

## Research Article

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# Relationship between TSH Level and Effective Half-life of I-131 in Differentiated Thyroid Cancer Patients

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## Abstract

Thyroid carcinomas account for approximately 1% of all human cancers with the incidence of Differentiated Thyroid Carcinoma (DTC) varying from 2 – 10 per 100,000 but having a high prevalence due to good prognosis. It is reported that the survival rates of patients with DTC can reach as high as 90% as a result of effective therapy consisting of total thyroidectomy; with or without radioiodine ablation. Iodine -131 therapy is an integral component in the management protocol for DTC worldwide. The effectiveness of radioiodine therapy is linked to sufficiently elevated serum TSH levels in DTC patients at the time of treatment and the effective half-life of <sup>131</sup>I in these patients respectively. Sufficiently elevated TSH is important in using thyroglobulin as a tumour marker especially in patients with total thyroidectomy. The effective half life of <sup>131</sup>I in DTC patients is linked to the effective radiation dose (absorbed dose) to the remnant thyroid tissue which in turn is linked directly to the effectiveness and efficacy of radioiodine remnant ablation (RRA). This study was aimed at finding the relationship between the two entities. We studied 38 patients with DTC, 18 patients (47.4%) had total thyroidectomy and 20 (52.6%) had non-total thyroidectomy (sub-total, near-total, partial thyroidectomy or lobectomy). There were 29 females (76.3%) and 9 males (23.7%), age range 20 – 58 years (mean 36.74 ± 9.61 years), mean weight 72.29 ± 18.24 Kg. The patients had <sup>131</sup>I treatment, mean dose 4.93 ± 1.93GBq (dose range 3.26GBq – 12.21GBq). The effective half life of <sup>131</sup>I in these patients as calculated from measurements of the retained activity in the patients after 24h of <sup>131</sup>I administration ranged between 0.31 – 0.96 days, (mean 0.61 ± 0.18 days and median = 0.6 days). The TSH results for the patients ranged between 25.6 – 499.8mIU/ml (mean = 179.49 ± 125.59mIU/ml and median = 148.4mIU/ml). There is a significant positive correlation between the patients' serum TSH and the effective half life (P = 0.00119, r = 0.506), therefore, it is concluded that there is a direct linear relationship between the serum TSH level of patients with differentiated thyroid cancer and the effective half-life of <sup>131</sup>I during radioiodine therapy.

**Keywords:** <sup>131</sup>I therapy; Serum TSH; Effective half-life; linear correlation

## Introduction

Thyroid carcinomas account for approximately 1% of all human cancers [1,2] with the incidence of Differentiated Thyroid Carcinoma (DTC) varying from 2 – 10 per 100,000 [3,4] but having a high prevalence due to good prognosis [5]. It is reported that the survival rates of patients with DTC could be as high as 90% [6] due to effective therapy consisting of total thyroidectomy and radioiodine ablation. Treatment of patients with combination of total thyroidectomy, <sup>131</sup>I ablation and thyroid hormone suppression result in a lower recurrence rate than surgery alone or surgery plus external radiotherapy or surgery plus thyroid hormone [7]. As a result of this <sup>131</sup>I has become an integral component in the management protocol for DTC worldwide.

Iodine-131 destroys any remaining normal thyroid tissue and occult microscopic carcinomas thereby decreasing the risk of recurrence [8]. This benefit of radioiodine ablation of thyroid tissues can be fully achieved if the thyroid tissues take up a great percentage of the radioiodine that is administered. High TSH (thyroid stimulating hormone) level is used to stimulate both normal thyroid tissue and DTC to increase its uptake of <sup>131</sup>I and also to stimulate the secretion of thyroglobulin (Tg) [9]. Hence, the effectiveness of Radioiodine therapy (RAI) depends on the patient's serum TSH being sufficiently elevated to about ≥ 30mU/L which is believed to increase NIS (sodium iodide symporter) expression and thereby to optimize radioiodine uptake [10].

For the RAI therapy to be effective, the patient must also be able to retain the radioiodine for significantly long period of time. The

effective half life of <sup>131</sup>I in DTC patients is linked to the effective radiation dose (absorbed dose) to the remnant thyroid tissue which in turn is linked directly to the effectiveness and efficacy of radioiodine remnant ablation (RRA) [11]. The effective radiation dose delivered to thyroid cancer tissue to destroy it is the ultimate goal of using <sup>131</sup>I to treat DTC patients. A positive correlation has been shown between effective radiation dose and the outcome of <sup>131</sup>I therapy in patients with distant metastases [12,13]. Since the level of serum TSH and effective half life of <sup>131</sup>I in DTC patients are both related to the effectiveness of RAI therapy, we decided to investigate the relationship between effective half life of <sup>131</sup>I in DTC patients and their serum TSH level at the time of administration of the radioiodine.

## Subjects and Methods

### Patients

This study included 38 patients with DTC selected from those

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treated at a Teaching Hospital in South West Nigeria, from September, 2007 to November, 2010. Five other DTC patients were excluded from the study due to inadequate information on the serum TSH level at the time of RAI therapy. Eighteen (18) patients (47.37%) had total thyroidectomy, while 20 (52.63%) had non-total thyroidectomy (sub-total, near-total, partial thyroidectomy and lobectomy).

The patients had  $^{131}\text{I}$  treatment (dose range 3.26GBq – 12.21GBq, mean dose  $4.93 \pm 1.93\text{GBq}$ ) after signing a written informed consent.

The patients' induced hypothyroid states were by T4 withdrawal and this was confirmed by thyroid stimulating hormone (TSH) levels of  $\geq 25\mu\text{IU/ml}$  (optimal level  $30\mu\text{IU/ml}$ ) prior to therapy. The period between the last TSH result and therapy may range from 4-6 week in our center. TSH was measure by a 3<sup>rd</sup> generation TSH immunoradiometric assay.

The activity of the  $^{131}\text{I}$  capsules were measured in the dose calibrator (Capintec CRC-15R – Capintec Inc. Pittsburgh, PA U.S.A) and then given to the patients to swallow.

### Calculation of Retained Activity and Effective Half-life

Iodine is absorbed rapidly, immediately after ingestion, so the measurement of the whole body external exposure rate from the patient at 1m was carried out immediately after ingestion [14,15] using a calibrated RADIAGEM 2000 dose rate meter (Canberra Eurisys, Montigny-le-Bretonneux). The retained activity at 24h for each patient was then calculated based on the external exposure rate measurement using the equation 1 below:

$$A_{24} = \frac{A_0 E_{WB-24}}{E_{WB-0}} \quad (1) [14,16]$$

Where  $A_{24}$  is the retained activity at 24h,  $A_0$  is the administered activity,  $E_{WB-24}$  the whole body external exposure rate at 1m from the patient at 24h and  $E_{WB-0}$  is the initial whole body external exposure rate at 1m immediately after ingestion of the  $^{131}\text{I}$  capsule. The measurement and calculations were carried out for each patient until the retained activity reached  $\leq 555\text{MBq}$ , the level at which patients are discharged from isolation at our centre.

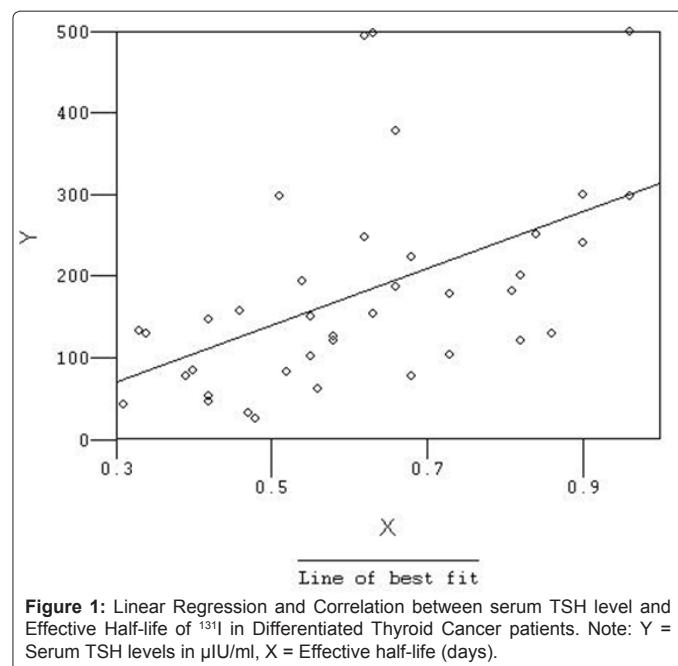
From the calculations of the retained activity, the whole body effective half life was calculated using equation 2 below:

$$A_{WB-t} = A_{WB-0} * e^{-0.693 * t / T_{\text{eff-WB}}} \quad (2) [16]$$

Where  $A_{WB-t}$  is the whole body retained activity at t days after administration as measured in equation 1 (in MBq),  $A_{WB-0}$  is the administered activity (in MBq), t is the post administration time (in days) and  $T_{\text{eff-WB}}$  is the whole body  $^{131}\text{I}$  effective half life (in days). Retained activity at 24h was considered for this work, hence, our t = 1 (in days). Linear regression and correlation of the serum TSH levels and the whole-body effective half lives at 24h post administration of therapy doses of  $^{131}\text{I}$  were computed. The computation was done using statistics software (Primer of Biostatistics for Windows, version 4.0, McGraw Hill, 1996).

### Results

Out of the 38 patients studied, 29 were females (76.3%) while 9 were males (23.7%), age range 20 – 58 years (mean age  $36.74 \pm 9.61$  years), mean weight was  $72.29 \pm 18.24\text{Kg}$  (range 44kg – 121.6kg).



Elevated TSH levels were achieved averagely after 4 – 6 weeks of discontinuation of levothyroxin. The effective half life of  $^{131}\text{I}$  in these patients ranged between 0.31 – 0.96 days (mean =  $0.61 \pm 0.18$  days and median = 0.6 days) while the TSH results for the patients ranged between 25.6 – 499.8mIU/ml (mean =  $179.49 \pm 125.59\text{mIU/ml}$  and median = 148.4mIU/ml). There is a significant positive correlation between the patients' serum TSH levels and the effective half life of  $^{131}\text{I}$  in these patients ( $P = 0.00119$ ,  $r = 0.506$ ), Figure 1.

### Discussion

$^{131}\text{I}$  retention in the body of patients determines its effective half-life in such patients. The effective half life of  $^{131}\text{I}$  in DTC patients calculated for our patients tallies with those of other authors based on different measurements and calculation procedures [16,17,18]. The mean effective half life presented by these authors, based on different number of patients, ranged from 0.32d to 7.3d with median values ranging from 0.35d to 0.74d respectively while our study found a mean of 0.61  $\pm$  0.18d, and a median of 0.6d for our patients.

Serum TSH secretion in thyroid cancer patients can be enhanced for radioiodine ablation or therapy by withdrawal of thyroid hormone replacement. The withdrawal of hormone replacement also stimulates endogenously potential residual or recurrent tumor foci. This procedure according to Podoba [19] is effective for therapy but has three drawbacks namely: its association with the predictable and almost universal morbidity of transient severe hypothyroidism with its attendant decrease in quality of life and diminished productivity, the prolonged stimulation of any residual cancer can occasionally induce tumor progression with clinical consequences in several special localizations of metastases, and the fact that some patients cannot surmount a sufficient endogenous TSH rise. So in a bid to elevate the TSH level of the patients for effective radioiodine therapy or ablation, the above drawbacks must be considered.

Linear regression and correlation of the serum TSH of the patients

and the effective half-life of  $^{131}\text{I}$  in these patients as computed in our study revealed a significant positive correlation. This finding suggests that effective half-life can thus be used as a marker for level of hypothyroidism during treatment for radioiodine should TSH result not be available. However, this condition could be affected by, the presence of metastases and intake of water and other fluids by the patient. The food content of the stomach of the patient can also influence absorption of the iodide from the stomach while the renal function can also affect the  $^{131}\text{I}$  retention and hence, it's effective half-life.

From the foregoing, and the fact that effective half could only be calculated after RAI treatment which ideally should not be instituted without confirmed hypothyroidism, the correlation can only be a retrospective confirmation of TSH value and cannot replace it in the pre treatment evaluation of patient for RAI treatment. It could however be informative to find the relationship between the effective half life, the tumour histology, age of the patient and effectiveness of therapy. Moreover literature search did not reveal previous use of effective half-life of Iodine-131 in DTC patients as a marker for level of hypothyroidism.

## Conclusion

Our study has shown a significant positive correlation between serum TSH level and effective half-life of  $^{131}\text{I}$  in Differentiated Thyroid Cancer patients. This study established a direct relationship between TSH and effective half life so the clinical significance of the study is to support existing information that significantly elevated TSH levels lead to high uptake and longer retention of Iodine-131 in DTC patients. Again, the scientific significance is still open to further research.

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