บทความวิจัย

Assessment of Urine Iodine Concentration after Low Iodine Diet in Differentiated Thyroid Cancer

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Abstract

Objective: Radioactive iodine (RAI) therapy in differentiated thyroid cancer need low iodine diet to increase the efficacy of I-131 ablation. The aim of this study was to evaluate the concentration of urine iodine in thyroid cancer patient prior to treat by radioiodine ablation in Siriraj Hospital.

Patients and Method: Seventy well-differentiated thyroid cancer patients with total thyroidectomy preparing for first ablation were enrolled. They were 54 (77%) females and 15 (23%) males age ranged between 18 to 79 years and the average was 45 years. All had I-131 uptake lower than 15% and serum thyroid stimulating hormone (TSH) concentrations above 30 mlU/L. All patients had undergone two week of LID before I-131 ablation. From each patient, morning spot urine specimens were obtained twice, before and two weeks after restriction LID. Analytical method is based on the Sandell-Kolthoff reaction. According to WHO criteria, UI concentrations < 50 µg/L were considered moderately iodine deficient, and the levels ≥50 µg/L but □100 µg/L correspond to mild iodine deficiency. These criteria are regarded as adequate LID preparation for I-131 ablation therapy. The cut off value of UI concentration, which indicates poor LID preparation, was ≥100 µg/L.

Results: After 2 weeks LID preparation, UI levels <50 µg/L were noted in 15 out of 70 patients (21.4%). The levels ≥50 µg/L but <100 µg/L was noted in 22 of 70 patients (31.4%). There were 33 patients (47.1%) inadequately prepared with UI levels over 100 µg/L after 2 weeks. The highest UI value in these patients was 601.12 µg/L. The median values of UI before and 2 weeks after LID were 133.54 µg/L and 99.99 µg/L. These values were not significantly different (p=0.09 by Wilcoxon signed-rank test).

Conclusion: Our results show that successful iodine depletion was accomplished only in 52.8% (37/70) of patients after 2 weeks LID. To obtain a higher LID success rates, a more strict LID program to all patients by specially trained personnel may be required to increase patient compliance with LID to achieve an adequate decreased of the body iodine pool before I-131 therapy.

Keywords: Well-differentiated thyroid cancer, Low iodine diet, Urine iodine concentration.

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Introduction

Thyroid cancer is one of the most common endocrine malignancies. Well-differentiated thyroid carcinomas, primarily papillary or follicular, accounts for over 90% of the malignant lesions [1]. The first treatment of choice is surgical excision follow by postoperative radioiodine treatment (RAIT) to destroy any remaining thyroid tissue in the thyroid bed area and any microscopic traces of thyroid cancer that remain in the body. For successive RAIT, appropriate radiation dose to the thyroid remnant or tumor must be delivered. In preparation for receiving RAIT, patients are usually asked to go on a low-iodine diet (LID) for a period of 1–2 weeks. Radioiodine are more binding to the cancer cells with a lower level of stable iodine in circulation and increasingly transfers to the thyroid gland via the sodium-iodine symporter [2]. The purpose of a low-iodine diet is to deplete the whole-body iodine pool to help increase the effectiveness of the RAIT from increases the binding ability of radioiodine to the cancer cell [3]. The ATA (American Thyroid Association) recommended a low iodine diet (<50 ug/d) starting 1–2 weeks prior to radioiodine administration [4]. To assess of iodine nutritional status, evaluation of body iodine pool by urine analysis is recommended before RAIT. The European Association of Nuclear Medicine (EANM) [5] remarked that a concentration of urine iodine higher than 150-200 µg/l is not suggested to treated by radioiodine. This indicates that the restriction of consuming food containing high levels of iodine is strongly recommended for thyroid cancer therapy.

Urinary iodine excretion reflects very recent iodine intake. Thereby the analysis of urinary iodine concentrations can be an alternative method to indicate nutritional status of iodine. It is a more popular method than other ways. In addition, urine is more easily collected than blood or serum. WHO (World Health Organization) recommends the median urinary iodine concentration of 100–199 µg//L as optimal iodine nutrition.

This study aims to measure and compare a concentration of urine iodine in thyroid cancer patients at Siriraj Hospital before and after the patients had limited themselves from consuming food containing high amounts of iodine.

Materials and Methods

Patients

Seventy patients with differentiated thyroid cancer (54 females and 16 males) were enrolled. Their mean age was 45±15 years (range 18-79 years). The TSH levels were greater than 30 mU/L in all patients. They were preparing for first ablation after thyroidectomy due to papillary and follicular thyroid cancer. Sixty-four patients (91%) had papillary and 6 patients (9%) had follicular cancer**.** Twenty-seven patients have median peak TSH of 80**.**3 mU/L and more than 100 mU/L in 43 patients**.** All patients had undergone two week of LID before RAIT

administration. The patient characteristics are summarized in Table 1. This study had been approved by the Institutional Review Board, Siriraj Hospital Medical School.

Table1. Patient characteristics

Patient characteristics	All (n=70)
Age (yr): Mean	45
Range	18-79
Sex: Female	54 (77%)
Male	16 (22%)
Histological type: Papillary	64 (91%)
Follicular	6 (9%)
TSH>30mU/L (n=27): Median	80.30
Range	30.52-99.11
TSH>100 mU/L (n=43)	
Administrated activity of I-131 (mCi)	30-150

Low iodine diet

Before receiving RAIT, patients are given instructions to deplete their body iodine stores by restriction of daily iodine intake through a low-iodine diet (LID). The usual time period is two weeks. Patients were also informed to strictly adhere to instructions, for their own benefits, to help increase the effectiveness of the RAIT.

Refer to World Health Organization (WHO) criteria for assessing iodine nutrition based on median urinary iodine concentration are : severe iodine deficiency (<20 μg/L); moderate iodine deficiency (20–49 μg/L); mild iodine deficiency (50–99 μg/L); optimal iodine nutrition (100–199 μg/L); more than adequate iodine intake (200–299 μg/L); and excessive iodine intake (>300μg/L)[6]. Median urinary iodine concentrations of >100 μg/L define a population that has no iodine deficiency. UI <50 μg/L were considered moderately iodine deficient, whereas levels ≥50 μg/L but <100 μg/L correspond to mild iodine deficiency. These two levels are regarded as optimum LID for RAIT. The cutoff value of UI indicating inadequate LID preparation was >100 μg/L.

Urine iodine measurement

The morning spot urine specimens were obtained twice from each patient because it is less subjective and also most convenient for the patient. The first urine specimen was collected a day before starting a low iodine diet and second sample after keeping low iodine diet for two weeks. The most common method recommended by WHO [6] was used. This method based on the spectrophotometric measurement of the Sandell–Kolthoff reaction [7] in which iodide catalyzes the reduction of ceric ammonium sulfate (yellow) to the colorless cerous form in the presence of arsenious acid. The ammonia persulfate was also used to dissolve organic substance that might influence the result [8]. It has an advantage of taking short analysis time. The sensitivity of the method is 8 μg/L.

Statistical Analysis

The data of median UI concentration before and after instruction were compared by Wilcoxon

Signed-Rank test. The statistical data was considered significant at $p< 0.05$.

Results

After 2 weeks of LID, UI concentration lower than 50 µg/L were noted in 15 out of 70 patients (21.4%). The levels 50–100 µg/L was noted in 22 out 70 patients (31.4%). There were 33 patients (47.1%) inadequately prepared themselves with UI levels over 100 µg/L after 2 weeks. The result is shown in Table 2.

Table 2. Patients in each level of UI concentration.

UI concentration (ug/L)	Patients (n=70)
<50	15 (21.4%)
50-100	22 (31.4%)
>100	33 (47.1%)

The median values of UI concentration before LID and 2 weeks after LID were 133.54 µg/L (range: 22.19 – 549.55) and 99.99 µg/L (range: 6.52 – 601.12). These values were not significantly different ($p=0.09$ by Wilcoxon Signed–Rank test). The highest UI concentration in the group of inadequately prepared was 601.12 µg/L.

Conclusion and discussion

According to the World Health Organization's (WHO) report, profile of UI in the morning urine specimens provides and adequate assessment of the recent dietary iodine intake [6]. UI concentrations $\leq$ 50 µg/L and 50–100 µg/L indicates a moderately and mild iodine deficient state respectively. These levels are regarded as adequate LID preparation for I-131 ablation therapy. The cut off value of UI, which indicated poor LID preparation, was > 100 µg/L.

The results showed that a successful iodine depletion was accomplished only in 52.8% (37/70) of patients, and 47.1% had the iodine sufficient status (>100) after LID for 2 weeks. Report from Tomoda, *et al* [8] demonstrated 70% of patients reduced their UI to < 100 µg/L after 2 weeks LID, and 35% patients had moderate iodine deficient. Margareta *et al* [9] reported 88% of patients were able to achieve iodine deficient status (82% to mild iodine deficient state, and 6% patients had gained moderate iodine status deficient state). The possible reason behind iodine reduction is that differences of iodine level in each country's food and it can be the eating habit of the patients themselves. Some of the patients have a very high iodine level and it is difficult to get back to normal level. To obtain a higher LID success rates, a more precise LID preparation program to all patients by specially trained personnel may be required to increase patient compliance with LID for achievement an adequate reduction of the body iodine pool before RAIT. Refer to Margareta *et al* [9], LID was explained to the patients and sent home with a list of dietary recommendations. Morsch *et al* [10] and Morris *et al* [11], participants received the instructions about the diet except for the duration, and they were also counseled on avoiding non-dietary iodine sources. These

results provide an essential data for future studies regarding preparation for radioiodine therapy.

In Thailand, ATA guidelines were adopted for management of thyroid cancer, which recommended a temporary LID prior to RAIT. The measurement of UI concentration is sufficiency and direct reflection of dietary iodine intake. However, this method is not widespread throughout Thailand. Therefore, this research aims to initiate an evaluation of UI concentration before RAIT in thyroid cancer patients following the ATA guidelines.

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