A retrospective study on fixed dose radioiodine therapy in patients with hyperthyroidism

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Abstract
Radioiodine therapy is an established mode of treatment of thyrotoxicosis with large range of etiologies. This study was carried out to assess the clinical outcome one year after administration of radioiodine therapy and also to identify whether any clinical features affect disease presentation and its response to treatment. Retrospective observational study was conducted in the nuclear medicine department of a multi-speciality hospital in which the records of 70 hyperthyroid patients were reviewed who were treated with the first dose of radioiodine during the inclusive period of August 2011 to August 2012. Among the 62 patients who completed follow-up, 24.3% of patients were euthyroid, 54.3% was hypothyroid while persistence or re-occurrence of hypothyroidism was seen only in 10% of patients. The incidence of hypothyroidism was 38.5% in first trimester, 12.8% in second trimester, and 2.8% in third trimester. There was no significant difference in the response rate to different doses of radioiodine treatment groups, age, gender, pretreatments with antithyroid drugs and its duration and presence of goiter and ophthalmopathy (p>0.05). The fixed dose RAI therapy was very effective treatment for patients with hyperthyroidism and has a high success rate. A total 88.7% of patients are successfully treated and only 11.8% is still hyperthyroid which suggest that a second dose is necessary in these patients. Hence it was proved that radioactive iodine treatment is an effective treatment modality for definitive treatment of hyperthyroidism with long term cure. The analysed demographic factors do not affect the outcome of I\textsuperscript{131} therapy in hyperthyroidism. A single fixed dose of radioiodine therapy is a simple, safe and effective treatment for hyperthyroidism.

Keywords: Radioiodine therapy, Hyperthyroidism, Graves’ disease, Hypothyroidism Euthyroidism.

INTRODUCTION
Hyperthyroidism refers to a clinical state of hypermetabolism and hyperactivity which results in enhanced function of the thyroid gland leading usually to a clinical state of thyrotoxicosis. The major causes of hyperthyroidism include Graves’ disease, solitary toxic adenoma, toxic multinodular goiter and thyroiditis. The less common causes include thyroid hormones producing tumours, pituitary resistance to thyroid hormones, trophoblastic disease and iodine ingestion [1-3]. The main treatment options for persistent hyperthyroidism are antithyroid drugs, radioactive iodine and surgery. All the three treatment options (ATDs, radioiodine and surgery) can be used as first line therapy. Graves’ disease is more common in females compared to males and is associated with firm diffuse goiter, as well as clinically evident ophthalmopathy. It is an autoimmune disease caused by an antibody that is active against thyroid stimulating hormone receptors.

ATDs are standard therapy for hyperthyroidism, either as first choice of treatment or as pretreatment before I\textsuperscript{131} therapy or surgery. Radioiodine therapy for hyperthyroidism was initially used in early 1940s. Saul Hertz and Arthur Roberts were the first to do so on March 31, 1941. I\textsuperscript{131} and I\textsuperscript{123} are the two isotopes of iodine used for imaging purposes and metastasis in differentiated thyroid cancers and quantifying thyroid function in hyperthyroidism. I\textsuperscript{131}, also called RAI has a physical half life of about 8.2 days. Because of its easy availability and emission of beta...
rays it is used for therapy in Graves’ disease, toxic nodules and TMNG. $^{123}$I has a physical half life of 13.2 hrs and its unavailability limits the use only in imaging.

Various techniques have been used to deliver the ample doses of radiation to the thyroid gland. They are calculated dose and fixed dose regimen. Calculated dose is determined according to the estimated weight of the thyroid gland and 24-hr uptake percentage. Calculated dose allows lower dosage and results in lower incidence of hypothyroidism but it has a higher recurrence rates. In fixed dose regimen an empirical dose of RAI is administered to the patients like 10 mCi for patients with GD and 15 mCi for TMNG. The incidence of hypothyroidism is similar regardless of the radioactive iodine dosage administered. There is little evidence that using a calculated dose has any benefit over a fixed dose regimen in preventing hypothyroidism. Hence the use of fixed dose regimen is convenient as it simplifies the approach to treatment [2,4].

Radioiodine is preferentially administered orally, but it can be administered in liquid form or intravenously in patients for whom vomiting is a problem. Compared to capsules, the liquid form is less expensive, can be stored easily and dispensed as needed, but the risk of contamination and spoiling is higher in capsules.

Hypothyroidism is the main side effect of radioiodine treatment. The rate of incidence varies and it increases over time, hence lifelong follow up is essential. Hormone replacement therapy is needed in all patients with elevated TSH after $^{131}$I therapy, and also in patients with subclinical hypothyroidism. There is an increased risk of the appearance or worsening of ophthalmopathy in patients with Graves’ disease on treatment with radioactive iodine. Autoimmune thyroiditis is observed in 1% of the patients following radioiodine therapy of goiter/ autonomous nodules. In patients with pre-existing thyroid peroxidase or $\text{Tg}$ antibodies, the risk is increased up to 10%. A small excess of mortality from radiation induced cancers has been reported. We aimed to determine the clinical condition of the patients receiving the first dose of radioiodine dose and whether any of the demographic factors influence the outcome of the therapy.

Regular review of thyroid function tests is essential to assess the efficacy of the treatment and for timely detection of developing hypothyroidism or post treatment immunogenic hyperthyroidism in patients who have undergone radioiodine treatment for thyroid disease. TSH and free T4 examination should be carried out 4-6 weeks after radioiodine therapy [5].

In patients with increased risk of endocrine ophthalmopathy, follow up should be done within a shorter interval of 2-3 weeks. In patients suffering from persistent hyperthyroidism, radioiodine treatment should be repeated after 6-12 months whereas in patients with post therapy immunogenic hyperthyroidism, ATDs taken for few months seems to be adequate and a second dose of radioactive iodine may not be required.

**Methods**

The study involved 70 randomly selected patients with hyperthyroidism, treated with $^{131}$I at the Department of Nuclear Medicine in Kovai Medical Center and Hospital. The study had the approval of the ethical committee of our institute. Informed consent was obtained from all participating subjects. The study was carried over a period from the month of Jan 2014 to July 2014.

The main objective of the study was to examine whether simple clinical features, such as gender, age and dose may affect both disease presentation and predict response to treatment in subjects with hyperthyroidism and also to study the incidence of hypothyroidism after radioiodine therapy according to time and assess the clinical outcome one year after administration of radioiodine therapy.

**Study Population**

Patients treated with the first dose of radioactive iodine for hyperthyroidism referred to the Nuclear Medicine Department of Kovai Medical Center and Hospital during the inclusive period of August 2011 to August 2012. Patients who were excluded from this study were those with severe Graves' ophthalmopathy, pregnant and Breast feeding women.

The data was collected from various sources such as patient’s case sheet, treatment chart, laboratory reports and nursing records. Patient information such as demographic data, diagnosis, RAI dose given, antithyroid drugs administered before and after RAI treatment, incidence of hypothyroidism or euthyroidism after treatment were collected. The thyroid hormone concentrations before and after treatment, incidence of goiter and ophthalmopathy were documented. Further, variables were analyzed
Studies done by Robert A.Nordyke proportion cured to change with age (p=0.899). In this study, there was no significant tendency for conditions in subjects above 35 years. According to indicated a higher incidence of hyperthyroid 49.06±9.05 and 49.21±10.21 years in females. This above 35 years, the mean age of male patients was 27.42±5.81 and 26.57±7.45 years respectively. The remaining 49 patients comes under the age limit of 27.42±5.81 and 26.57±7.45 years respectively. The mean age of study patients was found to be 42.56±13.44 years (range 15 to 72 years). 21 patients came under the category of less than 35 years with females and males with mean age of 27.42±5.81 and 26.57±7.45 years respectively. The remaining 49 patients comes under the age limit of above 35 years, the mean age of male patients was 49.06±9.05 and 49.21±10.21 years in females. This indicated a higher incidence of hyperthyroid conditions in subjects above 35 years. According to this study, there was no significant tendency for proportion cured to change with age (p=0.899). Studies done by Robert A.Nordyke et al so could not find any association between gender and outcome of therapy [6].

As hyperthyroidism is relatively more common in adult population, for convenient analysis patients were categorized based on the age limit into 2 groups i.e. less than 35 years and above 35 years. The mean age of study patients was found to be 42.56±13.44 years (range 15 to 72 years). 21 patients came under the category of less than 35 years with females and males with mean age of 27.42±5.81 and 26.57±7.45 years respectively. The remaining 49 patients comes under the age limit of above 35 years, the mean age of male patients was 49.06±9.05 and 49.21±10.21 years in females. This indicated a higher incidence of hyperthyroid conditions in subjects above 35 years. According to this study, there was no significant tendency for proportion cured to change with age (p=0.899). Studies done by Robert A.Nordyke et al so could not find any association between gender and outcome of therapy [6].

RESULTS AND DISCUSSION

At the beginning of the study 70 patients were included, but only 62 completed follow up. Among those 70 patients, 23 (32.9%) males and 47 (67.1%) females were enrolled. The female to male ratio was 2:1:1, showing a higher incidence of hyperthyroidism in females than in males. Even though females are more prone to hyperthyroidism, this had no influence on the outcome of therapy (p=0.2330). Similar studies conducted by Antony Lewis et al also could not find any association between gender and outcome of therapy [6].

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Clinical Graves’ ophthalmopathy was noted in 8 patients (11.4%) in which except one all others were female. About 62 patients (88.6%) were free from ophthalmopathy. Of the 8 patients who had ophthalmopathy, 5 patients was treated successfully and hence there was no significant risk of progression of ophthalmopathy among the study population. (p=1.00). Studies done by Wisam KG et al found out that there was no significant worsening or new development of ophthalmopathy post RAI treatment [9]. In contrast, a systematic reviews done by Shamasunder HA et al concluded that radioiodine therapy is associated with increased risk of progression of ophthalmopathy compared with antithyroid therapy and hence pretreatment with steroids is necessary [10].

Presence of goiter was assessed clinically by endocrinologists and was documented as either present or absent at the time of radioiodine administration. About 58 patients (82.9%) showed the presence of goiter and in 12 patients (17.1%) the signs of goiter were not present. No significant association was seen in this study on goiter and treatment success. (p=0.326). In contrast, previous studies done by Anthony Lewis et al revealed that patients with small or no goiter were more likely to be successfully treated by a single dose.
Prior use of antithyroid medication occurred in 63 patients (90%). Of these, 68.57% (48 patients) received treatment for more than one year whereas 21.43% (15) of patients received for a period of less than one year. Nearly 10% (7) of patients had no pre-treatment with antithyroid medication before RAI administration. Previous studies done by Joyce S Y Yau et al demonstrated that there was no significant association between anti-thyroid medication and radioiodine treatment within one year.

Among the study subjects who received pre-treatment, majority of the patients were treated with carbimazole (67.2%, 47 patients), followed by methimazole (15 patients, 21.4%). Only 1 patient among the 63 patients was treated with propylthiouracil (1.4%). All were advised to stop the drugs 7 days before radioiodine administration. There was no association observed between pretreatment with antithyroid drugs and treatment success (1.00). In a prior study done by Edward Prinat et al, treatment success was obtained in patients with no pre-treatment and those who have stopped ATD seven days before I\textsuperscript{131} administration, while in the group of patients who received MMI until I\textsuperscript{131} application, success was significantly lower. The primary objective of radioactive iodine therapy is to eliminate hyperthyroidism, but what is important to patients is the quickness of therapeutic effect. Figure 1 shows change in mean concentrations of TSH and T\textsubscript{4} before and after I\textsuperscript{131} administration. The result revealed an increase in TSH concentration after the RAI treatment whereas the T\textsubscript{4} level showed a decrease in the concentration which indicates that therapeutic effect is achieved in the hyperthyroid patients. Piotr Szumowski et al came up with a study which showed similar results [12].

Thyroid hormone concentrations before and after administration of radioiodine was analysed. A significant difference was found in the concentration of TSH and T\textsubscript{4} before and after radioiodine therapy in patients who are on thyroxine replacement therapy after RAI administration (p=0.000 & p=0.003 resp.). Whereas on comparing the concentration of TSH and T\textsubscript{4} prior and post therapy on who were not on drugs, there was no significant difference (p=0.533 & 0.057).

As the time after radioiodine administration elapses, the percentage of hypothyroid patients increases. The incidence of hypothyroidism was 38.5% (27) in first trimester, 12.8% (9) in second trimester and 2.8% (2) in the third trimester. A prior study done by Ajith S Shinto et al also reported a similar incidence of hypothyroidism after therapy [13]. (Figure 2).

The assessment of overall efficacy of treatment at one year after I\textsuperscript{131} administration showed that a euthyroid status was achieved in 24.3% (17) of patients, hypothyroidism was observed in 54.3% (38 patients), while persistence or recurrence of hyperthyroidism was seen in 10% of patients, which revealed that a second dose of radioiodine is required in these patients. This outcome meant that 75.7% of patients require further treatment. In that 38 patients requires further hormone replacement therapy and 7 patients requires a second dose of radioactive iodine. The achievement of euthyroid and hypothyroid status is considered as good result. Studies done by Mosako Tsuruta et al and Sirianong Namwongprom et al showed similar results. (Figure 3)

**Fig 1.** Thyroid hormone concentrations before and after therapy
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**CONCLUSION**

The analysed demographic and clinical factors had no effect on the outcome of $^{131}$I therapy in hyperthyroidism. On conclusion, high fixed dose RAI therapy is very effective treatment for patients with hyperthyroidism and has a high success rate. In this study 88.7% of patients are successfully treated and only 11.8% is still hyperthyroid which suggest that a second dose is necessary in these patients. Preventing the patient misconceptions is an important aspect of patient care. The concept that Clinical Pharmacist can have a positive impact on patient's Pharmaceutical care is becoming widely accepted. Hence clinical pharmacist can educate the patient about their medical conditions and the various treatment options available and the benefits of the treatments available.

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None.

**CONFLICT OF INTEREST**

None.
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REFERENCES


