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NOTE

Urinary Iodine Levels and Thyroid Diseases in Children; Comparison between Nagasaki and Chernobyl

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Abstract. We evaluated the incidence of childhood thyroid diseases and urinary iodine levels in Nagasaki, Japan and in Gomel, Belarus, which was greatly radio-contaminated by the Chernobyl accident, in order to obtain the comparative data of thyroid diseases between iodine-rich (Japan) and -deficient (Belarus) areas. In Nagasaki, the median level of urinary iodine, measured by ammonium persulfate digestion in microplate method, was 362.9 μg/L. In order to evaluate the geographical differences in Japan, other samples were collected in Hamamatsu and in South Kayabe, Hokkaido, where the median levels were 208.4 μg/L and 1015.5 μg/L, respectively. Furthermore, thyroid screening by ultrasound (US) in Nagasaki revealed only four cases that showed goiter (1.6%) and two cases (0.8%) that had cystic degeneration and single thyroid cyst. There was no evidence of thyroid nodule detected by US examination. In contrast, the median of urinary iodine level was 41.3 μg/L in Gomel. The incidences of goiter (13.6%) and echogenic abnormality (1.74%) in Gomel were much higher than in Nagasaki, suggesting the critical involvement of iodine deficiency in increased childhood thyroid abnormality around Chernobyl. Radioactive iodine released just after the Chernobyl accident may have influenced predominantly children residing in iodine-deficient areas. Our results suggest that management of thyroid screening for schoolchildren at ordinary times may be beneficial for monitoring the adverse effects of radioactive iodine from the standpoint of future prospective study.

Key words: Urinary iodine, Simple microplate method, Iodine prophylaxis, Chernobyl accident
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FOR fifteen years after the Chernobyl Accident, the worst nuclear plant accident in the world, efforts have been made to alleviate the medical consequences of this disaster. Medical examinations of about 210,000 children performed within the framework of the International Programme on the Health Effects of the Chernobyl Accident (IPEHCA) and Chernobyl Sasakawa Health and Medical Cooperative Project have shown a significant increase in the incidence of childhood thyroid diseases [1,2]. In particular, in the Gomel region of Belarus, incidence of thyroid cancer is 100 times higher than before the accident [2]. However, the influence of radiation and iodine deficiency in the development of thyroid cancer re-

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mains to be clarified. Shakhtarin *et al.* reported that ERR (excess relative risk) of thyroid cancer at the radiation dose of 1 Gy in population residing under the conditions of severe iodine deficiency is almost twice as high as those living without iodine deficiency around Chernobyl [3]. Our previous report has also supported the synergistic effect of radiation exposure and iodine deficiency on increase of thyroid nodular change around Chernobyl because of the highest incidence of childhood thyroid nodule and iodine deficiency [4]. Furthermore, the increase of juvenile hypothyroidism has been also reported around Chernobyl [5, 6].

In contrast, Japan is a so-called iodine-rich area, apparently due to the large amount of seafood containing iodine in the Japanese diet. However, changes in diet in the younger generation may influence the uptake of iodine to cause an increase in goiter and thyroid diseases. Therefore, it is important to clarify the current situation of iodine intake not only to understand their health conditions but also to make a preparatory plans in the event of a future unexpected nuclear accident.

In this communication, we screened the urinary iodine concentration in schoolchildren of Gomel and Nagasaki, using a recently developed simple microplate method [7], in combination with the ultrasound thyroid screening. Furthermore, we compared the urinary iodine (UI) data and incidence of the thyroid diseases between the two cities.

Materials and Methods

Subjects and Samples

The study was performed in the beginning of 2000. UI concentrations in morning spot urine were measured in 100 subjects (11–17 years old) in Gomel, Belarus and 250 subjects (7–14 years old) in Nagasaki (south Japan). In order to evaluate the geographical differences in Japan, samples were collected in Hamamatsu (middle Japan, 50 subjects, adults) and South Kayabe, Hokkaido (north Japan, 50 subjects, adults). All samples were kept at 4°C until assay. Before the collection of samples, informed consent was obtained from all subjects.

Measurement of urinary iodine

The UI concentration was measured by "simple microplate method", based on the Sandell-Kolthoff reaction [8], incorporating both the reaction and the digestion process in microplate format, the details of which are described elsewhere [7]. In brief, using a specially designed sealing cassette to prevent loss of vapor and cross-contamination among plates, ammonium persulfate digestion was performed in a 96-well microtiter plate (MicroWell; Nalge Nunc International) in an oven at 110°C for 60 min. After digestion, the mixture was transferred to a transparent microplate and the Sandell-Kolthoff reaction was performed at 25°C for 30 min. Finally, UI concentration in each well was measured by microplate reader at 405 nm. The sensitivity of this method was $>10\ \mu g/L$.

Thyroid ultrasound screening in schoolchildren in Nagasaki

To clarify the relationship between morphological changes of the thyroid and UI concentrations, ultrasound (US) screening of thyroid gland was performed in schoolchildren of Nagasaki. LOGIQ-α100 (GE Medical Systems, USA) was used for this screening. All US images were digitized and saved on MO discs for further evaluation. Thyroid gland volume was automatically calculated by LOGIQ-α100. Results were compared with data of Belarussian children, obtained from Chernobyl Sasakawa Health and Medical Cooperative Project [2]. The criterion for goiter in Gomel was a thyroid exceeding the volume calculated by the formula developed by us [9] and Parshin *et al.* [10], and the criterion for goiter in Nagasaki was a thyroid exceeding the volume calculated only by the formula developed by Parshin *et al.* [10]. Nodules more than 5 mm in diameter were considered to be "positive". Diagnosis of thyroid cancer in Gomel was initially inspected by fine needle aspiration biopsy (FNAB) and finally confirmed by histological examination after operation.

Results

Measurement of urinary iodine

UI concentrations of subjects in Gomel ranged from 13.1 to 210.8 μg/L. In contrast, UI concentrations in Nagasaki, Hamamatsu and South Kayabe widely ranged from 58.4 to 3225.9 μg/L, from 34.2 to 796.2 μg/L and from 121.5 to 7152.2 μg/L, respectively (Table 1). Furthermore, 90% subjects in Gomel showed low UI concentrations (<100 μg/L), whereas in three Japanese cities, only 3% subjects showed low UI concentrations (Fig. 1). The median of iodine concentrations in each city was 47.3 μg/L (Gomel), 362.9 μg/L (Nagasaki), 1015.5 μg/L (South Kayabe) and 208.4 μg/L (Hamamatsu).

Thyroid ultrasound screening in schoolchildren in Nagasaki and in Gomel

In Nagasaki, only four cases showed goiter (1.6%) and two cases (0.8%) had cystic degeneration and single thyroid cyst. There was no evidence of thyroid nodule detected by US examination. In contrast, the incidence of goiter and echogenic abnormality in Gomel was much higher than in Nagasaki (Table 2). Also, high prevalence of positive thyroid antibodies (anti-thyroglobulin antibody: 2.26% and anti-microsome antibody: 0.95%) and hypothyroidism (0.21%) had been observed in Gomel [2]. All cancer cases in Gomel were diagnosed as papillary carcinomas by FNAB and histological examination.

Table 1. Median levels of UI concentrations of each city and the number of cases (ratio) which manifested low levels (<100 μg/l).

	Median (μg/l)	<100 μg/l
Gomel, Belarus (schoolchildren)	47.3	90/100 (90%)
Nagasaki, Japan (schoolchildren)	362.9	9/250 (3.6%)
Sapporo, Japan (adults)	1015.5	0/80 (0%)
Hamamatsu, Japan (adults)	208.4	3/50 (6%)

Table 2. Comparison of thyroid abnormalities between Gomel, Belarus (n=19,660) and Nagasaki (n=250), detected by the ultrasound screening. Diagnosis of thyroid cancer in Gomel was finally confirmed by fine needle aspiration biopsy (FNAB). Data of Gomel was obtained from the results of "Chernobyl Sasakawa Health and Medical Cooperation Project"

	Number of abnormalities (%)		
	Goiter	Nodule	Cancer
Gomel, Belarus	2,669 (13.58)	342 (1.74)	39 (0.20)
Nagasaki, Japan	4 (1.6)	0 (0.0)	0 (0.0)

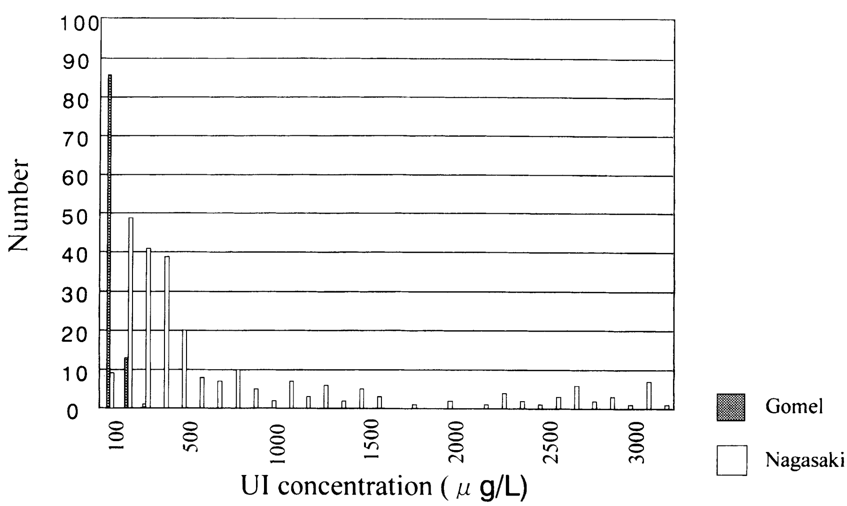

Fig. 1. Comparison of UI concentrations between Gomel, Belarus (n=100) and Nagasaki, Japan (n=250).

Discussion

We have done a comparative analysis of UI concentrations between Japan and Belarus. As expected, the amounts of iodine excretion in Japan (Nagasaki, Hamamatsu and South Kayabe) were larger than those in Belarus (Gomel).

In this study, a newly developed simple microplate method, based on the Sandell-Kolthoff reaction was applied. Since this original method is simple and sensitive, it has been extensively used. However, this method is time-consuming, and the amount of toxic waste generated is not negligible. To speed up the procedure and to minimize the amount of toxic waste, a simple microplate method has been developed [7]. In this method, the digestion system as well as the Sandell-Kolthoff reaction is completed in one microplate format. Furthermore, to prevent leakage of vapor and cross-contamination between the contents of the wells, a sealing cassette was designed.

It is well known that after the Chernobyl accident, a high incidence of childhood thyroid cancer was observed [12]. We showed that UI concentrations in Gomel schoolchildren were definitely lower than those of Japan. Furthermore, the incidence of thyroid morphological abnormalities in Gomel was much higher than in Nagasaki. These results strongly suggest the critical involvement of iodine deficiency in increased childhood thyroid abnormality around Chernobyl. In view of public health, iodine deficiency should be ameliorated for preventing endemic goiter around Chernobyl.

In 1999, an accident occurred at a uranium processing facility at the Tokaimura Nuclear Complex in Japan [13]. Since this accident, the effective prevention against nuclear accidents has been extensively discussed in Japan. For the basic discussion of this problem, it is important to screen the current thyroid function and the level of iodine sufficiency in Japanese, especially in schoolchildren, in order to evaluate the necessity of iodine replacement among population for the "unexpected" future nuclear accident.

Recently, changing dietary patterns among the Japanese younger generation has led to a decreased intake of seafood among them. In our study, the median iodine concentration in Nagasaki's schoolchildren (362.9 μg/L) was lower than that of South Kayabe's adults (1015.5 μg/L) but relatively higher than that of Hamamatsu's adults (208.4 μg/L). Dietary styles in these areas seem to be similar but details remains to be further clarified. This suggests that even in schoolchildren, iodine is still in sufficiently supply in Japan.

In this communication, we showed the different distribution of UI concentrations between Japan and Belarus, i.e. iodine-rich and -deficient areas. We here emphasize that standardized data collection and management of thyroid screening for schoolchildren at ordinary times are important to conduct for thyroid health and for determination how to monitor the adverse effects of radioactive iodine at the standpoint of future prospective study. Establishment of systematic screening, especially for schoolchildren, will be needed.

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