Estimation of the Release Time from Isolation for Patients with Differentiated Thyroid Cancer Treated with High-dose I-131

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Abstract

Purpose Patients receiving high-dose I-131 to treat differentiated thyroid cancer are isolated from visitors to limit radiation exposure to reasonable levels. The appropriate isolation time is unclear and has not been reported in Korea. The purpose of this study was to estimate the isolation time and investigate the possibility of earlier release from isolation.

Methods This study was a retrospective analysis of data from 71 patients (10 men and 61 women; mean age, 49 ± 11.1 y) who received 3.7 GBq (47 patients), 5.55 GBq (23 patients), or 7.4 GBq (1 patient) of I-131 between January 2008 and December 2008. The radiation dose was measured with a fixed probe placed inside the isolation room. The total estimated dose equivalent (TEDE) to family members, the time required for the external dose rate to become <0.07 mSv/h, and the time required for whole-body retention to become <1.2 GBq were calculated. **Results** By the TEDE criterion (<5 mSv), 70 of 71 patients (98.6%) could have been released without isolation. By the external dose rate criterion, 10 of 71 (14.1%) and 60 of 71 patients (84.5%) could have been released without isolation and within 24 h, respectively. With whole-body retention criterion, 19 of 71 (26.8%) and 48 of 71 patients (67.6%) could have been released within 24 h and within 48 h, respectively.

Conclusions Appropriate release times were estimated and compared using different criteria. Most patients could have been released without isolation or within 24 h of radiation treatment.

Keywords Thyroid cancer · Radioisotope therapy · I-131 · Radiation protection

Introduction

Radioactive iodine therapy following thyroidectomy is the standard treatment for patients with differentiated thyroid cancer. Patients with thyroid cancer who need high-dose radioactive iodine therapy (HDRIT) require isolation in a lead-shielded room for a certain period of time (usually 2 nights and 3 days in Korea). Since 1997, the US Nuclear Regulatory Commission (NRC) has continuously amended the release provision for thyroid cancer patients treated with HDRIT. The major principle of the provision is that the total effective dose equivalent (TEDE) to family, friends, and coworkers shall not exceed 5 mSv [1]. The radiation safety regulation of the Ministry of Education, Science and Technology in Korea is similar. According to the NRC, patients with remaining radioactivity in the body of less than 1.2 GBq or a measured dose rate less than 0.07 mSv/h at 1 m can be released from isolation.

Recently, the number of thyroid cancer cases detected in Korea has increased dramatically because of the widespread use of high-resolution ultrasonography and fine-needle aspiration cytology [2, 3]. Because most patients with differentiated thyroid cancer require HDRIT after surgery, a shortage of available isolation rooms has resulted. The number of isolation rooms is unlikely to increase in the short term because the reimbursement policy of the national healthcare insurance for isolation therapy is unfavorable in Korea.

Thus, if we can shorten the total admission time while maintaining safety regulations, more patients who need

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HDRIT can be treated. Some patients who receive HDRIT complain about the inconvenience of isolation and the anxiety that they experience from the solitude. A decrease in the total isolation time is likely to reduce the inconvenience and the anxiety.

To determine the adequate release time from isolation, the radiation level must be measured frequently. However, this practice exposes the medical staff to a radiation burden. Thus, we use a simple and safe method to measure the radiation dose as frequently as needed without a radiation burden to the medical staff. The details of and results from this method were reported previously [4].

The aim of this study was to calculate the TEDE, to determine the adequate release time from isolation, and to evaluate whether the isolation time could be shortened without increasing the radiation burden to family members of the patients. The time required to meet other release criteria (external dose rate <0.07 mSv/h and whole-body retention <1.2 GBq) was also calculated and compared.

Materials and Methods

Subjects

We measured the radiation dose rate in all patients admitted to an isolation room for I-131 therapy. This report is a retrospective analysis of data from 71 patients with differentiated thyroid carcinoma who received HDRIT between January 2008 and December 2008. Patients whose thyroid-stimulating hormone (TSH) level was less than $30 \mu\text{IU/ml}$ were excluded from the analysis.

The patients (10 men and 61 women) ranged in age from 23 to 75 years (49 ± 11.1 years). Total thyroidectomy was performed in all patients with or without cervical neck node dissection. All patients had papillary thyroid carcinoma. Patient characteristics are shown in Table 1. The amount of administered I-131 ranged from 3.7 to 7.4 GBq: 47 patients received 3.7 GBq, 23 patients received 5.55 GBq, and 1 patient received 7.4 GBq.

Methods

Patient Preparation

Thyroxine (T4) use was discontinued 4 weeks before I-131 administration, and triiodothyronine (T3) was prescribed for 2 weeks after the discontinuation of T4. T3 use was then discontinued for 2 weeks. All patients were requested to maintain strict diet control for 2 weeks and

received consultation from a nutritionist at the hospital to help with this goal.

Radiation Dose-rate Measurement and Calculation of TEDE

To measure the radiation dose rate from the patients without exposing the hospital staff to radiation, the probe of a dose meter was placed on the inside wall of the lead-shielded isolation room. The body of the dose meter was placed outside the isolation room so that hospital staff could read the dials of the dose meter without being exposed to radiation. The probe and body of the dose meter were connected with a long cable. To prevent possible contamination, the probe was placed inside a small box fixed at the wall at 1 m in height. The box had a small hole that was aimed at the patient, and the hole was sealed with a vinyl cover that could be replaced easily in case of contamination.

The patients were requested to stand on a picture of feet that had been drawn on the floor of the isolation room 1 m from the probe. Whether or not the patient was standing in the right position was confirmed by closed caption television, which was located in the isolation room. Closed caption television was installed to ensure the patients' safety during isolation, and written permission for its use was secured from all patients. The radiation dose rate was measured immediately after administration of I-131 and at 4-h intervals thereafter until discharge, except during sleep.

The measured data were plotted using a commercially available spreadsheet program (Microsoft Excel); λ and the effective half-life (T_{eff}) were derived using a curve fit function of the spreadsheet program assuming mono-exponential decay (Fig. 1). TEDE was calculated by integrating the area under the curve (AUC) from 0 time (administration of I-131 capsule) to infinite time (total AUC = $A^0 \int_0^\infty e^{-\lambda t} dt$, where A^0 = dose rate at $t=0$). The integral of the AUC is equivalent to the TEDE to a person who stands at a distance of 1 m from the patient from the time of administration of I-131 to infinite time. We also calculated the TEDE to family members with various occupancy factors.

On the basis of the derived formula of the curve, the time required for the external dose rate to become less than 0.07 mSv/h [from the equation of the curve $A = A^0 e^{-\lambda t}$, the time required for the dose rate to become 0.07 mSv/h is calculated as $t = -\lambda \ln(A/A^0)$, where $A = 0.07$ mSv/h and A^0 = dose rate at $t=0$] and the time required for the retention of I-131 in the body of the patient to become less than 1.2 GBq [the time required for whole-body retention to become less than 1.2 GBq is calculated as $t = -\lambda \ln(D/D^0)$, where $D = 1.11$ GBq or

Table 1 Patient characteristics

Characteristics	
Age, years (range)	49±11.1 (23–75)
Gender, male/female	10/61
Serum creatinine, mg/dl (range)	0.8±0.2 (0.5–1.5)
Serum TSH, μ IU/ml (range)	52.9±8.9 (31.6–77.6)
Serum thyroglobulin, ng/ml (range)	35.9±152.7 (0.1–1180.6)
Serum thyroglobulin antibody, IU/ml (range)	45.7±136.86 (2.0–1116.9)
Number of treated patients	
3.7 GBq	47
5.55 GBq	23
7.4 GBq	1

30 mCi, D^0 = administered dose] were calculated in each patient.

Results

Calculation of Adequate Release Time According to the TEDE Criterion

The estimated TEDE ranged from 0.86 to 8.54 mSv (0.22 ± 0.12 mSv). The TEDE was less than 5 mSv in all patients except one, a 56-year-old woman with diabetes who received 3.7 GBq of I-131 and whose serum creatinine level was 1.5 mg/dl (the highest of all the subjects). On the basis of the TEDE criterion (<5 mSv), 70 of 71 patients (98.6%) could have been released without isolation.

If an occupancy factor less than 1 is applied, the TEDE becomes smaller. Estimates of TEDE made using various occupancy factors, from 1 to 0.25, are shown in Table 2.

Calculation of Adequate Release Time According to the External Dose-rate Criterion

Estimated times for the external dose rate to become less than 0.07 mSv/h ranged from 0 to 26.6 h (8.7 ± 6.44 h). The

first external dose rates for 10 patients, which were measured immediately after administration of I-131, were less than or equal to 0.07 mSv/h. On the basis of the 0.07 mSv/h criterion, 10 of 71 patients (14.1%) and 60 of 71 patients (84.5%) could have been released without isolation and within 24 h, respectively, and 1 of 71 patient (1.4%) could have been released within 30 h of isolation (Table 3)

Calculation of Adequate Release Time According to the Whole-body Retention Criterion

On the basis of the whole-body retention criterion (<1.2 GBq), 19 of 71 patients (26.8%) could have been released within 24 h, and 48 of 71 patients (67.8%) could have been released within 48 h, respectively (Table 4). A statistically significant correlation was observed between the serum creatinine level and the duration of time that the whole-body retention of I-131 became less than 1.2 GBq ($P < 0.0001$, $r = 0.56$).

Discussion

Patients who receive HDRIT are isolated for a given time period until the amount of radiation they emit reaches acceptable levels. The radiation level should be measured to determine the release time of the patients from isolation. Because frequent measurements of the radiation level subject hospital staff to possibly unacceptable levels of radiation, isolation of HDRIT patients for a predetermined time (usually 2 nights and 3 days), generally longer than is necessary, is the customary practice in Korea.

In our hospital, we routinely measure the radiation dose rate until the release time in patients who receive HDRIT using the method described in Methods. The formula of the time-dose rate is used to calculate TEDE for each patient. If appropriate occupancy factor (OF) is applied, TEDE can be converted to a reasonable total radiation dose that reflects

Fig. 1 Changes in the external dose rate over time (♦). The dashed line represents the fitted curve. The formula of the curve is shown in the box

Table 2 The TEDE for various occupancy factors, and the number of patients who could have been released without isolation

Occupancy factor	TEDE (mSv)	Possible outpatient treatment
1	2.31±1.12 (0.80 – 8.54)	70/71 (98.6%)
0.75	1.74±0.84 (0.60 – 6.40)	70/71 (98.6%)
0.5	1.16±0.56 (0.40 – 4.27)	71/71 (100%)
0.25	0.58±0.28 (0.20 – 2.14)	71/71 (100%)

the daily activity of the patient's family members. Park et al. [5] interviewed 11 patients before HDRIT and determined the OF (OF=0.125–0.5) of each patient. They used the OF to calculate the maximum permissible I-131 dose that can be given to outpatients while limiting the radiation burden to family members to less than 5 mSv. According to their calculation, the maximum permissible I-131 dose was 4.07–8.51 GBq. Our patients received a dose of 3.7–7.4 GBq.

On the basis of the TEDE criterion that a person standing 1 m from a patient should be exposed to less than 5 mSv, 70 of 71 (98.6%) patients could have been released immediately after administration of I-131 without isolation. The one patient whose TEDE was greater than 5 mSv was a 56-year-old woman with diabetes who received 3.7 GBq of I-131. Her serum creatinine level was 1.5 mg/dl, which was the highest of all the patients.

When an OF of 0.5 was used, 71 of 71 (100%) patients could have been released without isolation. This means that all patients could have been treated at home. However, compliance with safety precautions is important, because “if someone spends 1 or 2 h closer than 0.5 m to the patient during the first hours after administration, the dose limit could quickly be reached or exceeded” [6].

Barrington et al. [7] measured the whole-body dose rate during admission and after hospital discharge for up to 11 days using a dose meter and then calculated the dose rate to the public (annual dose <1 mSv). According to their calculation, patients who receive HDRIT can be allowed to travel home 4 h (dose: 3.7 GBq) or 2 h (dose: 7.4 GBq) in a private car on the day of treatment.

The cumulative radiation burden to family members can also be calculated using readings from thermoluminescent dosimeter (TLD) badges. Pant et al. [8] measured the radiation dose using TLD badges until 15 days after the

release of patients and reported that only 1 of 342 family members were exposed to more than 5 mSv, even though those family members cared for the patients in an isolation room and after discharge to home. The one who received more than 5 mSv (8.5 mSv) was a close relative of the patient who was disabled and unable to move.

Calculation of the total radiation dose using readings from a TLD badge more closely approximates the actual radiation exposure than does the theoretical calculation and prediction of the TEDE, because the results derived from the TLD readings are not based on assumptions about the contact time between patient and family. Rutar et al. [9] used personal monitoring devices to measure the radiation exposure to family members of patients who received I-131-B-1 antibody treatment. They derived effective half-lives using readings from these devices and calculated the total radiation dose to infinite time. According to their calculation, the predicted doses were higher than the measured doses.

The estimated isolation time based on the external dose rate criterion (<0.07 mSv/h) was longer than that based on the TEDE criterion. According to the TEDE criterion, 70 of 71 (98.6%) patients required no isolation. In contrast, according to the external dose rate criterion, only 10 patients could have been released without isolation, 60 of 71 (84.5%) patients could have been released from isolation within 24 h of admission, and 1 patient could have been released from isolation within 30 h of admission.

The number of patients who could have been released from isolation became smaller when we applied the whole-body retention criterion. The time required for the whole-body retention of I-131 to become <1.2 GBq ranged from 17.2 to 120.4 h (30.3±13.79 h). Only 19 of 71 (26.8%) patients could have been released within 24 h of isolation, and another 48 of 71 (67.6%) patients could have been

Table 3 The number of patients who could have been released from isolation at given times based on the external dose rate criterion of <0.07 mSv/h

Time	Patient numbers
0 h	10/71 (14.1%)
<6 h	16/71 (22.5%)
<12 h	28/71 (39.4%)
<18 h	12/71 (16.9%)
<24 h	4/71 (5.6%)
<30 h	1/71 (1.4%)

Table 4 The number of patients who could have been released from isolation based on whole-body retention criterion of <1.2 GBq

Time	Patient numbers
0 h	0/71 (%)
<24 h	19/71 (26.8%)
<36 h	41/71 (57.7%)
<48 h	7/71 (9.9%)
<72 h	3/71 (4.2%)
>72 h	1/71 (1.4%)

released within 48 h of isolation. One patient required more than 72 h of isolation.

Required isolation time calculated by the external dose rate criterion or TEDE criterion is shorter than the isolation time calculated by the whole-body retention criterion, which may have been due to an attenuation effect of radiation in the patient's body itself that affected the dose rate measurement.

Because the purpose of isolating HDRIT patients is to limit the radiation burden to others, the use of the TEDE or external dose rate criterion to determine the release time appears to be more appropriate than the use of whole-body retention criterion.

Whole-body retention of I-131 is affected by the renal clearance of free I-131 in the blood. A statistically significant correlation was observed between the serum creatinine level and the duration of time that the whole-body retention of I-131 to become less than 1.2 GBq.

Renal clearance is not affected when recombinant human TSH (rhTSH) is used for the preparation of I-131 therapy (rhTSH patients). Remy et al. [10] reported that the mean T_{eff} was 10.5 h in rhTSH patients and was 15.7 h in thyroid-hormone-withdrawal patients. The T_{eff} of our patients (thyroid-hormone-withdrawal patients) was 16.0 h, which was similar to that reported by Pacilio et al. [11]. The T_{eff} of rhTSH patients is shorter than that of thyroid-hormone-withdrawal patients. Therefore, the whole-body retention of I-131 should be lower in rhTSH patients, and the radiotoxicity in these patients should be lower than that in conventional thyroid-hormone-withdrawal patients. Rosario et al. [12] observed acute sialadenitis, hyperamylasemia, neutropenia, elevation of FSH (damage to ovaries), and elevation of 8-epi-PGF 2α (oxidative injury) more frequently in thyroid-hormone-withdrawal patients than in rhTSH patients. Furthermore, the TEDE should be less in rhTSH patients than in thyroid-hormone-withdrawal patients.

It is believed that diuretics enhance the renal clearance of I-131. However, Matovic et al. [13] recently reported that blood radioactivity was greater in patients who received furosemide than in controls, even though the patients who received furosemide passed larger volumes of urine. The mechanism responsible for this paradoxical effect is unknown. Whether the external dose rate in the forced-diuresis group was greater (or not lower) than that in the control group was not reported.

In conclusion, we measured the external radiation dose rate and calculated the TEDE to family members of patients who received HDRIT, the time required for the external dose rate to become less than 0.07 mSv/h, and the time

required for whole-body retention of I-131 to become less than 1.2 GBq. According to our calculations, most patients who receive HDRIT can be released from isolation earlier than the conventional time in Korea of 2 nights and 3 days.

This study was a retrospective analysis. If the radiation dose is measured frequently and sufficient data are obtained to generate time-dose rate curves earlier after administration of I-131, the release time may be able to be predicted prospectively and the appropriate release time tailored to individual patients.

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