Original Article

Estimation of Effective Half-Life of I-131 in Differentiated Thyroid Cancer Patients in a Tertiary Care Hospital in India: A Retrospective Study

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Abstract

**Introduction:** Patients having differentiated thyroid cancer (DTC) undergo radio-iodine (I-131) therapy to ablate normal residual thyroid tissue after surgery and this is known to reduce rates of death and recurrence. The objective of the study was to assess the effective half-life of I-131 clearance in differentiated thyroid cancer patients.

**Material and Methods:** The exposure rate (mR/hr) of ninety one patients treated for remnant thyroid ablation with I-131 were analyzed. These measurements were taken immediately after dose administration at a distance of one meter from the patient at the level of abdomen and then on subsequent days at the level of maximum activity, till the patient is discharged under recommended regulatory limits (<50uSv/hr, 5mR/hr).

**Results:** We found the effective clearance of I-131 as bi-exponential and the t-significant amount (65%) of activity was excreted through the urine within 20 hrs. In the group of patients administered 3.7GBq (100mCi) I-131, the first phase clearance was found to be at 13.72 hour and final phase clearance was at 18.91 hr (range 8.84-177.42hr). We also found the differences in effective half life in two groups viz 3.7GBq and 5.55 GBq.

**Conclusion:** The mean effective half-life in the 3.7GBq (100mCi) group was 13.72 hrs at initial phase and 18.91 hrs at the final phase. The data generated in this study will be useful in formulating guidelines for the staff and the person coming close proximity to the patients during and after the high dose I-131 therapy.

**Keywords:** effective half-life, differentiated thyroid cancer and remnant ablation.

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**Introduction**

Thyroid cancer is the most frequently occurring endocrine cancer and 90 to 95 percent of cases of differentiated thyroid cancer (DTC) have high survival rates of 10 years (1). Patients having DTC undergo radio-iodine therapy to ablate normal residual thyroid tissue after surgery and this is known to reduce rates of death and recurrence (2-5).

Generally, high doses of I-131 more than 1.11 GBq (30mCi) are administered for these patients. Since these patients pose stochastic radiation risks to the person coming close to them, they are hospitalized and then released when exposure rate drops below safe limit set by local authority in radiation protection.

The information regarding effective half-live clearance of I-131 in DTC patients helps the health physicist/ Radiation Safety Officer / Regulatory Authority in designing recommendation of radiation protection guideline from time to time. It helps in defining the time period during which extra precautions are required and designing/ developing set of instructions for patients and their attendant so that radiation exposure to their attendant is as low as reasonably achievable. International recommending agencies such as ICRP and IAEA or others dealing with radiation safety aspects during and after radio-iodine therapy also need updated data on the subject while finalizing their recommendation (6).

Few studies have estimated the effective half-life clearance of I-131 in patients with DTC and in India since then little attention have been given (7,9). It is known that I-131 therapy / treatment protocol of DTC varies among the institutions (that is total thyroidectomy or hemithyroidectomy, low dose or high dose I-131, pretherapy and during therapy instructions given to patients, patient discharge limits from the hospital, seriousness observed in following instructions by the patient before and during therapy etc that can affect the estimation of effective half-life of I-131 in DTC Patients. Therefore, there was a need to assess the effective half-life clearance of I0131 in DTC Patients. The purpose of this retrospective study is to assess the effective half-life of I-131 in DTC Patients.

**Materials and Methods**

This was a retrospective study. No ethical approval was required as the study involved only the analysis of exposure rates measured immediately after the oral administration of I-131 and thereafter on daily basis during the period of hospitalization in isolation.

In order to assess the effective half life, the exposure rate record of the DTC patients treated with I-131 was analyzed. Patients who had undergone treatment during June 2011 to December 2012 at the department of nuclear
medicine, Army Hospital Research & Referral, Delhi cantt were considered in this study.
The Patients with histological conformation of the DTC requiring radio-iodine therapy after total thyroidectomy were included. Following patients were excluded:
1. Patient unable to self-care
2. Anaplastic or medullary carcinoma thyroid
3. Pregnancy
4. During menstrual period
5. Patient unable to take oral I-131
6. Patients with azotemia

Patients underwent physical examination and their bio-chemical parameters were evaluated before the radio-iodine therapy. In order to assess the remnant thyroid tissue and extent of metastasis present, they were given a diagnostic dose of 74MBq (2mCi) I-131 and whole body scan were performed after three days on the gamma camera (Philips forte dual head gamma camera) with high energy parallel hole collimator. Patients were administered therapeutic dose based on the following criteria:

**Therapeutic High Dose therapy immediately after total thyroidectomy:**
- Papillary carcinoma without lymph node metastasis and capsule infiltration and follicular carcinoma with no distant metastasis in all age group were given 3.7 GBq (100mCi).
1. Papillary carcinoma with lymph node metastasis and capsule infiltration in all age group were given 5.55 GBq (150mCi).
2. Papillary / follicular with distant metastasis given 7.4GBq (200mCi).
- Palliative high dose therapy during follow up for residual group/ recurrent group:
  - 100mCi irrespective of the histopathology report.

Before therapy, patients were off tablet L-Thyroxine for 4 weeks period. All patients were instructed to follow iodine restricted diet for 4 weeks before therapy. Cut off TSH level (more than 30u I.U. international unit as per Society of Nuclear Medicine guideline for therapy) before administration of therapy was ensured.

Radio-iodine in liquid form as sodium iodide is procured from BRIT, measured in the dose calibrator (Capintec, CRC-25R, 151) was measured in the dose calibrator ((Capintec, CRC-25R, 151) before oral administration. The patients were demonstrated as how to drink the oral I-131 activity and prevent contamination while drinking. The concept of distance, time and shielding to minimize the radiation dose and instructions to be followed during the isolation period were explained to their attendant. Patient and attendant were counseled to follow given oral / written instruction so that essential hazards of external and internal contamination to the attendant can be minimized during the isolation period. Our instruction lists also include the use of lemon candy immediately after the oral administration of I-131 so that the radiation dose to the salivary glands can be minimized, encouraged to take plenty of fluids and to empty the bladder frequently to minimize radiation dose to the kidney and bladder.

The patient exposure rate measurement were made immediately after the oral administration of I-131 and thereafter on daily basis at one meter distance from the patient at the level of maximum activity concentration in the body with empty bladder during the period of isolation. The calibrated exposure rate meter RAM GAM (Model 4-0003, Rotem Industries, Range 0-999mR/hr) was used. The patients were discharged when the exposure rate at one meter was less than 50µSv/hr (5mR/hr) and were clinically fit for the discharge.

The natural logarithm of the exposure rate (µSv/hr) versus the time of measurement (hrs) graph show the bi-exponential curve, fast decay before 24 hour (initial phase) and slow thereafter (final phase). Mono exponential fit were performed on the initial phase data that is taking first two measurements one measured immediately after the administration of I-131 and another on the 2nd day morning. Then linear fit was made and from the equation of linear fit
decay constant (slope of the equation) was obtained and the effective half-life clearance was calculated by dividing 0.693 by the decay constant. Similarly for the final phase all the data points (radiation exposure, time of measurement) available after next day were taken and calculated the effective half life of clearance of I-131.

Results
There were 91 patients included in this study, the male: female ratio was 39:52. The distribution of patients based on the activity administered has been in the figure 1. Sixty five percent patients were administered 3.7 GBq (100mCi) and 26 Percent patients were administered 5.55GBq (150mCi) of I-131.

Figure-1: The pie chart shows the distribution of patients based on the administered I-131 activity. 65%, 26%, 5%, 2%, 1% and 1% of patients were administered 3.7GBq (100mCi), 5.5GBq (150mCi), 7.4GBq (200mCi), 4.4GBq (120mCi), 2.22GBq (60mCi) and 3.16GBq (80mCi) I-131 respectively.

69 Patients were discharged on after 48hr. 18 Patients were discharged after 72 hour in which 8 patients were from the 3.7GBq (100mCi) group and 10 was from the 5.55 GBq (150mCi) group. 4 patients were discharged after 96 hours from 7.4 GBq (200mCi) group.

The mean radiation exposure rate measured immediately after administration of 3.7GBq (100 mCi) of I-131 at one meter distance from the patient at the abdomen level was 183.9µSv/hr (18.39mR/hr) with a standard deviation of 27.1 µSv/hr (2.71mR/hr). On 2nd and 3rd day, at the level of maximum activity in the body it was 63.7µSv/hr (6.37mR/hr) at 19.57 hrs and 22.9 µSv/hr (2.29 mR/hr) at 43.49 hrs respectively. Similarly the mean exposure rate measured immediately at 19.57 hr and 43.49 hr after administration of 5.55 GBq (150mCi) was 255.0 µSv/hr (25mR/hr), 86µSv/hr (8.6mR/hr), and 34.1 µSv/hr (3.41mR/hr) respectively. The effective half-life clearance of I-131 from the DTC patients had followed bi-exponential relationship with time.

The mean effective half-life in the 3.7GBq (100mCi) group was 13.72 hrs at initial phase and 18.91 hrs at the final phase. The summary statistics of the effective half-life of the initial and final phase of the initial and final phase for both the groups (3.7Gbq and 5.55GBq) was given in Table -1.

Table-1: Shows effective half-life clearance of I-131 from the patients. The mean effective half-life clearance at the initial and final phase in the group 3.7GBq (100mCi) I-131 was found to be 13.72±4.21hr (range: 8.08 – 29.50) and 18.91± 21.55 hr (range: 8.84 – 177.42) respectively. Similarly, in 5.55GBq (150mCi) group, the effectively half-life in the initial and final phase was 12.43±1.90 hr (range: 7.70 – 16.06) and 19.25±6.39 hr (range: 10.41 – 34.13) respectively.

Since the number of patients in the groups of 80mCi, 120 mCi and 200 mCi were very less therefore we have not provided the statistical analysis.
Discussion
This study estimated effective half-life clearance of I-131 in DTC patients during the initial phase to be 13.07 hours (13.72 hrs in 3.7GBq (100mCi) group and 12.43 hours in 5.55GBq (150mCi) group. It is in good agreement with 11.2 to 15.4 hr as the effective half-life estimated on the Indian Population by Ravichandran et al (7) and also with the study conducted by Barrington et al who studied 86 patients and found the effective half-life to be 9.4hr, 13.4hrs and 12 hrs (8).

This study observed bi-exponential function of I-131 clearance. Barrington et al have found bi-exponential (7,8) and Sasikala A C et al (9) found it to be tri-exponential function. This difference may be due to the difference in the time of exposure measurement, Sasikala AC et al have measured the exposure rate at 1, 3, 5, 8, 24, 48m, 72 hr after post administration of activity and in our study it was measured immediately after I-131 dose administration, and after 19.57hr, 43.49hrs, 68.20hrs, 90.87hrs and in most of the cases only first three measurement points was available (Patients discharged after following regulatory discharged limit).

This study found faster clearance of I-131 in 5.55GBq (150mCi) group as compared to 3.7GBq (100mCi) group within 24 hrs. Tabei F et al (10) have found difference in effective half life in 3.7GBq (100mCi) and 5.55GBq (150mCi) group. Their difference is of approximately 4 hours (the initial phase) between 5.55GBq (150mCi and 3.7GBq (100mCi) group while in our study it was one hour.

In both the 3.7GBq (100mCi) and 5.55GBq (150mCi) group we found the difference in effective half-life between initial and final phase clearance of I-131. Tabei et al have also found the similar result, again in this case also, their difference is greater (27Hrs in comparison to 5 hours) than that of ours. This may be due to factors: patient population, remnant thyroid tissue present, frequency of measurement of exposure rate, and population size. In selected population if there is lot of variations in amount of remnant tissue, there will corresponding variation in retained activity. Tabei F et al (10) have measured exposure rate at five different times in each patient, in their country the discharge limit was less than 1mR/hr and was possible to have exposure data on consecutive five to six days. In our study the discharge limit was less than 50μSv/hr (5mR/hr) and hence our study had data upto 48hours and therefore we took 24hr and 48hr data points to calculate the final phase clearance.

The faster clearance of I-131 observed in case of 5.55GBq (150mCi) group in comparison to 3.7GBq (100mCi) group may be due to high degree of remaining activity after saturation of thyroid cancer tissues are available in the blood pool to be cleared through the renal or gastric route.

The amount of retained activity at 19.57hours was calculated and it was found that 64.32% and 65.95% of the activity is cleared from the body in case of 3.7GBq (100mCi) and 5.5GBq (150mCi) group respectively. Since around 65 % activity is released during the first 19/57hr, as the amount of administered activity increases, the excreted activity is very high, for example approx 6.66GBq (99mCi) in case of 5.55GBq (150mCi), and poses radiation risk to public and therefore these patients needs isolation and hospital requires delayed tank to store the excreta for decay up to the discharge limit set by radioactive waste disposal rule before releasing it to the environment. The period of isolation is pathetic for the patient. The creating space for isolation wards, delayed tank and its maintenance as per regulatory requirement is difficult for hospital administration.

Recently, Mallick U et al (11) has shown that the ablation success rates of low dose radio-iodine are similar to that of high dose radio – iodine. More studies of the similar kind is required and if the ablation success rate of low dose is found to be similar to the high dose then low dose precaution should be followed, this will reduce the financial cost involved in the treatment of the thyroid cancer with I-131 and isolation will not be required.
The final phase of the bi-exponential function has implication regarding the giving instructions to the patients after post therapy. The wide range of effective half-life of I-131 emphasized the incorporation of individualized restriction period for the patients. We recommend to tailor individualized the post therapy instructions based on the effective half-life clearance of the I-131.

It has been observed that few patients do not adhere to the instructions given after the post therapy scan and it had led to an accident in the past. K Laxman Parthasarathy’s observation was that after discharge, when patient was at home he developed cough and cold and due to this negligence didn’t followed instruction he threw used facial in dustbin and was collected as garbage by the truck carrying the non-radioactive garbage\[12\]. Negligence of not following the instructions ahs led other radiation accidents in India, however, not related with I-131 therapy. We recommend that while giving the instructions after post therapy it must be kept in mind that few patients do not follow the instruction and if in doubt, instructions need to be modified accordingly.

The exposure rate measured on 1st day but not exactly at 24hours, the mean time of measurement was 19.57hrs with a standard deviation of 1.45 and range was 7.83 (minimum 16.25 to maximum 24.08)

**Limitation of the study:** Our study was a retrospective study. The method or procedures adopted at the time of exposure rate measurements can influence the result of effective half-life clearance. Suppose for example, a patient have vertebral metastasis then exposure rate measured antero-posterior (AP) and posterior-anterior (PA) will differ in value and in both the cases the effective half-life will be difficult. This uncertainty may exist in our study and nothing can be done at this stage.

The data generated in this study is useful for the recommending the agencies in the radiation safety or regulatory authority to provide health providers with reasoned instructions on radiation safety for patients, their families, caregivers, and the public after radioiodine (I-131) therapy. These agencies derive recommendations from a review of current practices, expert opinions, and the literature.

The knowledge of effective half-life of I-131 is useful at the planning the next investigation to be carried out on the patient in which I-131 can introduce the scattered photons. It will also be useful in simulation and modeling studies related with radiation safety in DTC patients.

**Conclusions**

The mean effective half-life in the 3.7GBq (100mCi) group was 13.72 hrs at initial phase and 18.91 hrs at the final phase. The data generated in this study will be useful in formulating guidelines for the staff and the person coming close proximity to the patients during and after the high dose I-131 therapy.

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