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CLINICAL NUTRITION RESEARCH

The Impact of Low Adherence to the Low-iodine Diet on the Efficacy of the Radioactive Iodine Ablation Therapy

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To improve the efficacy of radioactive iodine (RAI) therapy for differentiated thyroid cancer patients, a low-iodine diet (LID) prior to the therapy is recommended. In iodine-rich areas such as Korea, however, a strict LID is very difficult to maintain. We experienced the cases of three patients showing low adherence to the LID before initial RAI therapy, and analyzed the main food source supplying iodine during the LID, and examined the influence of the poorly maintained LID on the efficacy of RAI therapy. The dietary intake during the LID periods were assessed using three-day dietary records and remnant thyroid activity after the second RAI administration was also evaluated. All patients' mean daily iodine intake during two-week LID periods exceeded the 100 μg guideline set by the Korean Thyroid Association (median 110.9 μg, ranges 100.4-117.0 μg). Although the typical food sources of iodine intake are seaweeds in Korea, salted vegetables were the main contributor to the patients' iodine intake during the LID periods. Remnant thyroid activity was shown on a follow-up scan in all of 3 patients suggesting low efficacy of RAI therapy. In summary, the patients with low adherence to the LID guideline showed unsuccessful remnant ablation, and the main food source of iodine was salted vegetables. Further studies are necessary to examine the relationship between adherence of the LID and RAI efficacy according to dietary iodine intake levels, as well as food sources that cause low adherence to the LID. These data can then be used to develop more practical LID guidelines.

Key Words: Thyroid cancer, Iodine, Radioactive isotopes, Dietary management, Patient adherence

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Introduction

Thyroid cancer is the most common type of cancer in Korea [1], with differentiated thyroid cancer (DTC, includes papillary and follicular thyroid cancer) accounting for the vast majority of cases [2]. The standard treatment for DTC is thyroidectomy followed by ^{131}I (radioactive iodine, RAI) therapy and thyroxine suppression to decrease serum thyroid stimulating hormone (TSH). RAI therapy eliminates microscopic residual tissues after thyroidectomy which decreases the likelihood of thyroid cancer recurrence [2,3].

Prior to RAI therapy, the patient is advised to maintain a low-iodine diet (LID) to facilitate ^{131}I uptake, maximizing the efficiency of RAI therapy [4,5]. Appropriate levels of dietary iodine intake or duration of the LID are not yet standardized over regions or countries. The American Thyroid Association recommends the LID with less than 50 μg/day of dietary iodine for 1-2 weeks prior to RAI therapy [2], but the Korean Thyroid Association recommends a low-iodine diet with less than 100 μg/day and provide a dietary guideline for the LID where allowed or restricted food items are listed during the LID [6].

In iodine-rich areas such as Korea, the recommended level of iodine intake during the LID is important to facilitate maintaining the LID, because a strict guideline may negatively impact the LID compliance [7]. A few studies were reported results of less strict diet [8,9] or short periods of the LID [10], however, the general consensus among clinical dietitians in Korea regarding appropriate degree or duration of the LID have not yet elucidated. According to Moon et al. [11], clinical dietitians should develop a practical dietary strategy in order to improve and facilitate the LID compliance.

To improve the compliance of the LID, dietary iodine levels should be evaluated comprehensively. Most previous studies used urinary iodine measurements due to the lack of an iodine database and the difficulties in dietary survey. Urinary iodine excretion is a good measure for dietary iodine intake [12], but evaluating the dietary iodine intake using multiple days of dietary records would provide a more comprehensive measure of dietary iodine intake in order to develop a practical dietary strategy for the LID.

Therefore, this study aims to assess dietary iodine level using three-day of dietary records and to search food sources that cause low adherence to the LID. In addition, we attempted to evaluate the ablation rate of remnant thyroid by compliance of the LID.

Case

We experienced three patients showing the diet composing iodine levels over 100 μg/day despite their efforts for the LID before initial RAI therapy. The protocol of case report was approved by the institutional review board of College of Medicine at Seoul National University (H-1308-066-513), and all the patients provided their written informed consent to participate. The clinical characteristics of the patients are shown in Table 1. The patients had stage II or III papillary thyroid cancer, classified based on the cancer staging manual in the 7th edition of the American Joint Committee on Cancer (AJCC) [13].

All three patients were educated on the preparation and management of the LID prior to RAI therapy in a two-and-a-half-hour intensive education session. During the session, a clinical dietitian explained patients of the importance and methodology of maintaining the LID in a half-hour. Then the patients maintained the LID for two weeks prior to ^{131}I administration (1.1 GBq) and a Whole Body Scan (WBS), which was done three days after the ^{131}I administration. To elevate their TSH levels, recombinant human TSH (rhTSH; Thyrogen^{TM}, Genzyme, Cambridge, MA, USA) was injected two days times: at two and one day before ^{131}I administration.

Table 1. Clinical characteristics of the patients

	Patient 1	Patient 2	Patient 3
Sex	Female	Female	Female
Age, yr	53	48	59
BMI, kg/m^2	22.7	24.6	17.7
Histology	Papillary	Papillary	Papillary
Tumor size (H x W x D), cm	2.5 x 2.0 x 1.5 0.6 x 0.5 x 0.4	1.1 x 0.8 x 0.6	2.4 x 1.9 x 1.4 1.9 x 1.1 x 1.0 0.5 x 0.4 x 0.3 0.7 x 0.5 x 0.5
BRAF mutation	None	NA	None
Tumor multiplicity	+	-	+
Bilaterality	One lobe	One lobe	Both lobe
Extrathyroid extension	None	Gross	Microscopic
TNM	pT2N0M0	pT1bN1aM0	pT3N0M0
Stages*	Stage II	Stage III	Stage III

*Classified according to the American Joint Committee on Cancer (AJCC) cancer staging manual [13].
BRAF: gene for the B-type Raf kinase, TNM: Tumor size, lymph Node status, distant Metastasis.

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Dietary intakes for patients were assessed using three-day dietary records during usual diet period and the LID period respectively. Patients were taught how to record their diet and asked to record three-day dietary records at two weekdays and one weekend day.

Energy and nutrient intakes, except for iodine, were calculated using a Diet Evaluation System (DES) [14]. Iodine intake was estimated using the database recently established by Han et al. [15] and modified for this study. Blood test results were collected from electronic medical records.

The efficacy of RAI therapy was evaluated by successful thyroid ablation. Successful remnant ablation is defined as an absence of visible RAI uptake on a subsequent diagnostic RAI scan or an undetectable stimulated serum thyroglobulin (off-Tg) level [2].

Figure 1 presents the dietary iodine intake in both the usual diet and LID periods. Although the patients tried to maintain their LID according to the guideline of less than 100 µg/day their mean daily iodine intakes during two-week LID period were more than 100 µg. For Patient 1, the mean iodine intake level for usual diet and the LID were 317.2 and 117.0 µg/day respectively. Patient 2's levels were 125.2 and 110.9 µg/day and Patient 3's levels were 217.7 and 100.4 µg/day.

We also performed urinary iodine measurements. The values in all three patients were reduced after a two-week LID period, but the iodine/creatinine ratio in spot urine exceeded 66.2 µg/g (iodide/creatinine), that was the cutoff value for a poorly maintained LID set by Kim et al. [16].

Table 2 presents the adherence of the LID guideline by each food item. All three patients followed five items out of nine food items in the LID guidelines that were using refined salts instead of sea salts and avoiding seaweeds, egg yolk, processed food, and consumed adequate amount of meat and its product, which was less than 120 g/day. Patient 1 and Patient 3 also followed three more items that were avoiding fish, milk and dairy products consumption, soybean pastes and soy sauce made with sea salts. Patient 2, however, did not follow three items and consumed fish, milk and dairy products, condiments including sea salts. The food item in the guideline that all three patients did not follow was avoiding salted vegetables, mainly kimchi during the LID. Patient 2 showed the lowest adherence to the LID and the mean iodine intake level during the LID periods was not much different from Patient 2's usual intake level.

Table 3 presents the clinical outcomes of thyroid remnant ablation therapy. Remnant ablation was unsuccessful in all three patients. Though serum off-Tg levels became undetectable (< 1.0 ng/mL) for Patients 1 and 2, Patient 3's off-Tg level was 1.07 ng/mL and all three patients showed visible RAI uptake.

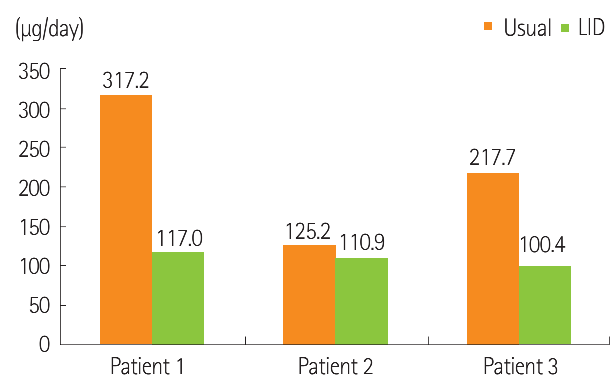

Figure 1. The iodine intake during usual and the low-iodine diet (LID) periods.

Table 2. Adherence to the low-iodine diet guidelines

Item	Patient 1	Patient 2	Patient 3
Avoiding salted vegetables (< 0.25 serving/day)	No	No	No
Eating adequate amounts of meat and its product (< 120 g/day)	Yes	Yes	Yes
Avoiding egg yolk (< 0.25 ea/day)	Yes	Yes	Yes
Avoiding fish (< 0.25 serving/day)	Yes	No	Yes
Avoiding seaweeds (< 1 g/day)	Yes	Yes	Yes
Avoiding milk and dairy products (< 0.25 serving/day)	Yes	No	Yes
Avoiding processed food products	Yes	Yes	Yes
Avoiding sea salts	Yes	Yes	Yes
Avoiding soybean pastes and soy sauce that is made by sea salts	Yes	No	Yes

Table 3. Clinical outcomes of thyroid ablation

	Patient 1	Patient 2	Patient 3
1st 1.1 GBq of RAI			
TSH, μIU/mL	50.0	50.0	281.5
Preablative off-Tg, ng/mL	1.23	1.80	3.73
Iodide/Creatinine ratio in spot urine, μg/gCr	85.5	177.8	117.9
2nd 1.1 GBq of RAI, 6 months after 1st RAI			
Off-Tg, ng/mL	< 0.1	< 0.1	1.07
Remnant thyroidal activity at Whole Body Scan	Positive	Positive	Positive
Completion of remnant thyroid ablation by 1st RAI	Fail	Fail	Fail

Off-Tg: stimulated TSH thyroglobulin, RAI: radioactive iodine, TSH: thyroid stimulating hormone.

Discussion

We evaluated dietary iodine during LID and successful ablation of the RAI therapy for three differentiated thyroid cancer patients. All three patients showed low adherence to the LID guideline, in particular for salted vegetable and exhibited remnant thyroid activity in the second post-RAI therapy scan.

Dietary assessment of iodine intake is challenging because the large day-to-day variation makes it difficult to quantify the "usual" iodine intake. However, the dietary iodine intakes are comparable with the previous findings where dietary iodine intake was reported 478 μg/day for Korean healthy adults using food frequency questionnaire [17] and 312 μg/day in men and 413 μg/day in women for Japanese using 7-day dietary records [18]. In besides, we measured urinary iodide excretion in both usual diet and the LID periods along with dietary iodine and both two values showed the same trend of being markedly reduced.

Although our patients were intensively educated on maintaining the LID, all of their dietary iodine intake levels exceeded the less than 100 μg guideline set by the KTA. Patient 2 did not follow the LID guidelines such as avoiding dairy, fish and kimchi. Patients 1 and 3 followed KTA guidelines except for the restriction on kimchi.

Maintaining the LID is challenging for Korean patients, whose regular diet consists of foods with very high iodine content, such as seaweeds, seafoods, soy sauce, soy bean pastes, and salted vegetables such as kimchi. According to Moon et al. [11], thyroid cancer patients had considerable knowledge of high iodine content foods but they had a difficulty to prepare low iodine dishes not using sea salts.

Though seaweed has the highest iodine content and is by far the biggest contributor to dietary iodine consumption, the patients' main source of iodine was kimchi during the LID period. Kimchi is a main side dish in our Korean diet and is usually made of large amounts of sea salts, garlic, red pepper, salted fish and other spices.

According to analytical values determined by the Korean Food and Drug Administration (KFDA), the iodine content per 100 g of radish kimchi, napa cabbage kimchi, and young radish kimchi are 198.4, 143.4, and 107.4 μg [19] respectively. Therefore, avoiding foods with a high sea salts content, such as kimchi, is very important for successful RAI therapy.

Although clinical dietitian put enough emphasis on avoiding sea salts or replacing sea salts with refined salts, it is very challenging for patients to distinguish the dishes made by refined salts from all dishes or to prepare their own dishes with refined salts in daily life. To increase the adherence of the LID, more practical dietary strategy for avoiding sea salts or for replacing sea salts in our Korean dishes should be considered.

In conclusion, low adherence to the LID guideline with more than 100 μg/d of dietary iodine intake level negatively influenced the efficacy of RAI therapy. Future studies are required to explore the influence of various dietary iodine intake levels on the efficacy of RAI therapy and to develop more practical guidelines to facilitate the LID maintenance.

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Conflict of Interest

We declare that we have no conflict of interest.

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