No Evidence of Radiation Risk for Thyroid Gland among Schoolchildren around Semipalatinsk Nuclear Testing Site

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Abstract. To assess thyroid status among the schoolchildren around Semipalatinsk Nuclear Testing Site (SNTS), Kazakhstan, and to evaluate the current status of iodine deficiency in this area, we performed medical screening of schoolchildren in two villages, Kaynar and Karaul villages, East Kazakhstan Region, Republic of Kazakhstan, located within 100 km of SNTS. A total of 196 schoolchildren were chosen at random. Control groups comprised 250 schoolchildren from Nagasaki, an iodine-rich area, and 100 schoolchildren from Gomel, an iodine-deficient area contaminated by the Chernobyl Nuclear Power Plant accident. Ultrasound screening of thyroid revealed three cases of benign thyroid disease (two cases of goiter and one single cyst), but no cases suspicious of malignancy. The urinary iodine (UI) concentrations of subjects in Kaynar and Karaul ranged from 21.8 to 735.8 μg/L, 4.3% of whom showed low UI concentrations (<50 μg/L), compared with 0% in the Nagasaki group and 52% in the Gomel group. The median UI concentration in Kaynar and Karaul was 153.2 μg/L, which was significantly lower than that in Nagasaki (366.3 μg/L, p<0.0001) but higher than that in Gomel (47.3 μg/L, p<0.0001). In conclusion, there was a low incidence of morphological abnormalities in the thyroid, and no evidence for severe iodine deficiency among the Kazakhstani children studied. These results suggest that there is no transgenerational risk for schoolchildren born from parents irradiated as a result of tests carried out in SNTS.

Key words: Semipalatinsk Nuclear Testing Site, Urinary iodine, Thyroid gland, Transgenerational risk

(Endocrine Journal 50: 85–89, 2003)

ON 29 August 1949, the first nuclear bomb test was conducted at the Semipalatinsk Nuclear Testing Site (SNTS), located in the northern part of the Republic of Kazakhstan. Over the subsequent 13 years a further 26 above-ground and 87 atmospheric nuclear tests were performed in the area [1]. Several hundreds of thousands of people are estimated to have been irradiated during this period. Unfortunately, there is little data on the health effects among the population around SNTS, partly because of difficulties in estimation of the radiation dose, but also be-
cause of the uncertainty of diagnostic reliability in this area. However, we know from studies of the radiation-exposed populations in Nagasaki and Hiroshima that it is important to evaluate the late effects of irradiation, i.e. the incidence of radiation induced malignancies such as leukemia, colon, breast, lung and thyroid cancers [2]. In addition, a dramatic increase in childhood thyroid cancer after the accident at the Chernobyl Nuclear Power Plant in 1986 showed the importance of medical screening for irradiated victims in the immediate area [3, 4].

In addition to late effects of exposure to radiation, one of the most serious problems among population in this area is the possibility of the transmission of increased risk of malignancies to second and third generations (transgenerational risk) as a result of exposure to radiation. Although there are several reports suggesting an increased incidence of genetic abnormalities (mental disturbance, neural tube defect, etc.) in this area, it is very difficult to determine a causal relationship between such abnormalities and the dose of irradiation to the first generation.

To further complicate the issue, the Republic of Kazakhstan, including Semipalatinsk region, is considered to be an area of “generally moderate iodine deficiency” (http://www.sph.emory.edu/PAMM/present/2-Gregory/sld013.htm). Iodine deficiency causes impairment of mental function, retardation of mental and physical development, and diminution of school performance, as well as goiter and hypothyroidism. Furthermore, it has been suggested by some studies carried out after the Chernobyl accident that iodine deficiency might contribute to the accumulation of $^{131}$I in the thyroid gland [5, 6]. Previously, we have reported a high frequency of thyroid autoantibodies among adult population [7] and the rearrangement of ret proto-oncogene in patients with thyroid cancer of this region [8]. However, there is no data on the systemic evaluation of thyroid abnormalities among schoolchildren of the SNTS region. In this study, we performed medical screening of schoolchildren in Kaynar and Karaul villages, located within 100 km of SNTS, and clarified the morphological status of the thyroid, to determine the transgenerational effect of parental exposure as a result of the nuclear tests. Furthermore, we measured the concentration of urinary iodine (UI) to evaluate the level of iodine deficiency of this area.

Methods

Subjects

Medical screening was performed on August 2001 in Kaynar and Karaul villages, East Kazakhstan Region, Republic of Kazakhstan with the permission of the local health departments of Semipalatinsk. A total of 196 children (101 boys and 95 girls: 5-15 years old) were chosen at random in both villages. All urine samples were kept at 4°C until assay. Before the collection of samples, informed consent was obtained from each subject via the Semipalatinsk City Health Bureau.

Thyroid ultrasound screening in schoolchildren

Ultrasound (US) screening of thyroid gland was performed by LOGIQ-x100 (GE Medical Systems, USA). All US images were digitized and saved in MO discs for further evaluation. The results were compared with data from children from Nagasaki (Japan), obtained from our previous study [9]. Thyroid volume was calculated from the following formula [10]; Height × Side length × Thickness × 0.7. The volume of each lobe (right and left) was calculated and then the two values were summed. The criterion for goiter is a thyroid volume exceeding the volume calculated by the following formula [11, 12]: LIMIT = $1.7 \times 10^6 \times 0.013 \times \text{age} + 0.025 \times \text{height} \times (\text{body weight}^{0.15}$, where age is the age in years at the time of examination, height is in centimeters, and body weight in kilograms. Finally, obtained data were compared with the results from 232 schoolchildren from Nagasaki, Japan; an “iodine rich area”, and analyzed by means of a distribution-free test (Wilcoxon) with a significance limit of p<0.05.

Measurement of urinary iodine

The UI concentration was measured by “simple microplate method”, based on the Sandell-Kolthoff reaction [13], incorporating both the reaction and the digestion process into a microplate format. Details of this method have been described elsewhere [13]. In brief, using a specially designed sealing cassette to prevent loss of vapor and cross-contamination among plates, ammonium persulphate digestion was performed in 96-well microtiter plate (MicroWell;
Nalgen 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, concentration of urinary iodine in each well was measured by a microplate reader at 405 nm. The sensitivity of this method was >10 μg/L. Since it is known that lower creatinine excretions frequently occur in areas of malnutrition, which are also the areas most likely to harbor iodine deficiency disorders (IDD), we expressed UI concentrations in μg/L, not relating it to creatinine [15].

We adopted epidemiological criteria for assessing severity of iodine deficiency proposed by World Health Organization, United Nations Children’s Fund and International Council for the Control of Iodine Deficiency Disorders [16], i.e. <20 μg/L of UI was defined as a “Severe IDD”, 20–49 was as a “Moderate IDD”, 50–99 as a “Mild IDD”, and ≥99 as a “No deficiency”.

Data obtained from this study was compared with the data from Nagasaki (Japan, iodine-rich area) and Gomel (Belarus, iodine-deficient area), the area exposed to the highest levels of radioactive contamination after the Chernobyl accident [9]. Finally, distribution of UI concentrations of three groups was analyzed statistically using a distribution-free test (Wilcoxon) with a significance limit of p<0.05.

Results

Thyroid ultrasound screening in schoolchildren

In Kaynar and Karaul, we detected only 2 cases with goiter (7-year-old boy and 10-year-old girl), and 1 child with a single cyst (5-year-old girl). The incidence of echogenic abnormality in Kaynar and Karaul was much lower than Gomel (Table 1). There was no case of suspected thyroid malignancy. Median thyroid volume for Kaynar and Karaul was determined for each sex and age group. In each group, it was smaller than that for the corresponding group from Nagasaki (p<0.0001, Table 2).

Measurement of urinary iodine

The UI concentrations of the subjects in Kaynar and Karaul ranged from 21.8 to 735.8 μg/L (Fig. 1).

Table 1. Comparison of thyroid abnormalities between Kaynar and Karaul (n = 196), Nagasaki (n = 230) and Gomel (n = 19,660). Data of Gomel were obtained from the results of Chernobyl Saksawa Health and Medical Cooperation project, and those of Nagasaki were from our previous study [9].

<table>
<thead>
<tr>
<th></th>
<th>Goiter (%)</th>
<th>Nodule</th>
<th>Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kaynar and Karaul</td>
<td>2 (1.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Nagasaki</td>
<td>4 (1.6)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Gomel</td>
<td>2,664 (13.6)</td>
<td>342 (1.74)</td>
<td>39 (0.20)</td>
</tr>
</tbody>
</table>

Table 2. Comparison of median thyroid volume for Kaynar and Karaul, and Nagasaki.

<table>
<thead>
<tr>
<th></th>
<th>Kaynar and Karaul</th>
<th>Nagasaki</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thyroid volumes (mm³)</td>
<td>boys</td>
<td>girls</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>2.52</td>
<td>2.53</td>
</tr>
<tr>
<td>8</td>
<td>3.15</td>
<td>2.57</td>
</tr>
<tr>
<td>9</td>
<td>3.41</td>
<td>3.24</td>
</tr>
<tr>
<td>10</td>
<td>3.67</td>
<td>2.08</td>
</tr>
<tr>
<td>11</td>
<td>3.73</td>
<td>5.45</td>
</tr>
<tr>
<td>12</td>
<td>3.98</td>
<td>4.28</td>
</tr>
</tbody>
</table>

There was no significant correlation between thyroid volumes and urinary iodine levels (data not shown). On the other hand, urinary iodine in Nagasaki showed a wide range from 78.8 to 4103.6 μg/L, compared with 8.8 to 210.8 μg/L in children from Gomel.

Interestingly, 4.3% subjects in Kaynar and Karaul showed low UI concentrations (<50 μg/L), and 52% showed low UI concentrations in Gomel, whereas no subject showed a low UI concentration in Nagasaki. The median UI concentration in Kaynar and Karaul was 153.2 μg/L; significantly lower than that in Nagasaki (366.9 μg/L, p<0.0001) but higher than that in Gomel (47.3 μg/L, p<0.0001).

Discussion

After the break-up of the former USSR and following termination of nuclear testing at SNTS, a limited amount of information about these tests has become available. Because of the scanty data and the difficulty of radiation dose reconstruction, it is very difficult to clarify the causal relationship be-
tween radiation exposure and its effect on health. It has been especially difficult to explore the possible effects transmitted to the second and third generations present in this area.

In this study, however, we could demonstrate a low incidence of thyroid morphological abnormality, and provide evidence for the lack of iodine deficiency among schoolchildren around SNTS. The smaller size of thyroid gland in schoolchildren around SNTS might be partly due to constitutional difference compared to that in Nagasaki. After the Chernobyl accident, a high incidence of childhood thyroid cancer was observed and so it was important to accurately evaluate thyroid status in the area close to SNTS. Recently, we showed that UI concentrations of schoolchildren in Gomel, the area most heavily contaminated by the Chernobyl accident, were definitely lower than those in Japan, suggesting the critical involvement of iodine deficiency in the increase in childhood thyroid abnormality around Chernobyl. In contrast, the low incidence of thyroid abnormality around SNTS may be a result of appropriate supplement with iodine during and after the time of nuclear testing. Alternatively, there may be no direct radiation effect on the thyroid gland of children currently residing around the SNTS area.

Recently, it was shown that the exposure to radioactive fallout might increase germline minisatellite
mutation rate among the population around SNTS [17]. However, nonreproducible results should be reevaluated through the introduction of the medical screening system for objective and accurate diagnosis into this area. Since May 2002, the medical screening using a mobile diagnostic bus donated by Japan International Cooperation Agency (JICA) has been started around SNTS, which will give more accurate population-based data on thyroid abnormalities because the bus contains ultrasound equipment and blood analyzing equipment for further analysis. So far there is no evidence of transgenerational markers on irradiation damage in human. We should carefully evaluate the cause-and-effect relationship of irradiation on thyroid gland among children around SNTS.

References