Determination of kinetic parameters for 123-I thyroid uptake in healthy Japanese

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Abstract. The purpose of this study was to compare the kinetic parameters for iodide thyroid accumulation in Japanese today with previously reported values. We determined the thyroid uptake of 123-I at 24 hours after the oral administration in healthy male Japanese without any diet restriction. The mean value was 16.1±5.4%, which was similar or rather lower than those previously reported in Japan (1958-1972). Kinetic model analysis was conducted to obtain the clearance for thyroid uptake from the blood circulation. The thyroid uptake clearance of 123-I was 0.540±0.073 ml/min, which was almost similar to those reported previously. There is no obvious difference in the thyroid uptake for 24 hours, and kinetic parameters in healthy Japanese for these 50 years. The fraction of distributed to the thyroid gland is lower than the ICRP reference man, and such difference must be taken into consideration to estimate the radiation exposure upon Fukushima accident in Japan.

1 Introduction

It is well known that thyroid accumulation of radio-iodide depends on the ingestion of stable iodides because of non-linearity in the thyroid accumulation. Because Japanese food contains content of stable iodides, Japanese accumulates radio iodide upon exposure with lower magnitude than the ICRP reference man. Indeed, in previously studies (conducted in 1958-1967, the mean value of the thyroid uptake of radio-iodide for 24 hours after administration was 21±8 (mean±SD) %.

After Fukushima accident, we have a concern if the thyroid uptake and kinetic parameters of radio-iodide in Japanese today remains to be similar to those previously reported values. To address this issue, we designed clinical study in healthy subjects with no diet restriction to determine the thyroid uptake of 123-I in Japanese subjects with normal thyroid function.

2 Clinical studies in healthy subjects

2.1 Study Design

Clinical study was conducted in Nagasaki University Hospital PET/Molecular Imaging Center (Nagasaki, Japan). Fifteen Japanese male subjects were enrolled in this study (Age 41.8±0.4 years old, body weight 68.9±8.0 kg, BMI 23.5±0.5, and normal thyroid function). The subjects received no diet restriction. Following oral dose of 123-I (Sodium Iodide Capsules, Nihon Medi-Physics, Co., Ltd, Japan; 4.53-7.98 MBq), the blood was collected at 20 min, 40 min, 1, 1.5, 2, 4, 6, 9 and 24 hours after administration, and urine was collected for 10 hours after administration. The total radioactivity associated with blood and urine specimens were measured by gamma-counter. The thyroid uptake of 123-I was determined at 20 min, 40 min, 1, 1.5, 2, 4, 6, 9 and 24 hours after administration. This study was approved by the Ethics Review Boards of Faculty of Pharmaceutical Sciences, The University of Tokyo, and Faculty of Pharmaceutical Sciences, Nagasaki University.

The area under the blood concentration time profile (AUC) was calculated as trapezoidal approximation method. The renal clearance (CL_r) of 123-I was determined by dividing the amount of total radioactivity excreted into the urine by the area under the blood concentration time profile.

2.2 Result

Thyroid uptake of 123-I were increased along with time, and reached to 16.1±5.4% (mean±SE) of the oral dose after 24hours in average (ranging from 9.1-26%). The total radioactivity recovered for 10 hours after administration was 49.7±6.2%. CL_r of the total radioactivity was 36.1±8.4 ml/min.

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2.3 Comparison of the thyroid uptake for 24 hours

The thyroid uptake of 123-I for 24 hours determined in this study was compared with previously reported values which were collected from literatures (include published in Japanese). As shown in Figure 1, the mean value of the thyroid uptake was similar or rather slightly lower in the Japanese subjects today. Kunii Y et al also conducted similar study in another area in Japan (Tokyo) where the mean value (12.8±5.7%, [1]) was similar to our study. These values were lower than the corresponding value in ICRP reference man (30%).

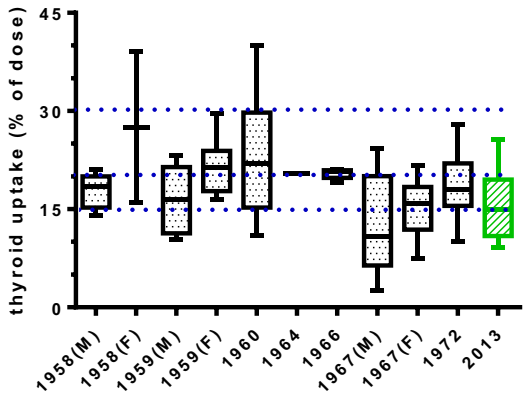

Figure 1 Comparison of the 24 hour-thyroid uptake of radioiodide in Japanese

3 Model analyses

3.1 Kinetic models

One- or two compartment model was employed in the analysis of blood concentration time profiles, and thyroid accumulation. The kinetic parameters such as distribution volume, and thyroid uptake clearance were obtained by iterative non-linear least square method using Napp software [2] on Macintosh computer.

3.2 Result of model analysis

Blood concentration time profiles followed one or two compartment model depending on subjects; in 9 of 15 subjects, the blood concentration time profiles were accounted for by the 1 compartment model where 1st order absorption was considered.

The distribution volume in the central compartment was 21.2±4.1 l, and thyroid uptake clearance was 0.540±0.073 (mean±SE) l/hr.

3.3 Comparison of thyroid uptake clearance in Japanese population

Nagataki S et al reported the thyroid uptake clearance in healthy subjects in 1967 [2]. The mean and standard error were compared with those in our study (Figure 2). Our data was almost comparable with previously reported value.

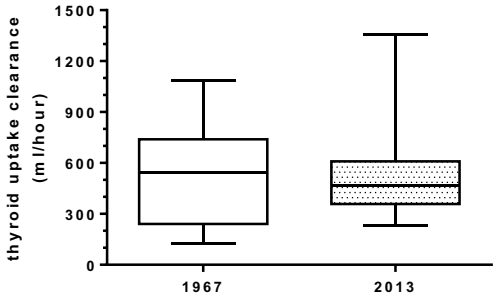

Figure 2 Comparison of the thyroid uptake clearance of radio iodide in Japanese

Conclusion

For these 50 years, no significant difference was observed in the thyroid accumulation of radio iodide for 24 hours, and thyroid uptake clearance. The present study confirmed that thyroid accumulation of radio iodide is lower in Japanese than the ICRP reference man. This was also confirmed in another study independently conducted in Tokyo. Such difference must be taken into consideration to estimate the radiation exposure upon Fukushima accident in Japan.

This study also determined the distribution volume and renal clearance in Japanese population. Using the kinetic model, and parameters, the thyroid accumulation of radio iodide will be estimated according to the exposure scenarios during evacuation. The kinetic parameters in virtual subjects can be generated with means and coefficient of variations. Monte Carlo method may allow estimation of the likely distribution of thyroid accumulation based on each exposure scenario.

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