

Incidence of Post Radioiodine Ablation Hypothyroidism in Cases of Toxic Diffuse Goitre

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Abstract

Background: Radioiodine (I-131) is one of the first line therapy for Toxic Diffuse Goiter (TDG) / Graves Disease (GD) with three possible outcomes – patient becomes euthyroid or remains thyrotoxic or permanently hypothyroid.

Aim: The present retrospective study aims to evaluate and estimate percentage of patients developing hypothyroidism often treatment with Radioiodine for TDG and assess its efficacy during concomitant use of thionamide medication.

Materials & Methods: 74 case records of patients attending Nuclear Medicine department of King George Hospital between 2012 Feb to 2013 Jan were reviewed thyroid hormones T₃, T₄, TSH were estimated by Radioimmunoassay (RIA) and Radioactive Iodine uptake (RAIU) was performed on 19 men and 55 women with a median age of 35 years. 22 patients were pretreated with Thionamide medication I-131 ablation was done with 2.5- 5.5 mci of calculated therapeutic dose.

Result: 74 patients were evaluated 19 were men 55 were women with the mean age of 35 years .9.46% (n=7/74) were hypothyroid within 3 months with a cumulative incidence of 43.2% (n= 32 / 74) in 1 year. 44.595 were euthyroid following therapy (n= 33 /74), 29.7 % (n=22/74) within 12 months while 14.86% (n=11/74) required more than a year. 12.2 % (n=9/74) had persistent hypothyroidism. Incidence of hypothyroidism was lower in the group that received thionamide medication 26.6% (n=8/30) compared to the group which was not pretreated with Antithyroid drugs (ATD) 68.57 % (n=24/35) was statistically significant

Conclusion: Smaller doses of I-131 2.5-5.5 mci may have contributed to the lower incidence of hypothyroidism as well as a smaller percentage of cure rates. While Intrathyroidal depletion by prior thionamide therapy was the causative factor that interfered with efficacy of Radioiodine and resulted in the apparent radio protective effect.

Keywords: Radioactive Iodine, Toxic Diffuse Goiter, Hypothyroidism, Antithyroid drugs (ATD)

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I. Introduction

Radioiodine therapy considered first line therapy in most adults with graves disease¹ is safe and effective^{2,3,4}. The goal of therapy is to induce permanent hypothyroidism. Overall 50% of patients become hypothyroid within one year. Most patients develop subnormal thyroxin that evolves into permanent primary hypothyroidism⁵. It is hypothesized that ATD pretreatment may interfere with the efficacy of radioiodine by acting as free radical scavengers with in the gland and exerting a potential radio protective effect^{6,7,8,9}. The present study aims to evaluate the percent of patient progress towards hypothyroidism within one year and assess the effect of outcome in patients treated with ATDs.

II. Materials & Methods

Case Records of 74 patients treated for TDG/GD between 2012 Feb to 2013 Jan at the department of Nuclear Medicine, King George Hospital (KGH), Visakhapatnam were evaluated. KGH is a tertiary referral hospital for patients from coastal Andhra Pradesh. Case records were selected based on the following

Inclusion criteria

1. Elevate blood levels of thyroid hormones . T₃, T₄, TSH estimated by RIA
2. 24 hr I-131 uptake elevated levels.

Exclusion Criteria-

1. All patients with multinodular goiter after appropriate RIA tests and diagnosed by fine needle aspiration cytology done at department of pathology Andhra Medical College, Visakhapatnam.
2. Patients with solitary toxic nodule
3. Complicating medical problems.

The determination of hypothyroidism was based on symptoms and

- (a) Low serum T₄
- (b) Increased TSH

(c) Disappearance of goitre¹⁰ T₃, T₄, and TSH hormones were assayed by RIA with strict adherence to protocols The patient's age range was 18 to 55 years with 19 males and 55 females. 22 patients had received pretreatment with thionamide preparation. Ablation done was calculated based on an estimated size of thyroid gland which is multiplied by the desired

delivered dose per gram of tissue (100-180 mci of I- 131) and this number is divided by the 24 hours uptake expressed as a decimal (ex: 80% uptake is converted to 0.80). The doses ranged between 2.5 to 5.5 mci. All variables were expressed as percentage and statistical significance was calculated as chi- square with probability value of < 0.01.

III. Results

74 patients received calculated doses 2.5 -5.5 mci of I-131 as treatment for TDG with the following outcome .55 were females & 19 were males .Their ages ranged between 18 and 55 years with median age of 41 years for men and 33 years for women . 22 cases had been pretreated with thionamide preparation before receiving therapy with I-131.hypothyroidism noted in 7 cases within 3 months was 9.46% (n=7/74) , 43.2%(n=32/74) was the cumulative incidence of hypothyroidism within 12 months of therapy. (Table.1, Fig. 1)

Table-1 - Outcome For Cases Of Tdg After Therapy With I-131 Calculated DOSES 2.5-5.5mci

NUMBER CASES AGE & SEX	HYPOTHYROID		EUTHYROID		PERSISTENT HYPERTHYROIDISM
	3 MONTHS	1 YR CUMULATIVE	1 YR	>1 YR	
74 19- MEN 55- WOMEN	7 (9.46%)	32 43.2%	22 29.7%	11 14.86%	9 12.2%

Figure-1 - Percentage Distribution For Outcome Euthyroid Cases In Present Study



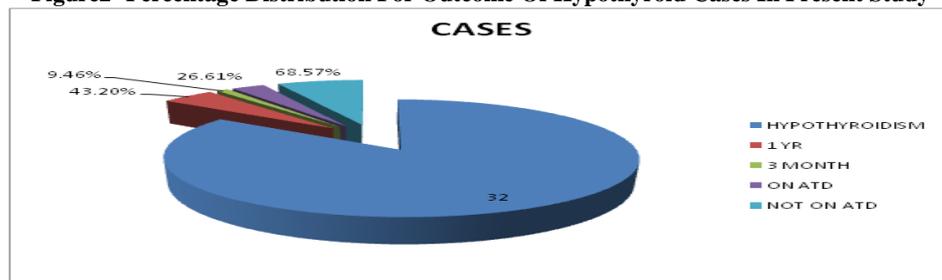
Their mean T4 (RIA) was 4.69 µg/dl with the range of 0.9 to 9.7µg/dl (normal range 7.8 to 14 µg/dl); mean T3 (RIA) 0.90 ng/dl, range of 0.1 to 1.4 (normal range 0.5 to 4.0 ng /dl) ;serum TSH(IRMA) values were elevated in 32 patients which ranged between 16 to >100 µIU/ml with the mean of 51.03µIU/ml. 24 hours RAIU(Radioactive Iodine Uptake) 48.10 % with the range of 16 -87% (Table 2)(.Fig2)

Table-2 - Distribution Of Cases And Thyroid Hormone Values And Raiu

CASE	T3 µg/dl	T4 ng/dl	TSH µIU/ml	RAIU %
HYPERTHYROID n= 74	5.14 (1.19-10)	23.76 (14.6-43)	0.17 (<0.01-0.1)	48.10 (16-87)
HYPOTHYROID n= 32	0.90 (0.1-1.4)	4.69 (0.9-9.7)	51.03 (16-100)	-
EUTHYROID n= 33	1.96 (0.5-4)	11.28 (7.8-14)	0.52 (0.30-4.30)	5-30%

*data for 9 cases of persistent. Hypothyroidism not shown.

Figure-2- Percentage Distribution For Outcome Of Hypothyroid Cases In Present Study



46% of patients had severe hypothyroidism with definite symptoms. The remaining had minimal symptoms and modest elevation of thyrotropin levels. All were started on replacement therapy L-Thyroxin including those with minimal

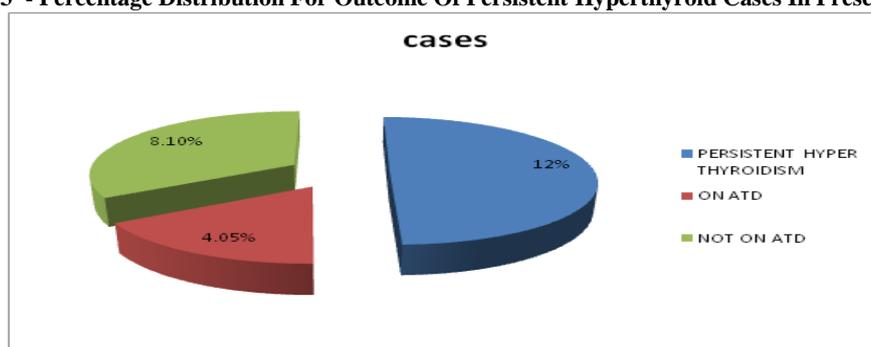
symptoms and definite shrinkage of goiter. 42 of the 74 patients did not become euthyroid during the first year. After a single dose (Table 3) (Fig3)

Table-3 – Thyroid Function Tests In Patients Of Tdg Before And After Therapy

STATUS	TOTAL	HYPOTHYROID	EUTHYROID	PERSISTENT HYPERTHYROID	EUTHYROID WITHIN 1YR
ATD +	33 (44.59%)	8 (26.6%)	22 (29.7%)	3 (4.05%)	10 (45%)
ATD 0	41 (55.40%)	24 (66%)	11 (14%)	6 (8.1%)	12 (54.5%)
TOTAL	74	32	33	9	22

ATDs-antithyroid drugs

Figure 3 - Percentage Distribution For Outcome Of Persistent Hyperthyroid Cases In Present Study



22 patients were euthyroid (29.7%) and 11 patients (14%) after more than one year and in 9 patients (12.2%) in whom persistence of hyperthyroidism was noted were treated with a second dose of I -131. Patients pretreated with thionamide were selected for such treatment according to the preference of the individual referring physicians and not due to clinical profile, gland size or their thyroid hormone test results but persistent TDG after 8 to 12 months of therapy with thionamide. This incidence of hypothyroidism was significantly lower 26.6% (n=8/30) compared to 68.57% patients (n=24/35) not pretreated with these medications (P<0.01 by chi square)

Hence thionamide therapy may have been a significant variable that determined the degree of response to I-131 therapy among the 2 groups.

IV. Discussion

Most patients with GD are effectively treated with one therapeutic dose of I – 131. After oral administration, I -131 is completely absorbed and rapidly concentrated in TFCs where Beta particles emitted by I -131 destroy TFCs which results in reduced thyroid hormone synthesis. Symptomatic improvement occurs within 3 weeks of therapy. Full effect takes 3 -6 months because stored hormone must first be released. Radioiodine therapy may not initially be effective in up to 10% of patients. They required repeat treatment usually with a higher administered dose. Dose selection takes into consideration size of gland and percentage of RAIU μ where large glands require a relatively higher dose and high percentage of RAIU need a lower dose. In estimation by palpation gland size is often underestimated in large glands. Low doses may be administered to minimize the radiation to patients. The two general approaches to decide on the approximate therapeutic dose comprise calculated dose (100- 200 μ Ci and fixed dose (10-15 mci) while Retrospective prospective studies^{11,12} have not shown major differences in outcome for the two methods of dose determination. Kehrana D et al¹³ recommend a calculated dose regimen from their study which had a 32% incidence of hypothyroidism at 3 months and 55% at one year. In a retrospective study¹⁴ of patients with graves diseases treated with a standard dose of 555 MBq 64% were hypothyroid at one year. The present study has followed calculated dose regimen erred on the side of caution perhaps on the side of caution with very low doses of 2.5- 5.5 mci of I-131. The 3 month incidence was low i.e 9.46% and 1 year incidence being 43%.

Because of release of preformed hormones can precipitate thyrotoxic crisis in the weeks following Radioiodine treatment^{15, 16} worsening of thyroid function is likely due to transient increase in TRAB¹⁷ in older patients or patient with severe disease are commonly given ATD agents before or after^{18, 19} Radioactive Iodine to maintain normal thyroid function and exert a radio protective effect.

Prior use of ATDs decreases thyrotoxic crisis and reduces chances of working ophthalmopathy. Recent prospective randomized studies²⁰ have shown that PTO has a negative effect on radio iodine outcome but methimazole did not have such an effect^{21, 22, 23}. Metso.S et al²⁴ in their 2004 study reported a cox regression model risk ratio (R.R 0.47) for antithyroid medication. Preceding radioactive iodine therapy decreased and female gender (RR 1.53) increased risk of hypothyroidism in patient with graves disease. Similar results were observed in the present study. Out of 7 cases which became hypothyroid within 3 months of therapy 6 were female and 66% (n=33) who on prior ATD became euthyroid. Study of Vanhope et al²⁵ noted similar radio protective effect of ATDs. Only 55% cases on thionamide became hypothyroid compared to 76% who

were not on these medications. In the present study only 27% (n=8/30) who received prior ATDs were hypothyroid vs 66% (n=24/35) who were not on thionamide medication with a similar outcome, while the overall incidence of hypothyroidism was 43.2% (n=32/74). The present study is limited by small sample size and single group of patient population. Our finding should be verified in a larger sample size of patients with inclusion of toxic adenoma, multinodular goiter along with graves disease.

V. Conclusion

As the development of hypothyroidism is inevitable the objective of Radioactive iodine therapy should be to minimize the persistence of hyperthyroidism. The low incidence of hypothyroidism in the present study may be explained by the calculated low doses used and the large percentages of patients were protected by thionamide medication.

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