Effect of administrated activity, admission number and TSH level on radiation retention curve of patients taking iodine-131 therapy for differentiated thyroid carcinoma: Looking beyond established regulations

Original Article

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ABSTRACT

Introduction: Retention of I-131 in the body of patients with differentiated thyroid carcinoma (DTC) has a direct effect on therapeutic outcome of radioiodine therapy. There are several factors that may influence retention time of radioiodine in the body of these patients. In this study we are going to assess effects of administered radioiodine activity, serum thyroid stimulating hormone (TSH) level and also admission/administration number on the retention of I-131 in the body of DTC patients.

Methods: Number of 92 DTC patients, with different TSH levels ranged from 32 mIU/ml to 250 mIU/ml, was treated with different I-131 activities ranged from 1850 MBq to 7400 MBq. They received one, two or three sessions of radioiodine therapy based on severity of cancer. Post-therapy dosimetry for all the patients was performed immediately, 6 hours, 12 hours, 24 hours and one week after the administration of activity to calculate clearance rate of the I-131.

Results: Based on our observations, there was a direct correlation between administered radioiodine activities to the patients and clearance rate of the activity from their bodies. Also, those patients who had been admitted for the third time to receive their third radioiodine administration had higher clearance rate as compared to those who had their first or second admissions. TSH level above 32 mIU/ml did not show any effect on clearance rate of I-131.

Conclusion: Based on our findings, clearance rate of I-131 is affected by amount of administered radioiodine activities to the patients and number of radioiodine therapy sessions, but serum TSH level above 32 mIU/ml had no effect on this quantity.

Key words: Thyroid carcinoma; TSH; Dosimetry; Clearance rate; Radiation dose rate; I-131

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INTRODUCTION

Differentiated thyroid carcinoma (DTC) is a common malignancy that includes papillary and follicular histologies [1]. While incidence of this type of cancer is relatively high, but in comparison to other types of cancer it is associated with a favorable prognosis [2], and it is expected for DTC patients to have survival rate of up to 90% [3]. Vrachimis et al. in a study on 1497 DTC patients found that overall survival rates in stages I, II, III and IV were excellent [4]. Such a promising outcome is mainly because of the current efficient treatment, post-thyroidectomy radioiodine ablation that exists for DTC patients. Results of the several studies have indicated that application of I-131 in combination with total thyroidectomy and thyroid hormone suppression enhance effectiveness of these therapeutic procedures [5-7]. In one of these attempts, Baranauskas et al. observed that administration of thyroidectomy + radioactive iodine treatment + hormonotherapy with thyroxine to treat patients with follicular thyroid carcinoma is associated with overall survival rates of 91.2% for 10 year, 81.9% for 20 years and 77.1% for 30 years [8]. Application of I-131 after thyroidectomy destroys microscopic remaining carcinoma cells and consequently decrease recurrence probability of the malignancy [9, 10]. For this reason radioiodine is an important complementary component in the protocols used for treatment of DTC patients [11].

In radioiodine therapy, similar to other radiation therapy procedures, the ultimate goal is to deliver the highest dose to the target tissue while minimizing side effects in surrounding normal tissues. However, amount of the radioiodine activity necessary for an optimal therapeutic outcome is not clear yet [12]. While it seems that administration of high activities may lead to enhanced therapeutic effect, it is usually not recommended due to some implications.

In order for the patients to have an effective radioiodine therapy it is necessary that after I-131 administration, activity retain for a significant time in their bodies, providing enough time for I-131 to effectively expose thyroid gland. It's shown that absorbed dose to the blood, which determines activity available for thyroid tissue is a better predictor than administered activity to treat DTC patients [13]. Verburg et al. in their study that was performed on 499 DTC patients to assess effect of I-131 retention on ablation success, showed that successful ablation is better correlated with blood absorbed dose rather than with administered activity [13].

Retention of radioiodine in the blood of DTC patients not only depends on the function of the thyroid and renal systems but also can be influenced by the method used to prepare patient for radioiodine therapy. In a study performed by Papadimitriou et al. on 191 DTC patients with total or near-total thyroidectomy, they evaluated effect of recombinant human thyrotropin on preparation of patients for radioiodine therapy. Results of their study showed that retention and effective half-life of I-131 in the group of patients who were prepared for radioiodine therapy with recombinant human thyrotropin is less than the group who were prepared for therapy by discontinuation of levothyroxine suppression [14]. Also in a guideline provided by Luster et al. it's indicated that serum TSH level of ≥ 30mIU/ml may increase expression of sodium iodide symporter and consequently enhance I-131 uptake in the thyroid tissue [15].

Beside TSH level, it seems that admission\administration number of patients as well as amount of administered radioiodine activity have influence on clearance rate of radioiodine. The possible reason behind the first hypothesis is the change in the function of the thyroid after the first session of radioiodine ablation. Due to the cell damage occurred after the first radioiodine ablation, function of thyroid to absorb and keep iodine may decrease. As a consequent, clearance rate of radioiodine in the patients who receive their second or third radioiodine ablation may be more than those who receive their first I-131 therapy session.

The reasoning behind the effect of the amount of activity on clearance rate seems to be in the different response of the thyroid and renal systems to the different amount of the administered radioiodine activity. In order to investigate effects of these factors on the clearance rate of radioiodine in DTC patients, we studied effects of admission/administration number of patients and amount of administered radioiodine activities on I-131 clearance rate. Relation of TSH level of these patients with clearance rate of I-131 was also investigated.

METHODS

Number of 92 DTC patients (68 female and 24 male) were recruited into the study. All patients had a prior history of a total, or near total thyroidectomy. After the patients were explained by the nuclear medicine consultants about the procedure and got aware of the possible risks associated to the procedure they were accepted for their treatments in our nuclear medicine clinic. The I-131 dose taken was based on some parameters, including regional or distal metastases, levels of TSH and Tg. Level of TSH serum of the participants was measured by a 3rd generation TSH immunoradiometric assay and treatments were started 4 to 6 weeks after the last TSH measurement was done. After receiving the radioiodine capsules from the provider, their activities was measured using a dose calibrator (Capintec CRC-15R – Capintec Inc. Pittsburgh, PA U.S.A) then they were labelled and stored in the temporary storage. Before administration, activities of radioiodine were measured again to give the required amount of activity to the patient. After administration, the patients were restricted in the wards that was equipped with specialized disposal facilities for radioactive waste during their staying period. Based on the amount of the activity patients were received as their treatment, they were divided into four groups of treated with the I-131 activity of less than 1850 MBq, between 1850 and 3700 MBq, between 3700 and 5550 MBq, and between 5550 and 7400 MBq of I-131. Based on the stage of the thyroid cancer of each patient, they received one, two or three sessions of the radioiodine therapy. In order to assess effect of admission\administration number of the patients that is the number of radioiodine therapy sessions, on clearance rate of activity, patients were categorized into three different groups. After completing the radioiodine therapy, post-therapy monitoring were repeated in appropriate intervals until the patients were discharged. Measurement of external dose rate of treated patients was performed at a distance of 1m by a radiation-detection survey meter with an ionization chamber [Geiger (GM X5C plus) Counter, Graetz, Germany] calibrated in microsieverts per hour (μSv/h). During the measurements, each patient seat on a chair and the dosimeter was positioned in front of them approximately 1 meter above the ground. All dose rate measurements were performed after patients had emptied their bladders and in all measurements background dose rates were subtracted from the recorded values of the dose rates. The study complied with the Helsinki declaration and was accepted by the Institutional Ethics Committee of Isfahan University of Medical Sciences.

Statistical analysis

To determine clearance rate of I-131 in the body of patients over the time, the post-therapy dosimetry was performed immediately, 6 hours, 12 hours, 24 hours, 48 hours and one week following the administration of radioiodine. A repeated measurement ANOVA was performed to compare the dosimetry values at these six different time points. A P value of < 0.05 was considered statistically significant. All Statistical analysis was performed using an IBM computer and PASW software, version 18.0 (SPSS, Inc., Chicago, USA).

RESULTS

From the 92 patients included in the study 26% were male and 74% were female with 16.30% under 25 years old, 57.61% between 25 and 50 years old, 25% between 50 and 75 years old and 1.09% over 75 years old.

Based on the administered activity, patients were categorized into four groups of A≤1850 MBq (2.17% of patients), 1850<A≤3700 MBq (60.87% of patients), 3700<A≤5550 MBq (23.91% of patients) and 5550<A≤7400 MBq (13.04% of patients). Comparing clearance rates of these four groups, given in Table 1, showed that amount of administered activity had significant effect on retention of radioiodine in the body of patients (P=0.00). Patients who had received higher amounts of I-131 showed higher clearance rate in comparison to those who had received lower activities (Figure 1).

Of the patients who referred to our clinic to receive radioiodine therapy, 60 patients (65.22%) were treated with one radioiodine therapy session, first admission/administration, 26 patients (28.26%) were treated with two sessions, second admission/administration, and 6 patients (6.52%) were treated with three sessions, third admission/administration. After evaluating clearance rates of these three groups, we observed that there was significant difference among retention times of these groups of patients (Figure 2).

Based on our observation, patients who were admitted three times and had three radioiodine administrations showed higher clearance rate in comparison to other groups.

Table 1: Dose rates (µSv/h) of patients with different amount of administered radioiodine activities (MBq) over the time.

Time point post I-131 Administration (hours)	Mean of external dose rates			
	A ≤ 1850	1850 < A ≤ 3700	3700 < A ≤ 5550	5550 < A ≤ 7400
0	72	101	129	171
6	64	86	112	134
12	56	75	95	112
24	34	50	60	72
48	21	37	44	52
168	1.25	2	3	3

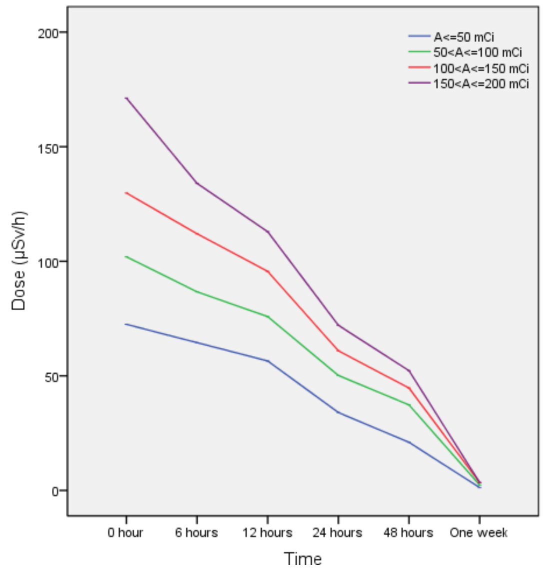

Fig 1. The figure demonstrates retention curves of I-131 in the body of patients with different administered activities.

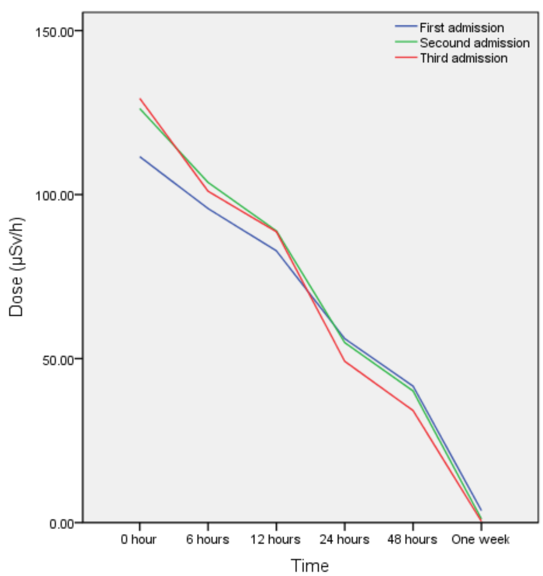

Fig 2. The figure demonstrates retention curves of I-131 in the body of patients with first, second and third admission.

According to the history of the patients, serum TSH level of the patients were in the range of 32 mIU/ml to 250 mIU/ml (mean=95.84 mIU/ml and median=85 mIU/ml). In order to asses effect of TSH level on the I-131 retention in the body of patients over the time, they were divided into three groups of TSH level <=85 mIU/ml (47 patients), 85 mIU/ml < TSH level <= 170 mIU/ml (39 patients) and TSH level > 170 mIU/ml (6 patients). Statistical analysis of the dosimetry data of each of these groups revealed that serum TSH level of the patient's body has no effect on clearance rate of radioiodine from the body of these patients (P=0.76) (Figure 3).

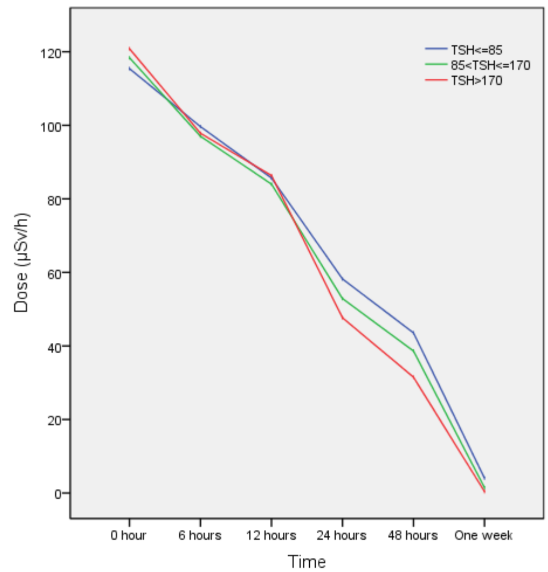

Figure 3. The figure demonstrates retention curves of I-131 in the body of patients with different serum TSH levels.

DISCUSSION

DTC is a common malignancy which includes papillary and follicular histologies [16-18]. For this type of cancer radioiodine ablation after thyroidectomy is a common proposed procedure, which is usually associated with favorable outcome [19]. In this therapeutic procedure, amount of administered radioiodine activity required to treat DTC patients has always been of controversial issues. In a study it's indicated that administering more than 100 mCi of radioiodine after thyroidectomy of patients with papillary thyroid cancer does not necessarily improve outcome of the therapy [20], and it was recommended that possible benefits of high activities should be outweighed with its corresponding potential risks. In another study performed on patients with papillary or follicular thyroid carcinoma who were treated with 30 mCi and 100 mCi of radioiodine following thyroidectomy, it was revealed that administration of low activity can be associated with a high risk of unsuccessful ablation [21]. While there is a discrepancy in the mount of administered activity for DTC patients, it is indicated that absorbed dose to the blood can be a more suitable indicator than administered activity to predict ablation success in patients with DTC. The reason behind this finding is based on this fact that absorbed dose to the blood determines amounts of activity available for the thyroid. As radioiodine retention in the body of the DTC patients is a predictor of the amount of activity available for thyroid glands and absorbed dose to the target, therefore we investigated whether administered activity, number of administration\admission and also serum TSH level influence I-131 retention in the body of DTC patients. These finding can be useful to enhance insight towards effective radioiodine ablation in these patients while avoiding possible side effects of administration of high amounts of radioiodine activity.

Measurement of the external dose rate of DTC patients treated with radioiodine is one of the established post-therapy methods used for estimation of activity in the body of patients [22]. Assessment of those parameters that may affect clearance rate of radioiodine from the body of these patients not only can provide useful information from radiation protection point of view but also can be used to improve protocol of radioiodine therapy. Results of previous studies have shown that clearance rate of radioiodine can significantly differ from one to another and mean effective half-life of I-131 in the body of patients may vary from 0.32 to 7.3 days [23, 24].

It is indicated that there is significant relation between administrated radioiodine activity and external dose rate of DTC patients treated with radioiodine. In a study by Azizmohammadi et al. on 100 DTC patients treated with 100 mCi, 150 mCi and 200 mCi of radioiodine, they showed that dose rate of patients increase as administered radioiodine activity increases [25]. In our study, in order to measure effect of administered radioiodine activity on its clearance rate we assessed four groups of patients with different administered activities. Based on our finding, there was a direct correlation between administered activity and clearance rate and higher clearance rate was observed in those groups who were administered with higher amounts of activities, leading to wash out of a significant portion of activity at the first hours after administration. While it seems that high amounts of activities may provide significant absorbed dose to the target, yet falling trend of radioiodine clearance is sharper in these patients in comparison to those who were treated with lower amounts of activities. This observation when it comes to the outcome of therapy, is an important issue to be considered while making the decision about the amount of administered activity. Patients who receive high amount of radioiodine activity are usually those whose grade/stage of their cancer is high and need considerable retention time of activity because of loco-regional or distant metastases. However, as we observed here, high activities are associated with high clearance rate that is a negative factor considering therapeutic effects of radioiodine therapy in these patients with the worst prognosis. This can make it even more difficult to come to an agreement regarding the optimum empirical administered activity for patients. Administration of high activities dose not necessarily lead to significant dose to the target. This finding more highlights the importance of patient specific dosimetry in estimating amount of administered radioiodine activity to the patient needed to reach to an optimum outcome.

One possible reason for this finding is the different functions and responses of the renal and thyroid systems to different amounts of administered radioiodine activities. It seems that thyroid gland reaches to a saturation status for higher activities of I-131 (>150 mCi) and consequently considerable portion of I-131 is cleared from the body of the patients in the first hours after radioiodine administration, increasing overall clearance rate of radioiodine. This is in a good agreement with the results of a previous study [26]. We also found that for all amounts of administered activities clearance curve of I-131 shows a rapid fall in the first hour's post-administration and significant portion of the I-131 is excreted in the first two days.

Patients were also assessed based on their radioiodine therapy sessions. We observed that there is a significant correlation between admission/administration number and retention time of radioiodine. Patients who were treated in their first admission, with one session of radioiodine therapy, showed slower clearance rate of radioiodine in comparison to the other patients. Slow radioiodine clearance means that the activity retains in the body for a long time, which in turn leads to a high dose delivered to the thyroid cancerous cells and probably batter therapeutic outcome. This finding may be because of the function of thyroid tissue that changes after radioiodine ablation. After radioiodine therapy of the thyroid gland, vast majority of cancerous thyroid cells are damaged. Since these cells retain radioiodine in the thyroid region, therefore after the first radioiodine therapy capability of thyroid to keep I-131 in its tissue decreases. Consequently, clearance rate of activity in patients' body increases as admission/administration number increases.

Based on the findings of Ejeh et al. that was performed on DTC patients with serum TSH level of 25.6 – 499.8 mIU/ml, level of serum at the time of radioiodine therapy of these patients was associated with improved therapeutic outcomes [27]. The reasoning behind this finding is that stimulation of serum TSH for radioiodine ablation stimulates the secretion of thyroglobulin and increases uptake of I-131 in thyroid tissue. Also Schneider et al. reported that there is a significant positive correlation between effective half-life of the radioiodine and serum TSH level of DTC patients [28]. However, results of our study revealed that TSH was not an effective factor on retention of I-131 in the body of patients and there was no significant difference in clearance rate of patients with different levels of TSH at the time of receiving I-131. One reason for this controversy may probably be in the small number of patients in our study. This limitation especially is seen in the group of patients with high TSH level (>170 mIU/ml) (6 patients) that may affect our findings and leads to disagreement with findings of previous studies. In another similar study on DTC patients treated with 100 mCi, 150 mCi and more than 150 mCi of radioiodine, the TSH levels were assessed in three different groups based on their cumulative doses and there was no difference in TSH level between these three groups [29].

The present study suffers from some limitations. Lack of sufficient number of patients in some groups as well as non-uniform distribution of patients in studied groups may have a negative impact on our findings. Therefore, for future studies it is recommended to perform a study with a larger number of patients and more uniform distribution of patients to have a more comprehensive assessment of factors that may affect clearance rate of I-131 in DTC patients.

CONCLUSION

We may conclude that administration of high amounts of activity in radioiodine therapy of DTC patients does not necessarily provide high amount of accumulated absorbed dose to the thyroid glands as clearance rate increases with increasing radioiodine activity. This should be considered while deciding about the optimum required activity for DTC patient. Radioiodine can retain for a longer time in the body of DTC patients in their first administration as compared to their second or third administration.

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