Analysis of Iodine Content in Salts and Korean Sauces for Low-Iodine Diet Education in Korean Patients with Thyroid Cancer Preparing for Radioiodine Therapy

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Abstract

Purpose A low-iodine diet is necessary in patients about to undergo radioiodine therapy for thyroid cancer to decrease the competitive absorption of ingested nonradioactive iodine. This study aimed to assess the iodine concentrations in salts and basic Korean sauces, and to provide fundamental data for guidelines on a low-iodine diet before radioiodine therapy.

Methods The iodine contents of refined salts, solar sea salts, fish sauces, and commonly used Korean sauces with added refined salt were determined by ICP-MS.

Results The iodine content of refined salts was found to be very low (0.033 ± 0.05 µg/100 g) compared with that of solar sea salts (434 ± 73.6 µg/100 g). The iodine contents of Korean soy sauce, Korean soybean paste, Gochujang seasoned with refined salt were also very low (0.010, 0.044, 0.002 µg/100 g, respectively). However, the mean iodine contents of the shrimp and fish Jeots analyzed in this study were found to be 41.3 ± 4.2 and 24.8 ± 4.5 µg/100 g, respectively.

Conclusion This study is the first to investigate the iodine contents of the salts and basic sauces used in Korea. The results show that refined salts and Korean traditional sauces seasoned with them can be safely used in low-iodine diets before radioiodine therapy.

Keywords Low-iodine diet · Thyroid cancer · Radioiodine therapy · Salts · Korean sauces

Introduction

Patients with thyroid cancer should keep to a low-iodine diet for 1 or 2 weeks before radioiodine therapy. The purpose of the low-iodine diet is to decrease ingestion of nonradioactive iodine that is absorbed in competition with radioiodine. The American Thyroid Association recommends dietary iodine restriction to as low as 50 µg/day, which is one third of the adult daily iodine intake recommended by WHO [1]. Japanese and Koreans have a high-iodine diet that includes various seaweeds. In Japan the individual daily iodine intake has been estimated at about 1,500 µg/day, whereas in the USA the individual daily iodine

intake is in the range 200–600 µg/day [2]. The Korean Thyroid Association (KTA) recommended in 2012 that low-iodine diets for radioiodine therapy should provide less than 100 µg/day, considering the iodine-rich dietary style as well as the poor compliance by Korean patients [3].

Previous studies have shown much higher levels of daily iodine intake in Korea compared with intake levels worldwide, even though the daily iodine intake levels in Korea reported by different organizations vary widely, as shown in Table 1 [4–9]. For example, Kang et al. estimated the mean daily iodine intake to be 1,083.9 µg/day using ICP-MS [7]. The Korea Food and Drug Administration have also presented data on infant formula obtained using the ion selective electrode (ISE) method [8]. The high daily iodine intake in Korea is also clearly shown by the high levels of iodine in urine. Lee et al. investigated the iodine status of Korean preschool children in terms of urinary iodine excretion using ICP-MS and found a median urinary iodine concentration of 438.8 µg/L, which can be considered excessive (>300 µg/L) [10]. Using the ISE method, the 24-h urinary iodine excretion in Korean adults after a 2-week stringent

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Table 1 Estimates of daily iodine intakes and evaluation of iodine content of Korean foods

Reference	Author/Organization	Food items					Mean adult iodine intake ($\mu\text{g}/\text{day}$)
		Number	Salts ($\mu\text{g}/100\text{ g}$)	Korean seasoning ($\mu\text{g}/100\text{ g}$)	Kimchi ($\mu\text{g}/100\text{ g}$)	Analysis method	
[4]	Moon et al.	64		ND		NAA	468.9 ± 481.9
[5]	KHIDI	107	ND	ND	ND	ISE	
[6]	KFDA	30				ICP-MS, IC	1,580.8
[7]	NIFDS	129	Solar sea salt 0.4–3.6	Soy sauce 1.4, 2.4 Gochujang 6.5–9.5 Soybean paste 1.1–37.5	96.4	ICP-MS, ISE, IC	$1,083.9 \pm 23.6$
[9]	RDA	438		Soy sauce 0.000 $\mu\text{g}/100\text{g}$		ICP-MS, ISE	

ND not detectable, NAA neutron activation analysis, ISE ion selective electrode, KHIDI Korea Health Industry Development Institute, KFDA Korea Food and Drug Administration, ICP-MS inductively coupled plasma mass spectrometry, IC ion chromatography, NIFDS National Institute of Food and Drug Safety, RDA Rural Development Administration

low-iodine diet was found to be $782 \pm 2,242\text{ }\mu\text{g}/\text{day}$ [11]. Thus, there is no argument that traditional Korean foods contain high levels of iodine, resulting in high daily iodine intake. Therefore, reducing iodine consumption from typical Korean foods is of paramount importance in patients preparing for radioiodine therapy, in order to achieve better therapeutic efficacy.

Generally, Korean meals are composed of steamed rice and various types of stew, which contain simmered animal bones, dried fish, and seaweed with various sauces such as soy sauce, red pepper paste sauce, and soybean paste. The primary reason for patients failing low-iodine diets could be the difficulty in repressing or abandoning the Korean dietary pattern. Some patients even experience hyponatremia as a result of extremely low food intake during the period of the low-iodine diet. Strict guidelines for the low-iodine diet often result in poor compliance [12, 13]. Most patients preparing for radioiodine therapy in Korea feel negative about low-iodine diet education and complain that keeping to the low-iodine diet is more difficult than the radioactive iodine therapy itself. They lose enjoyment in eating, and even experience depression during the period of the low-iodine diet.

In our hospital, we provide an education program to teach patients to make their own Kimchi based on the low-iodine diet guidelines which restrict the use of various Korean sauces. However, there have been no studies investigating the iodine contents of the various types of salts and fish sauces used in Kimchi. The patient educational guidelines of 2012, for example, recommend refined salt, flavored salt and iodine-free salt for patients with thyroid cancer undergoing radioactive iodine therapy [14]. Currently, no detailed analytical data are available concerning refined salt and its iodine content.

The purpose of this study was to provide basic and essential data on which to base our low-iodine diet education program. Specifically, the iodine contents of the various types of salts and fish sauces used in Kimchi were precisely determined. In addition, basic Korean sauces, including soy sauce, soybean paste and red pepper paste seasoned with refined salt, were analyzed to help patients with thyroid cancer easily understand the low-iodine diet guidelines. This is, to our knowledge, the first study investigating the iodine contents of the various types of salt and traditional Korean sauces for such a purpose.

Table 2 Iodine contents of the samples of various salts as measured by ICP-MS

Salt type	Sample				Overall mean ± SD
	A	B	C	D	
Refined salt					
Mean iodine content (µg/100 g)	0.005	0.011	0.008	0.110	0.033 ± 0.05
Relative standard deviation (%) ^a	15.6	9.6	15.9	12.6	
Solar sea salt					
Mean iodine content (µg/100 g)	402.7	476.0	510.6	346.7	434 ± 73.6
Relative standard deviation (%) ^a	3.2	3.5	4.2	9.5	

A iodine-free salt, B reworked salt (brand H), C reworked salt (flower salt, brand H), D processed salt (seasoning salt, brand D)

^a Standard deviation/mean $\times 100$

Table 3 Iodine contents of the samples of various traditional Korean sauces with added refined salt as measured by ICP-MS

	Soy sauce (<i>N</i> = 1)	Soybean paste (<i>N</i> = 1)	Gochujang (<i>N</i> = 1)
Mean iodine content (μg/100 g)	0.010	0.044	0.002
Relative standard deviation (%) ^a	12.9	10.9	6.9

^a Standard deviation/mean × 100

Materials and Methods

The materials were those that could be purchased easily in several commercial markets near our hospital. Thus, the iodine contents of the following 19 materials were analyzed in this study: four refined salts (one imported iodine-free salt, two reworked salts and one processed salt according to the food code of Korea), four solar sea salts, eight fish sauces (three shrimp Jeots and five fish Jeots), Korean soy sauce, soybean paste and Gochujang seasoned with the refined salts as shown in the ingredients list.

The iodine contents of these materials were analyzed using inductively coupled plasma mass spectrometry (ICP-MS) in the Yonsei Center Research Facilities at Yonsei University. Before measurement of their iodine concentrations, those materials comprising mixtures of solids (soybean paste, Gochujang, fish sauce) were prepared by acid digestion. Teflon containers were used in all the preparation steps. A PerkinElmer Nexion 300 ICP-MS instrument was used to measure the iodine concentrations of triplicate samples held in Teflon or white gold tubes. Measurements were made at the interface with the following parameter settings: 1,050 W RF power, 1 mL/min sample uptake rate, and 15 L/min plasma gas flow, 0.93 L/min nebulized gas flow and 1.2 L/min auxiliary gas flow, 3,124 ms for replicates, 127 *m/z* mass-to-charge ratio detected, and 50 ms sample dwell time.

Iodide standards for developing a standard concentration graph were prepared from a 1,000 mg/L solution containing 0.10 g of KI of purity 99.9995% diluted with 0.5% tetramethylammonium hydroxide (TMAH) to give standard solutions of concentrations 1, 5, 10, 20 and 100 mg/L [9]. Each sample of 0.1–0.5 g was weighed into a Teflon tube

and mixed with 5 mL distilled water to obtain a homogeneous suspension. After the addition of 1 mL 0.5% TMAH to the sample, 5 mL nitric acid and 1 mL peroxide were added. Each sample tube was placed on a hot plate set at 120 °C for 24 h. The sample tubes were placed in an oven at a temperature of 120 °C after rapid cooling for 20 min. Each sample was transferred to a 50-mL Teflon flask and diluted with distilled water to measure its iodine concentration.

Results

On ICP-the mean iodine contents of the four refined salts and the four solar sea salts were found to be 0.033 ± 0.05 μg/100 g and 434 ± 73.6 μg/100 g, respectively (Table 2). The iodine contents of the sauces seasoned with the refined salts were also very low: 0.010 μg/100 g for Korean soy sauce, 0.044 μg/100 g for Korean soybean paste, and 0.002 μg/100 g for Gochujang, respectively (Table 3). The mean iodine contents of the shrimp and fish Jeots were, in contrast, 41.3 ± 4.2 and 24.8 ± 4.5 μg/100 g, respectively (Table 4).

Discussion

Iodine is an essential micronutrient which is obtained from food. It is an essential component of thyroid hormones in humans. However, iodine is absorbed in competition with radioiodine in patients with thyroid cancer receiving radioiodine therapy. Based on this rationale, a low-iodine diet has been recommended for successful ablation of thyroid remnant as well as for better therapeutic efficacy of radioiodine

Table 4 Iodine contents of samples of various fish sauces as measured by ICP-MS

Sauce	Sample					Overall mean ± SD
	A	B	C	D	E	
Shrimp Jeot						
Mean iodine content (µg/100 g)	37.4	40.8	45.8	—	—	41.3 ± 4.2
Relative standard deviation (%) ^a	13.1	10.4	10.0			
Fish Jeot						
Mean iodine content (µg/100 g)	23.3	24.3	26.7	30.9	18.7	24.8 ± 4.5
Relative standard deviation (%) ^a	18.7	14.2	11.4	7.8	13.7	

^a Standard deviation/mean × 100

therapy in treating distant metastases. It has been reported that higher urinary iodine excretion is significantly associated with ablation failure [15, 16]. In contrast, in a study comparing the success of radioactive iodine ablation therapy between patients receiving a very strict low-iodine diet and patients receiving a less strict low-iodine diet, there was no difference in the success rates between the two groups [17]. These inconsistent results may be because of the retrospective study designs and differences in urinary iodine excretion status. So future large prospective studies are needed to evaluate the impact of low-iodine diets on not only ablation efficacy but also disease-free survival in patients with differentiated thyroid cancer.

Korea has a relatively high-iodine dietary pattern. In a study of the iodine contents of common Korean foods, evaluating data obtained by interview, high iodine intake levels were found in patients with thyroid disease ($n = 184$; up to $673.8 \pm 794.9 \mu\text{g/day}$) [16] and in patients with thyroid cancer ($1,460.6 \pm 1,044.8 \mu\text{g/day}$), compared with $468.9 \pm 481.9 \mu\text{g/day}$ in normal subjects ($n = 207$) [4]. However, we found a wide range of measured iodine levels among the relevant organizations. This observation can be ascribed to limitations in food research including differences in sample selection and preparation methods to treat the samples, low reproducibility, and poor reliability of data acquired by recall from individuals (Table 1). The resulting uncertainty makes it difficult for physicians and dietitians to provide low-iodine dietary education to patients in Korea. Thus it is necessary to develop recommendations based on more detailed information for important minerals in food such as iodine obtained using standardized analysis and sample preparation methods for specific foods.

There are three types of iodine molecule that exist in a state of equilibrium: iodine (I_2), iodide (I^-) and triiodide (I_3^-). Since ISE is very simple, yielding fast results, and is relatively inexpensive in use, it has been widely used for the analysis of iodide in liquid, environmental, and biological samples. However, ISE has some disadvantages. It can detect only iodide. The minimum measurable concentration can differ depending on the type and structure of the ion electrode, leading to potential errors at low concentrations. ICP-MS is a cost-effective method that provides better limits of detection and a greater linear range. Earlier studies before 2006 were

performed using the ISE method to evaluate iodine levels in food [6, 8]. ICP-MS is currently the best method for the analysis of the iodine content of sodium-containing foods such as Kimchi and sea weed, providing better sensitivity than ISE [7]. We carefully chose the external Yonsei Center Research Facilities for the ICP-MS measurement of the iodine content of the samples.

It should be noted that the aim of this study was not to provide accurate iodine contents of all processed food materials on the market. We attempted only to find the type of salt that should be used to restrict the amount of iodine in Kimchi recipes to improve our confidence in the patient education program. We measured the iodine concentrations in the basic sauces before cooking rather than in the final food products because the cooking method and the ingredients added in food processing could have affected the analytical results.

Kimchi is one of the favorite foods in Korea. It is made with nappa cabbage which is pretreated with sea salt for several hours and rinsed with water, after which salt, red pepper powder and various types of fish sauce are added. We calculated the iodine content of the iodine-restricted Kimchi which we suggested for the patient education program in our hospital, and compared it with that of Kimchi prepared with the generally used recipe, as summarized in Table 5. The daily Kimchi intake level found by the 2012 Korea National Health and Nutrition Examination Survey (KHANES) was a mean of 112.2 g/day, and by the 2008–2010 KHANES was 120–150 g/day [18]. Kang et al. found that the iodine level of Kimchi is $96.4 \mu\text{g}/100 \text{ g}$ by direct measurement [7]. In contrast, the iodine content of the iodine-restricted Kimchi was as low as 14–23 μg per 70-g serving, demonstrating that this recipe could be used safely during the low-iodine diet period.

The low-iodine diet guidelines of the KTA are commonly used in hospitals. Our study provides substantial experimental data covering the basic Korean sauces that also support the KTA low-iodine guidelines. Such low-iodine diet guidelines are very important for patients, since they may allow the patient to comply with the iodine-restricted diet more easily when preparing for radioiodine therapy while avoiding unacceptably low calorie intake and an unbalanced diet.

Table 5 Iodine contents of various types of Kimchi

Kimchi type	Basis of analysis of iodine content	Iodine content
Iodine-restricted Kimchi	Based on 3–5 g refined salt per 70-g serving	0.01 $\mu\text{g}/70 \text{ g}$
General recipe	Calculated from the recipe: sea salt 3–5 g + shrimp Jeot 1.5 g + fish Jeot 1.5 g per 70-g serving	14–23 $\mu\text{g}/70 \text{ g}$
Kimchi samples	Direct measurement of two samples	65.5 $\mu\text{g}/100 \text{ g}$, 149.9 $\mu\text{g}/100 \text{ g}$
General recipe Kimchi	Based on daily Kimchi intake level [18]	30–69 $\mu\text{g}/150\text{--}210 \text{ g}$

According to Kang et al. [7]

Conclusion

This study is the first to investigate the iodine contents of various salt types and basic Korean sauces based on accurate analysis using ICP-MS. Our results demonstrated low iodine contents of refined salts and of traditional sauces including Gochujang, soy sauce, and soybean paste seasoned with refined salts, suggesting that the low-iodine diet guidelines of the KTA can be used for patient education.

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Compliance with Ethical Standards

Conflicts of Interest Soo Young Kim, Jung Mi Park, and Jae Pil Hwang declare that there is no conflict of interest.

Ethical Approval This article does not describe any studies with human participants performed by any of the authors.

Informed Consent This article does not describe any studies with human participants performed by any of the authors.

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