PREVALENCE OF NONTOXIC NODULAR GOITER AFTER A NEARLY TWO-DECADE UNIVERSAL SALT IODIZATION IN A LITTORAL REGION OF SHANDONG PROVINCE, CHINA

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Abstract

Introduction. With the introduction of iodized salt, more and more people are exposed to iodine sufficiency in some regions. The purpose of this study was to investigate the prevalence of nontoxic nodular goiter (NTNG) in the littoral region with high iodine supply after a nearly two-decade universal salt iodization.

Subjects and Methods. Eight hundred and thirty-five participants (from 25~65 years; males 421 and females 414) were invited for the study from Huan-cui District of Weihai City, Shandong Province from January 2013 to September 2014. All participants were inspected and diagnosed by endocrinologists according to the thyroid function tests and the thyroid gland imaging. After the normal diet of three days, the urine samples of the participants were collected between 8:00AM and 9:00AM and the urinary iodine (UI) concentrations were analyzed using Urinary Iodide Test Kit.

Results. The overall prevalence of NTNG in the region was 40.1%, and different prevalence occurred in the different age ranges ($p < 0.01$). The prevalence of NTNG was 32.51%, 37.44%, 49.70%, 58.57 and 74.77% in the age group of ≤ 30 , 31-40, 41-50, 51-60 and > 60 years, respectively. Meanwhile, the prevalence of NTNG in women (42.08%) was higher than that in men (34.29%, $p < 0.05$). The median of UI concentrations were 139.4 $\mu\text{g/L}$ and 101.5 $\mu\text{g/L}$ for the group with NTNG and without NTNG, respectively ($p < 0.01$). However, there was no significant difference in UI concentrations among the groups with different age ranges ($p > 0.05$), and statistical difference was not observed for UI concentrations between women and men ($p > 0.05$). Intriguingly, higher UI concentrations were found in the group with larger thyroid size ($p < 0.01$).

Conclusion. The iodine excess can lead to the high occurrence of nodular goiter in the littoral region, and individual UI concentration detection is recommended for the iodine nutritional status analysis among normal people when Universal Salt Iodization (USI) continues to be implemented in the region.

Key words: heart rate variability, metabolically healthy obesity, metabolically unhealthy obesity.

INTRODUCTION

Iodine is an essential micronutrient for normal human growth and development. Iodine deficiency can cause not only endemic goiter and cretinism, but also a wide spectrum of disabilities (1). In 1999, WHO estimated that 130 of its 191 Member States had a significant iodine deficiency disorders (IDD) problem, and there remain challenges for the future although the last decade has seen the greatest progress in the fight to conquer IDD (2). IDD was common in China so a universal salt iodization (USI) program has been implemented by the Chinese government since 1995 (3).

Nontoxic nodular goiter (NTNG) is one of the most prevalent thyroid disorders worldwide and sometimes impairs health and well-being. NTNG is characterized by a nodular increase of the thyroid resulting from multifocal monoclonal or polyclonal proliferation of thyrocytes to produce groups of new follicles (4). The prevalence of thyroid nodules depends to a great extent on the method used for detection. Approximately 2~6% of people are found to have nodules by neck palpation, 19~35% with ultrasound, and 8~65% in autopsy data (5, 6). Several factors, e.g., iodine intake, the age and sex of the subjects, may explain the variability of thyroid nodules prevalence (7).

Iodine excess is currently more frequent than iodine deficiency due to the extensive environmental iodine exposure such as USI in some regions and poor monitoring. Iodine excess is an important environmental factor in the development of thyroid goiter (8, 9). The mechanisms by which iodine induces this disease are still unclear, but it has been proposed that excess iodine induces the production of cytokines and chemokines, which recruit immunocompetent cells to the thyroid. Meanwhile, the excess iodine in thyroid epithelial cells may result in elevated levels of oxidative stress, leading to harmful lipid oxidation and thyroid tissue injuries (10).

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The purpose of the study was to determine the overall NTNG prevalence in a littoral region with high iodine-containing diet after a nearly two-decade USI. Additionally, we also determined the relationship between the iodine intake and the prevalence of NTNG.

PATIENTS AND METHODS

Study population

This study was conducted in compliance with the institutional ethical board of Weihai Municipal Hospital affiliated to Dalian Medical University, which situates in the littoral region (Huan-cui District) of Weihai City, Shandong Province, China. This region is located in the eastern tip of Shandong Peninsula, across the sea from Korea and Japan, with a population of 2.816 million people.

In the study, 20 blocks on the city maps were randomly selected and the addresses of all homes in each block were obtained from the government of Huan-cui District. A total 1500 addresses from the list supplied by government were randomly selected for this survey.

A total of 835 participants (from 25~65 years, mean age 45.7 ± 13.5 years; males 421 and females 414) were included in the study from January 2013 to September 2014. All subjects had lived in the area for over 20 years. All participants were not exposed to drugs (including any kinds of iodinated drugs), thyroid surgery or radiation. NTNG was diagnosed by endocrinologists according to the thyroid function tests, imaging of the thyroid gland and even the result of fine needle aspiration biopsy.

Research methods

The thyroids of all participants were examined by ultrasonography. For the assessment of reproducibility, intra-observer variation of the thyroid measurement was assessed by use of images from 10 normal people. Using the same ultrasound unit, thyroid value was determined again 3 weeks after the primary analysis.

UI concentrations were measured by Urinary

Iodide Test Kit (Beijing Zhongsheng Jinyu Diagnostic Technology Co., Ltd.) according to manufacturer's protocol. Urine samples were collected from all participants between 8:00Am and 9:00AM after having the normal diet in three days. After sample collection, UI was measured in two hours.

Basic information, including age and gender, had previously been collected for all participants. According to the results of the ultrasonic detection, participants were divided into: group A with NTNG and group B without NTNG.

Random salt samples were tested from the retail stores and the homes of the participants. A total of 200 salt samples were tested by the National standard method of titration (11).

Statistical analyses

The statistical calculations were performed using SPSS version 13.0 (SPSS, Chicago, IL, USA). The prevalence of NTNG between sex-groups was compared using McNemar's test. The difference of NTNG among different age range was compared using Cochran-Armitage test for trend. UI concentrations were expressed as medians (25th~75th percentiles) and difference in UI concentration between groups A and B were evaluated by Mann-Whitney's U-test. The differences in UI concentrations among different ages were evaluated by Kruskal-Wallis. All P values corresponded to two-sided tests and values less than 0.05 were considered significant.

RESULTS

The overall prevalence of NTNG was 40.1% in this region. The prevalence of NTNG was 32.51%, 37.44%, 49.70%, 58.57 and 74.77% in the age group of ≤ 30 , 31-40, 41-50, 51-60 and > 60 years, respectively (Table 1). Statistical analysis showed that the prevalence of NTNG increased significantly with the increase of the age ($p < 0.01$). Meanwhile, the prevalence of NTNG in women (42.08%) was significantly higher than that in men (34.29%, $p < 0.05$). Intra-observer variability of the thyroid measurements in the study was 4.0 to 7.2%.

Table 1. Prevalence of thyroid nodule and UI concentration in the different age ranges

Age	Group A		Group B	
	Prevalence of NTNG	UI concentration ($\mu\text{g/L}$)	Prevalence of NTNG	UI concentration ($\mu\text{g/L}$)
≤ 30	32.51% (119/366)	143.2	67.49% (247/366)	101.2
31~40	37.44% (82/219)	139.5	62.56% (137/219)	99.5
41~50	49.70% (82/165)	135.8	50.30% (83/165)	108.0
51~60	58.57% (41/70)	140.1	4.43% (29/70)	97.9
> 60	73.33% (11/15)	138.8	26.67% (4/15)	99.6

A total of 835 urine samples were collected to detect UI concentration in the study. The overall median level of UI concentration was 120.0 μ g/L. Based on the results of ultrasonography, 835 participants were divided into two groups: group A consisting of participants with NTNG (335/835) and group B consisting of participants without NTNG (500/835). The median level of UI concentration in NTNG group was 139.4 μ g/L, which was significantly higher than that in the non-NTNG group (101.5 μ g/L) ($p<0.01$). There was no significant difference in UI concentration among groups with different age ranges ($p>0.05$) (Table 1). UI concentration was not significantly different between women and men ($p>0.05$). The concentration levels of TT3, TT4 and TSH were similar between NTNG and non-NTNG group ($p>0.05$) (Table 2). UI concentration in the group with large thyroid size was significantly higher than that in the group with small thyroid size ($p<0.01$) (Table 3).

Of 200 salt samples tested, 98.5% of the samples had an iodine level of >20 ppm with a median level of 24.5ppm. The samples of salt sold at retail stores in the region were all well-packed, branded, powdered, and iodized as per the manufacturers' status.

DISCUSSION

Weihai is located at the eastern tip of Shandong peninsula (China), which has three country-level cities of Rong-cheng, Wen-deng, Ru-shan and one district of Huan-cui. Iodine deficiency also occurred in the regions of Weihai far from the oceans, and then USI program was implemented in the entire Weihai region since 1995.

Huan-cui district is a typical littoral city with high iodine-containing diet, and Seafood is a normal part of the diet in this region. Unfortunately, no study on the prevalence of NTNG and UI concentration has been conducted over the region (Huan-cui District) before the introduction of the USI program. However, one study reported that UI concentration was within the normal range from two villages of another region (Rong-cheng) similar to Huan-cui district before the

USI program (12). That study implied that iodine deficiency did not exist in Huan-cui District prior to salt iodination. Thyroid diseases can develop through a habitual intake of large amounts of iodine (13-15). Huan-cui District is not an iodine deficiency region, and there is no consensus on USI necessary for the residents in the region. In the present study, the participants living in this region were selected to evaluate the prevalence of NTNG in this district after a nearly two-decade of USI implementation.

The major finding of this study was that NTNG with the normal thyroid function was very common in the region. The prevalence of thyroid nodule examined by ultrasonography in this region (40.12%) is consistent with previous reports on the prevalence of thyroid nodule (50%) (5, 16). In contrast, the prevalence is higher than that in South Korea (13.8%) (17). While the prevalence of thyroid nodule in this study is higher than in the similar regions, the reason could be due to the fact that the different methods were used for detection (12). Consistent with previous reports (18, 19), we also showed that NTNG was more common as age increases, and it occurred more frequently in women.

Either high or low iodine intake can lead to thyroid disease. UI concentration is a sensitive indicator of recent iodine intake (2). Therefore, we measured UI concentration to evaluate the iodine intake in the study. Our results showed that the median levels of UI concentration were similar among different ages and no difference was found in the UI concentration between women and men. We infer that different prevalence of NTNG in different ages and gender is not due to different iodine intakes in this region. In contrast, it could be due to the fact that slightly enlarged, diffused glands in younger age are often not detectable. The female predominance in autoimmune thyroid diseases may explain the higher prevalence of NTNG in women than that in men. However, the exact mechanism for the differences remains to be clarified.

One of the other main aims in our surveys was to investigate the relationship between iodine intake and prevalence of NTNG. We showed that the median level of UI concentration is higher in the group with

Table 2. The concentration levels of TT3, TT4, TSH and UI concentration between group A and group B

	Group A	Group B
TT3(nmol/L)	1.86 $\pm$ 0.48	1.79 $\pm$ 0.55
TT4 (nmol/L)	89.6 $\pm$ 15.21	95.6 $\pm$ 12.08
TSH (uIU/mL)	3.24 $\pm$ 0.95	3.08 $\pm$ 0.88
UI concentration (μ g/L)	139.4	101.5*

* $p<0.01$

Table 3. The relationship between UI concentration and thyroid size

Thyroid size	<1cm	1~2cm	2~3cm	>3cm
Number of samples (335)	105	102	75	53
UI concentration (μ g/L)	116.2	129.1	138.6	145.6*

* $p<0.01$

NTNG than that without NTNG. Intriguingly, larger thyroid size groups tend to have higher UI concentration in the survey. These results are consistent with previous finding on the relationship between different iodine intakes and the prevalence of thyroid goiter and other thyroid diseases (20-22). We believe that excessive iodine intakes led to the high occurrence of NTNG in the region after a nearly two-decade USI.

In conclusion, NTNG in the littoral region of Shandong province (China) is more common than other regions. Excessive iodine intakes could affect the prevalence of NTNG in the region, and different prevalence of NTNG in age ranges and gender are not due to different iodine intakes.

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Conflict of interest

The authors declare that they have no conflicts of interest concerning this article.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of study formal consent is not required.

Informed consent

Informed consent was obtained from all individual participants included in the study. Additional informed consent was obtained from all individual participants for whom identifying information is included in this article.

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