A Comparison between High Ablative Versus Usual Dosages of Iodine-131 in Inducing Hypothyroidism After One Year of Therapy in Hyperthyroid Patients

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ABSTRACT

Background: Radioactive iodine-131 therapy is highly effective in treating patients with hyperthyroidism. An ablative dose is preferred by a number of endocrinologists, and, a fixed dose protocol seems to be better than a calculated dose in real practice.

Objective: To check for hypothyroidism in hyperthyroid patients one year after RAI therapy, comparing between the results of high ablative versus usual dosages of RAI-131.

Methods: This study included 174 hyperthyroid patients, 101 males and 73 females, divided into 2 groups, the first consisted of 162 patients given a usual fixed dose of RAI while the second consisted of 12 patients given a high fixed ablative dose of RAI. The study lasted about 2 years from August 2000 till July 2002 in the Specialized Centre for Endocrinology & Diabetes, Baghdad.

Results: Out of 162 patients in the first group, 11 patients (6.8%), developed hypothyroidism compared to 4 patients out of 12 (33.3%) in the second group ($p < 0.05$).

Conclusion: A high ablative dose RAI has a better outcome regarding hypothyroidism than a usual dose, although, endocrinologists have different opinions regarding this issue.

Keywords: hyperthyroidism, ablative dose, RAI-131.

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INTRODUCTION

The most common form of hyperthyroidism is Graves disease, which is an autoimmune disease, its main point in the pathophysiology is the presence of thyroid stimulating immunoglobulin (TSI), coming next is toxic nodular goiter due to autonomous solitary nodule or multiple thyroid nodules [(1)].

Hyperthyroidism has been treated with iodine-131 for over 50 years. The aim of therapy with iodine-131 in hyperthyroidism is to destroy sufficient thyroid tissue to end with euthyroid or hypothyroid state. Iodine-131 is a beta-emitting radionuclide with a maximum energy of 0.61 Mev. Iodine is the precursor of thyroxin, the radioactive form of iodine is taken up by iodine transporter of the thyroid, in the same way as the natural iodine [(2)].

Good number of patients is reluctant to be treated with radioactive iodine (RAI), especially in our country Iraq, as some believe that RAI might lead to cancer, others are concerned about the occurrence of permanent hypothyroidism. Radioactive iodine carries a small risk of aggravating eye problem in Graves disease, especially in smokers [(3)].

Contraindications to the use of RAI are pregnancy, lactation and active ophthalmopathy, but the relative contraindications to RAI with the last mentioned point are controversial [(4)].

The use of RAI therapy might be the 1st line of therapy for hyperthyroidism in some countries like the United States or when the patient has recurrence of the hyperthyroid state after completing a course of anti-thyroid drugs (ATDs), or when surgery is not a feasible way of treatment [(5)].

Although RAI may cause cell mutation and cell death, all iodine isotopes are rapidly taken up by the thyroid follicles, thus only thyroid follicles undergo organification, this will lead to highly localized destruction of thyroid follicles. RAI disrupts thyroid hormone biosynthesis and causes necrosis of follicles and blood vessels. RAI half-life is approximately 8 days and it results in euthyroidism in about 6-18 weeks. Most often, hypothyroidism is a long-term effect of RAI which makes life-long thyroxin therapy a necessity. Hypothyroidism usually occurs 1st year after RAI treatment, but it may manifest several years post-RAI

therapy, necessitating a long-term follow up [6].

METHOD

This is a prospective randomized comparative study which was conducted in the Specialized Center for Endocrinology and Diabetes-Baghdad and included 174 patients with hyperthyroidism (101 males, 73 females).

Every patient was followed for one year after RAI therapy. The study lasted about two years from August 2000 till July 2002. The age range was 30-65 years. The patients were divided into groups, the 1st included 162 patients (92 males and 70 females), and the 2nd group included 12 patients (9 males, 3 females). The 1st group patients were treated with a usual dose iodine-131 according to the fixed dose protocol, the 2nd group patients were treated according to a high-ablative fixed dose protocol.

Iodine-131 decays by emission of Gamma radiation of 365 kev (81.2%), and 637 kev (7.3%) and 284 kev (6.1%) and beta radiation of maximum energy 606 kev to stable xenon-131. Sodium iodide-131 is prepared in a capsule that is put in a suitable shielding container with activities of 50-3700 MBq per capsule at calibration date.

All patients were rendered medically euthyroid whenever possible before giving iodine-131 capsule. The dose of iodine-131 in the 1st ranged from 185 MBq to 555 MBq, while in the 2nd group it ranged from 296 MBq to 925 MBq.

Anti-thyroid drugs (ATAs) were stopped at least 5 days before giving RAI.

On RAI treatment day the patients were advised to take a little breakfast. Each patient was followed for one year to look for the appearance of hypothyroidism.

RESULTS

Table (1) shows some demographic data in both groups with male preponderance (58 % vs 41.95%). Table (2) shows the evidence of hypothyroidism in the 1st group after one year of RAI, Graves' disease constitutes 66.7% of cases, 10 having hypothyroidism after one year compared to one case with MNG and toxic adenoma ($p< 0.05$), the total (11 patients) contitute 6.8% out of 162.

Table (3) shows the evidence of hypothyroidism in the 2nd group after one year of RAI. Again, Graves' disease cases dominate (66.7%) compared to toxic MNG and toxic adenoma with 4 patients with Graves' disease showing hypothyroidism after one year which is equal to 33.3% of the total of 12 patients ($p<0.01$).

Table (4) shows a comparison of results of both groups regarding hypothyroidism after one year of RAI therapy, 6.8% in the 1st group versus 33.3% in the 2nd group ($p<0.05$).

Table 1: Demographic data in the two groups.

Group	No.	Male	Female
1st	162	92 (56.8%)	70 (43.2%)
2nd	12	9 (75%)	3 (25%)
Total	174	101(58%)	73 (41.95%)

Table 2: The evidence of hypothyroidism after one year in the 1st group.

Category	NO.	Hypothyroidism after1 year
Toxic Diffuse goiter (Graves' disease)	108 (66.7%)* 56 M, 52 F	10 3 M, 7 F
Toxic MNG	28 (17.2%) 20 M, 8 F	1 M
Toxic adenoma	26 (16.1%) 16 M, 10 F	Zero
Total	162 (100%) 92 M, 70 F	11 (6.8%)
***p-value<0.05 M=male, F=female.**		

Table 3: The evidence of hypothyroidism after one year in the 2nd group.

Category	NO.	Hypothyroidism after 1 year
Toxic Diffuse goiter (Graves' disease)	8(66.7%) *7 M, 1F	4 F
Toxic MNG	2(16.7%) M	Zero
Toxic adenoma	2(16.6%) F	Zero
Total	12 (100%) 9 M, 3 F	4 (33.3%) F
***p-value<0.01 M=male, F=female.**		

Table 4: Comparison of results in both groups.

Group	Total No. of hypothyroidism cases	Percent
1st	**11 (162)**	**6.8**
2nd	**4 (12)**	**33.3***
***p-value<0.05**		

DISCUSSION

In our study there is male preponderance, while in other studies, it is the opposite, this is because female patients in Iraq are reluctant to RAI therapy when compared to male patients, fearing of the possibility of post-RAI malignancy, as it is shown in Table 1 (58% males versus 41.95% females).

Graves' hyperthyroidism is the most common in both groups in the study (66.7%) compared to 33.3% of both other categories of patients (Toxic MNG and Toxic adenoma).

We can see in Table (2) that in the 1st group (162 patients) 10 Graves disease patients developed hypothyroidism after one year of RAI therapy compared to one patient of those with toxic MNG and zero in those with toxic adenoma ($p<0.05$). This No.of 11 is equal to 6.8% of the total No. of 162.

In Table (3) we can see 4 patients with Graves' disease developed hypothyroidism after one year of RAI therapy (in the 2nd group) which constitutes 33.3% of the total of 12 patients ($p<0.01$).

We can see in Table (4) the comparison between the two groups regarding the occurrence of hypothyroidism one year post-RAI, 6.8% out of 162 patients in the 1st group with usual doses compared to 33.3% out of 12 in the 2nd group who were given a high ablative dose RAI ($p<0.05$). This indicates the better effect of ablative therapy than giving a small dose of RAI which we encourage to use. Sunita study (2012) showed that 77% of cases of hyperthyroidism are due to Graves' disease followed by toxic single and/or multinodular goiter [(7)].

The occurrence of hypothyroidism is higher among cases of Graves' disease because the cells are mostly hyperfunctioning, so the RAI is taken up by the gland tissue in a uniform way and the destruction is more, so hypothyroidism occurs earlier than the other categories of toxic goiter.

Robert A. in 1992 mentioned that hypothyroidism follows sooner or later in nearly all patients and its occurrence within one or two years after RAI is related to dose, the author also mentioned that the fixed dose approach is a simpler alternative for deciding on the amount of iodine-131 to administer and the cure with fixed doses greater than 10 mCi [(8)].

Kakit Wong (2018) mentioned that the mean time between the diagnosis of hyperthyroidism and referral for RAI therapy was 325.9 days with 78.2% of patients referred within one year for RAI treatment and the longest interval was 18 years, showing the big delay in referral, and the same author mentioned that many endocrinologists prefer the ablative dose of RAI to treat Graves' hyperthyroidism [(9)]

The American Thyroid Association (ATA) recommends a wide range of RAI dosage

from 370-555 MBq for Graves' disease (GD) and 370-740 MBq for MNG and toxic adenoma [10, 11].

In most studies the cumulative evidence of hypothyroidism during the first year post-RAI was ranging from 50-75.9% (12-17), while it was low in our study which was 6.8% for the 1st group (162 patients) and 33.3% for the 2nd group (12 patients). This is because we measured the one year post-RAI evidence for hypothyroidism in contrast to other studies where hypothyroidism was tested after 3 months, 6 months, 9 months and 12 months post-RAI (cumulative evidence).

This is because most of our patients did not come regularly for follow up. This can be clearly shown in the study performed by Peacey S. R. and colleagues (2012) who stated that 67% of post-RAI patients developed hypothyroidism and the details are as follows: hypothyroidism was detected in 16% at <8 weeks, 46% at 8 to <16 weeks, 24% at 16 to <24 weeks, 9% at 24 to <36 weeks, 3% at 36 to <52 weeks, and 2% at > 52 weeks [18].

CONCLUSION

This study included a total of 174 patients divided in two groups (162 versus 12 patients), the first was treated with a fixed usual dose of RAI and the second treated with a high fixed ablative dose protocol. The second method is more effective in ablating hyperthyroidism than the first one (6.8% in the first group versus 33.3% in the second group) and we encourage using the second policy in order to ensure that hyperthyroidism will not recur and to abate the need for a second or a third dose of RAI therapy. The difference between our study and others is that other studies used the cumulative percent of hypothyroidism during the first year of therapy, while we checked for hypothyroidism after one year of RAI because our patients did not come for follow up regularly.

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