Sensitivity Analysis on the Effectiveness of Iodine Prophylaxis to Reduce Thyroid Gland Exposure in Nuclear Emergency

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1. INTRODUCTION

Stable iodine administration is one of the protective measure to reduce thyroid exposure dose in nuclear emergencies. In general, the thyroid dose due to inhalation of radioiodine for a person cared by a stable iodine is determined by 1) the inhaled amount of radioiodine, 2) the inhalation dose coefficient for the radioiodine, and 3) the fraction of dose averted owing to the stable iodine. In this report, we aimed to evaluate the thyroid dose in case of Japanese totally. Therefore, not only the effectiveness of the stable iodine prophylaxisis (the third factor) but also the first factor was considered. With a recognition that the first factor is related to the inhalation dose coefficient, this second one was included in the discussion though it was not wholly examined in this study. The main emphasis was put on the examination of the third one, the fraction of averted dose.

The effectiveness of the iodine prophylaxis and the resultant radiation dose to the thyroid gland are influenced by physiological conditions such as a) the deposition efficiency in the respiratory tract for inhaled radioiodine and b) the metabolic parameters for iodine. While its effectiveness has been studied by various researchers in volunteer experiments and using mathematical models, most studies involve Caucasian subjects and, thus, the findings for may not be applicable to races with different diets or with respiratory tracts of different sizes. For example, Japanese have a larger dietary iodine intake, in the form of sea weed, than do Americans and Europeans (Nagataki, 1993; Yokoyama, 1995). Since the metabolism of iodine depends on the dietary intake of iodine, the effectiveness of iodine prophylaxis for Japanese may differ from that for other groups (Yoshizawa & Kusama, 1976).

We performed a sensitivity analysis on the deposition efficiency in the respiratory tract for inhaled radioiodine and examined the metabolic parameters for stable and radioactive iodine to identify the critical parameters in evaluating iodine prophylaxis effectiveness and to determine the dose received by the thyroid in Japanese following radioiodine inhalation.

2. METHOD

2.1 Parameters involved in inhalation model

As described here, the amount of inhaled radioiodine denotes the amount of radioiodine transported to the body fluids from the respiratory tract or via the gastrointestinal (GI) tract after clearance from the respiratory system. Considering the relatively high retention of radioiodine in the respiratory tract and its complete absorption in the GI tract (ICRP, 1995), the amount of inhaled radioiodined is considered to be equal to the sum of the amount deposited in the respiratory tract regions, axcluding the extrathroractic region (ET1 and ET2). Accordingly, the sum of deposition efficiencies in each region (except in ET1 and ET2) was set to the objective variance in the sensitivity analysis. The sensitivity analysis on the parameters involved in an inhalation model of radioiodine followed the Human Respiratory Tract Model For Radiological Protection (ICRP, 1994). Concerning the deposition efficiency in the respiratory tract, the analysis was performed by using the LUDEP code (version 2) developed by National Radiological Protection Board (NRPB, United Kingdom; Jarvis et al., 1996).

The related parameters were estimated according to the method described in the ICRP publication no.66 using physical data on the reference Japanese. A regression analysis was used to elucidate the relationship between body height, or body weight, and various respiratory parameters used to define the deposition efficiency for Caucasian references in different age categories. Representative sizes and variances in height and weight of Japanese in different age categories derived by Tanaka and Kawamura (1996; Table 1) were used in this study. The relationship between body height (or weight) and the respiratory parameters was used with the Japanese reference to estimate the variances of the respiratory parameters in Japanese. A change in the deposition efficiency was examined when one parameter was moved to the maximum or the minimum value for Japanese (Table 2) while other parameters were set to be the values for Caucasians.

Table 1 Scattering of height and body weight of Japanese

Age/Sex	Height (cm)	Body weight (kg)
Adult/Male	164.2 - 175.6	55.0 - 73.7
Adult/Female	150.3 - 160.6	45.0 - 60.0
15 y/Boy	161.2 - 173.1	48.1 - 66.4
15 y /girl	151.6 - 161.7	44.5 - 58.7
10 y	131.5 - 145.0	26.3 - 39.0
5 y	105.0 - 115.1	16.1 - 21.8
1 y	75.2 - 84.6	9.1 - 12.4
3 month	57.2 - 63.6	5.2 - 7.2

(after Tanaka and Kawamura, 1996)

Table 2 Variation in the parameters of the inhalation model for Japanese

Parameter		Adult/Male	Adult/Female	15 y/Boy	15 y/Girl
FRC	cc	2587 - 3151	1994 - 2432	2449 - 3023	2047 - 2482
V_D(ET)	cc	41.4 - 49.7	32.1 - 38.5	39.4 - 47.8	32.9 - 39.2
V_D(BB)	cc	41.0 - 48.5	32.8 - 38.5	39.2 - 46.8	33.5 - 39.2
V_D(bb)	cc	39.2 - 45.8	33.5 - 39.5	37.6 - 44.3	34.2 - 40.1
H	cm	164.2-175.6	150.3-160.6	161.2-173.1	151.6-161.7
d_0	cm	1.55 - 1.65	1.42 - 1.51	1.52 - 1.62	1.43 - 1.52
d_9	cm	0.158-0.165	0.151-0.156	0.156-0.163	0.151-0.157
VR	m^3/hr	1.40 - 1.49	1.22 - 1.28	1.31 - 1.48	1.22 - 1.28
FR	/min	24 - 20	27 - 21	26 - 21	27 - 22
VT	cc	942 - 1283	747 - 1014	817 - 1150	738 - 991
VFR	cc/sec	777 - 827	680 - 710	729 - 821	677 - 712
Parameter		**10 y**	**5 y**	**1 y**	**3 month**
FRC	cc	1285 - 1761	610 - 827	265 - 327	249 - 268
V_D(ET)	cc	21.9 - 29.0	11.3 - 14.8	4.8 - 6.3	3.7 - 3.9
V_D(BB)	cc	23.4 - 29.9	13.5 - 16.8	7.0 - 8.5	5.5 - 5.8
V_D(bb)	cc	24.2 - 30.2	15.0 - 18.1	8.7 - 10.2	6.9 - 7.4
H	cm	131.5-145.0	105.0-115.1	75.2 - 84.6	57.2 - 63.6
d_0	cm	1.25 - 1.37	1.02 - 1.11	0.75 - 0.83	0.59 - 0.65
d_9	cm	0.140-0.147	0.124-0.130	0.107-0.112	0.097-0.100
VR	m^3/hr	0.82 - 1.11	0.54 - 0.70	0.30 - 0.42	0.17 - 0.24
FR	/min	35 - 29	41 - 38	46 - 44	49 - 48
VT	cc	422 - 652	234 - 339	105 - 166	32 - 69

VFR	cc/sec	458 - 614	297 - 391	170 - 232	92 - 132

2.2 Parameters involved in the metabolic model of iodine

Concerning the averted fraction of radiation dose to the thyroid gland caused by administration of stable iodine, we performed a sensitivity analysis on the metabolic parameters of iodine according to the metabolic model used by Ramsden et al. (1967) and Wootton et al. (1978; Fig.1). The basic concept of the model is based on the so-called three-compartment model of Riggs (1952), which has been adopted in the ICRP Publication no.56. The following equation expresses the kinetics of the “blocking”of iodine transport from body fluids to the thyroid gland.

$$k_t = f\,(1-Q_t/Q_s) \quad (1)$$

where,

k_t : rate constant of transport from a pool of inorganic iodine in body fluid to the thyroid gland (h^{-1})

f : rate constant coefficient (h^{-1})

Q_t : amount of stable iodine in the thyroid gland (mg-I)

Q_s : constant , corresponding to “saturated” amount of stable iodine (mg-I)

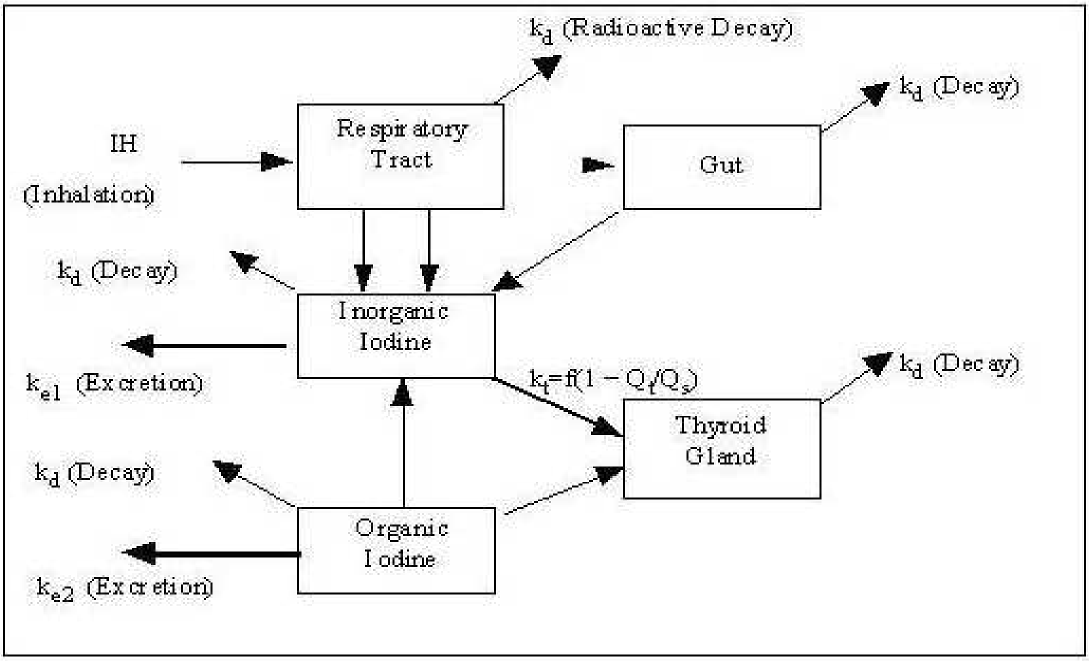

Fig.1 Compartment model for metabolism of radio/stable iodine (Ramsden et al. 1967; Wooton et al., 1978)

The appropriateness of this expression was proved by Ramsden et al. (1967) in an experimental study of elimination of injected radioiodine in the thyroid gland of volunteers with and without the use of stable iodine. A computer program was developed in this study to simulate the behavior of radio/stable iodine in the body according to their metabolic model; the present sensitivity analysis was performed using this program.

While Wootton et al. (1978) presented metabolic model parameters for an English group, those for Japanese were not determined. For the present study, we reviewed the literature thoroughly since 1930s to identify proper metabolic parameters of iodine for Japanese adults. Table 3 presents our findings.

The fraction of the averted dose, AVT, defined as follows, was set to be an objective variant in the sensitivity analysis.

$$AVT = (A - B)\,/\,A \quad (2)$$

where,

A : radiation exposure dose to the thyroid gland without administration of stable iodine

B : radiation exposure dose to the thyroid gland with administration of stable iodine

Table 3 Range of variation in the paramerters of the metabolic model in the sensitivuty analysis (see Figure 1 for definition of parameters)

	For Japanese			For Caucasian
Parameter	Upper limit	Central	Lower limit	Ramsden (1967)
Dietary intake DI [μ g/day]	3000	1000	100	240
Transfer rate k_a [/hr]	2.3	0.4	0.2	3.0
Transfer rate k_o [/day]	0.05	0.03	0.01	0.0096
Transfer rate k_i [/day]	0.11	0.06	0.01	0.048
Rate of excretion k_{e1} [/day]	2.40	1.92	1.44	1.92
Rate of excretion k_{e2} [/day]	0.013	0.007	0.001	0.0048
"saturated thyroidal iodine" Q_s [mg]	40.0	25.0	10.0	8.35
Coefficient of incorporation rate f [/hr]	0.14	0.08	0.02	0.97

Table 4 Range of maximum variation with change of parameters on the inhalation model

	Aerosol particle size (AMAD)					
	0.1 μm		1 μm		5 μm	
Age/Sex	Range of Max. Variation (%)	Sum of Deposition Efficiency	Range of Max. Variation (%)	Sum of Deposition Efficiency	Range of Max. Variation (%)	Sum of Deposition Efficiency
Adult/Male	-7.3 ～ +1	0.4240	-2.0 ～ +5.0	0.5273	-0.5 ～ +1.2	0.8292
Adult/Female	-10.1～ +1.1	0.4194	-2.6 ～ +6.1	0.5307	-0.4 ～ +1.4	0.8305
15 y/Boy	-5.1 ～ +3.8	0.4109	-1.6 ～ +3.7	0.5234	-0.4 ～ +0.9	0.8286
15 y /girl	-4.9 ～ +3.6	0.3997	-1.9 ～ +5.0	0.5333	-0.5 ～ +1.1	0.8326
10 y	-3.6 ～ +0.7	0.3706	-9.2 ～ +3.8	0.5689	-2.2 ～ +0.8	0.8461
5 y	-2.2 ～ +2.2	0.3467	-3.9 ～ +6.3	0.5537	-0.9 ～ +0.7	0.8410
1 y	-1.3 ～ +1.7	0.3562	-7.6 ～ +7.6	0.6406	-1.4 ～ +0.8	0.8652
3 month	-2.3 ～ +1.8	0.3597	-4.1 ～ +6.0	0.6357	-0.8 ～ +0.5	0.8633

A change in the fraction of the averted dose was examined when one parameter was moved to the maximum or the minimum value of the ranges for Japanese while other parameters were set to be the central values (Table 3) . This examination was carried out with a different time of administration of stable iodine from 20 hr before the inhalation of radioiodine to 20 hr after inhalation. The duration of inhalation was set to 1 hour with a constant rate of intake. The tested radioiodine was limited to iodine-131 because it is considered to have the largest potential health influence among the other iodine isotopes (Kai et al. 1985).

3. RESULTS

3.1 Sensitivity analysis on parameters involved in the inhalation model

Table 4 shows the ranges in the sum of the deposition rates with changes in each of the parameters listed in Table 2. The variances in the deposition efficiency due to changes in the respiratory parameters between the standard Caucasian (ICRP Publication 66) and our reference Japanese were relatively small.

However, the changes by age and radioiodine aerosol size were larger, suggesting an importance of understanding the physico-chemical status of radioiodine released in nuclear emergencies. The analysis of the metabolic parameters of iodine showed that the most critical ones are that reflect the intake blokage to the thyroid of inorganic stable/radioactive iodine from the blood (body fluids).

3.2 Sensitivity analysis on parameters involved in the metabolic model of iodine

Figure 2a – 2d shows the fractions of averted dose according to the maximum and minimum values of each metabolic parameter listed in Table 3. Changes in the parameter (k_a) that reflects the absorption of stable iodine from the GI tract have a small effect (Fig. 2a). The effect is largest when the administration time is near the inhalation time, since this parameter controls how fast the stable iodine reaches the thyroid gland. The sooner it reaches the thyroid gland, the earlier the blockage occurs and the lower the fraction of the averted dose. The rate constant (k_o) of the transport of iodine from the thyroid gland to body fluids as hormonal iodine has some effect when stable iodine is administered before radioiodine inhaled (Fig.2b). This is understandable since k_o is related to the duration of the blocking. The rate constants that reflect the recycling of decomposed hormonal iodine (k_i) and the excretion of iodine (k_{e1}, k_{e2}) had little influence (results not shown).

Among the metabolic parameters we tested, the largest influence was associated with the parameters f and Q_s (Fig.2c, 2d), from Eqn (1). According to the possible range of f, the difference in the fraction of the averted dose is 0- 0.3, and is especially large when stable iodine is administered a few hours before the inhalation of radioiodine. This feature is important from a viewpoint of radiological protection. Administration of stable iodine at a period of ten to a few hours before the inhalation of radioiodine is probable to maximize prophylaxis. On the other hand, differences in the effect of the prophylaxis due to individual differences in metabolism may occur in the same period. As for the parameter Qs, about 0.10 - 0.15 of the fraction of the averted dose may vary during this period (Fig.2d). The dietary iodine intake (DI) influences the fraction of the averted dose by about 0.1 - 0.15, with a weak dependency on the time of the administration of stable iodine.

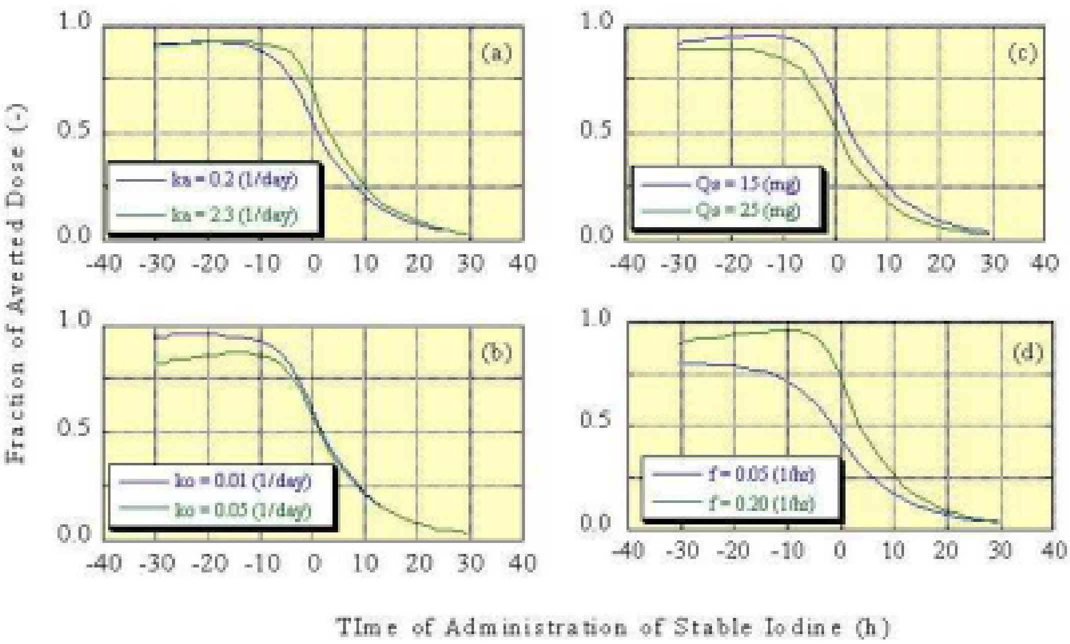

Fig. 2 Result of sensitivity analysis for the metabolic parameters of radio/stable iodine for Japanese

3.4 Fraction of averted dose for Caucasians and Japanese

Figure 3 shows a comparison of the fraction of the averted dose calculated using the metabolic parameters for Caucasians (Wootton et al, 1978) and those for Japanese in the present study. The calculation was made under a condition that the inhalation of iodine-131 continues one hour from the time 0 (Figure 3) for a male adult, and 130 mg-KI is administered at different time before or after the beginning of the inhalation. The metabolic parameters were after Wooton et al. (1978) for Caucacian, and the standard values found in the present study for Japanese (Table 3). The fraction is slightly smaller in the case of the Japanese, while the inhalation dose coefficient for radioiodine was evaluated as two-thirds of that for Caucasians (Togawa, 1992). Both of these differences reflect a lower fraction of transport of iodine to the thyroid gland among Japanese

(Yoshizawa & Kusama, 1976; Kai, 1983). It is probably the case that the smaller averted fraction is compensated for by the smaller inhalation dose coefficient in the case of Japanese. Accordingly, the thyroid dose following the use of prophylactic iodine will be similar for both Caucasians and Japanese.

4. CONCLUSION

The parameter Q_s and f , which reflect the rate transport of iodine from the body fluid to the thyroid gland, do not have simple physiological meanings; they can be determined by that rate of transport under normal condition and by changes in this rate after administration of stable. Therefore, we concluded that a complete identification of the blockage model and the related parameters for Japanese are critical in determining the effect of iodine prophylaxis in reducing thyroid gland exposure in Japanese.

To better understand the effectiveness of stable iodine prophylaxis in Japanese, we performed a sensitivity analysis for the parameters involved in an inhalation model of radioiodine and a metabolic model of stable/radioactive iodine. The difference in respiratory parameters between Caucasians and Japanese had a very small influence on their intake of radioiodine via inhalation. Based on the metabolic model of iodine proposed by others, our sensitivity analysis focused on metabolic parameters that were reviewed in the present study. The most critical parameters were found to be those that reflect the blockage at the thyroid gland of its intake of inorganic stable/radioactive iodine from the blood. Although some difference in the effectiveness of iodine prophylaxis is expected between Caucasian and Japanese, the thyroid dose under a condition of iodine prophylaxis will be similar for both Caucasian and Japanese because of compensation by a difference in the inhalation dose coefficient of radioiodine. Besides the examination on the physiological parameters, it is important to understand the physico-chemical status of the specific radioiodine released in a nuclear emergency since it was found that the aerosol size has some effect on metabolic parameters of inhaled radioiodine.

(This work was performed under the auspices of the Science and Technology Agency of Japan)

AKNOWLEDGEMENT

The authors are grateful to Dr. S. Nagataki, Dr. H. Baba and Dr. Y. Ishikawa for their helpful discussions on the iodine metabolism..

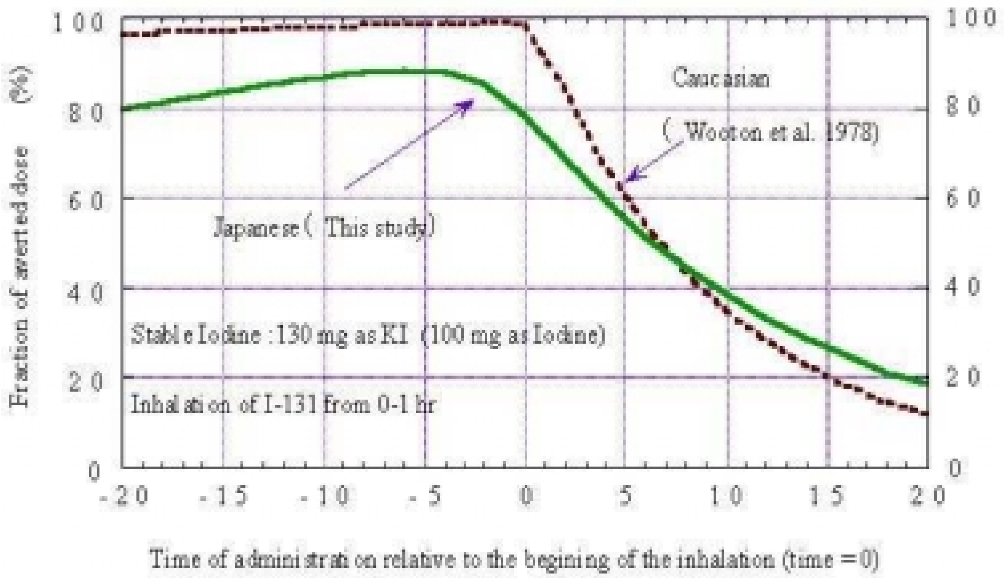

Fig.3 Comparison of the fracttion of averted dose between Caucasian and Japanese

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