at all (0)

One or two times (1)

Less than one week (2)

More than one week (3)

Total ( ) (0 – 3)

7) Medical resource utilization

7-1): During the preparation for 131RI treatment, did you consult your physician about related

symptoms?

Not at all (0)

One time (1)

More than two times (2)

7-2): During the preparation for 131RI treatment, were you treated in a hospital for relief of your symptoms?

Not at all (0)

One time (1)

More than two times (2)

7-3): During the preparation for 131RI treatment, did you take additional medications?

No (0)

Yes (1)

7-4): Did you have to be accompanied to the hospital?

Not necessary (0)

Necessary (1)

Total ( ) (0 –6)

< ABSTRACT(IN KOREAN)>

분화 갑상선암 환자에서 수술후 방사성 요오드 치료의 전처치 방법에 대한 비교: 기존의 갑상선 호르몬(LT4/T3) 중단요법 및 재조합 인간 갑상선 자극호르몬(rhTSH)주사법의 효과 및 삶의 질에 미치는 영향에 대한 비교

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이잔디

배경: 분화 갑상선암 환자에서 수술후 저용량(30mCi) 방사성 요오드 치료를 사용하는 경우 전처치방법에서 재조합 인간 갑상선 갑상선 자극호르몬(rhTSH) 사용시의 효과에 대한 연구는 많지 않다. 본 연구의 목적은 국내에서 널리 사용되는 저용량 방사성 요오드 치료시 전처치 방법으로 rhTSH 가 기존의 갑상선 호르몬 억제요법(LT4/T3 withdrawal)과 동일한 효과를 보이는 지 또한 삶의 질에 미치는 영향에 대해 비교하고자 하였다.

방법: 2006년 2월부터 2007년 3월까지 본원에서 분화 갑상선암 진단하에 갑상선 전절제술 및 중앙 구획 림프절 청소술후 저용량 방사성 요오드 치료 예정 환자 291예를 대상으로 무작위 전향적 연구를 시행하였다. 대상군을 방사성 요오드 치료의 전처치 방법에 따라 고식적인 LT4의 4주 중단법(group I)(ㅜ=89), LT3로 전환후 2주 중단법(group II)(ㅜ=133), 및 rhTSH 주사법(group III)(n=69)의 세군으로 분류하였고, 각각 전처치 방법의 효과를 비교 하였다. 도한, 방사성 요오드 치료직전 환자의 감정상태 및

삶의 질 정도를 평가 하였다.

결과: 세군 환자 모두 조직병리 검사 결과상 TNM 병기의 차이는 없었다. 전처치후 TSH의 상승은 세군 모두 양호한 결과(평균 82.24±18.21)를 보였으며, 세군간에 의미있는 차이는 없었다(p=0.5213). 방사성 요오드 치료후 12개월후 시행한 방사성 요오드 스캔, 경부 초음파 검사 및 TSH 자극후 thyroglobulin(Tg) 수치로 방사성 요오드 치료의 효과를 판단한 결과 세군간에 치료효과의 차이는 없었다(p=0.2061) . 삶의 질은 group III가 group I 및 group II에 비해 훨씬 양호한 결과를 보였으나(p<0.0001), group I과 group II는 의미있는 차이를 보이지 않았다.

결론: 본연구에서는 분화 갑상선암 환자에서 저용량 방사성 요오드 치료(30mCI)의 전처치방법중 rhTSH 주입법이 기존의 갑상선호르몬(LT4/LT3) 중단법과 동일한 유용성을 보인다는 것이 증명되었다. 그러나, rhTSH 주사법이 기존의 갑상선 호르몬 중단법에 비해 삶의 질 향상에 양호한 결과를 보이는 반면, LT3를 이용하여 갑상선 호르몬 중단기간을 줄이는 방법은 삶의 질에 영향을 미치지 못하였다.

핵심되는 말 : 재조합 인간 갑상선 자극호르몬, 저용량 방사성 요오드 치료, 삶의 질, LT3