A Study of Carbimazole Treatment in Hyperthyroidism Comparison with Radioiodine

Virupaksha K L, Prashanth S, Thota Naga Raghunandan, Sayed Afaque Hyder

1. Introduction

Hyperthyroidism is a pathological syndrome in which tissue is exposed to excessive amounts of circulating thyroid hormone. Hyperthyroidism is a disease in which the thyroid gland synthesizes and secretes excessive hormone [1]. Hyperthyroidism is ten times more common in women than men and has a prevalence of 2.5-4.7 per 1000 women [2]. Hyperthyroidism is common, affecting approximately 2 percent of women and 0.2 percent of men [3]. Various modalities of treatment (antithyroid drugs, surgery and radio iodine) can be offered to the patient to treat hyperthyroidism. The choice of therapy varies according to non biological factors – physician’s training and personal experience; local and national practice patterns; patient, physician and social attitude towards radiation exposure; biological factors including age, reproductive status and severity of disease [4].

2. Methodology

2.1 Source of data

Study included 75 patients attending outpatient department (OPD)/admitted in S.S. Hospital, Davangere, with signs and symptoms of hyperthyroidism during study period from August 2012 to August 2014.

2.2 Methods

Following collection of data in pretested proforma which included detailed history, physical examination and confirmation of hyperthyroidism by total triiodothyronine (T$_3$), thyroxine (T$_4$) and thyroid stimulating hormone (TSH) measured by Chemiluminiscence immunoassay on fully automated ACS:180:SE. Routine laboratory investigations like Haemoglobin (Hb), total count (TC), differential count (DC), erythrocyte sedimentation rate (ESR), peripheral blood smear (PBS), Random blood sugar (RBS), blood urea, serum creatinine, Electro cardiomgram (ECG) and Chest x-ray postero anterior (PA) view were done for all patients. Patients with drug therapy group received carbimazole (neomercazole) 10 milligrams thrice daily followed by maintenance dose of 10mg twice daily once patients achieved euthyroid state or radioiodine therapy group received 10-15 milli curies (mCi) of radio iodine 131. Total triiodothyronine (T$_3$), thyroxine (T$_4$), thyroid stimulating hormone (TSH) and total count (TC) were done once in every 3 months and patient was followed-up for minimum of 6 months and maximum of 18 months period following initiation of treatment.

Results: Study included 75 patients with hyperthyroidism in which 50 patients were in drug therapy group and 25 patients were in radioiodine therapy group. After antithyroid drug therapy, 90.9% of patients with hyperthyroidism became euthyroid in 12 months of therapy, 6% of patients remained hyperthyroid at the end of 18th month, 5.6% of patients developed hypothyroidism at the end of 18th month. There was no incidence of adverse side effects with antithyroid drug. After radioiodine therapy, 36% of patients were euthyroid after 3 months, 76.5% of patients developed hypothyroidism at the end of 12th month, 14.3% of patients remained hyperthyroid at the end of 18th month.

Conclusion: Among the available treatments for hyperthyroidism, radioiodine is the most effective treatment for controlling the hyperthyroidism but hypothyroidism is a common complication. There was a good response to antithyroid drug with lesser side effect of hypothyroidism.

Keywords: Hyperthyroidism, Antithyroid drug, Radioactive iodine, Euthyroid, Hypothyroid.
2.3 Inclusion Criteria

a) Age between 20-60 years.
b) Patients with history and clinical features suggestive of hyperthyroidism.
c) Laboratory criteria include increased triiodothyronine (T3) and thyroxine (T4) with decreased thyroid stimulating hormone (TSH) levels.
d) Only those cases of thyrotoxicosis that are caused by increased thyroid function.

2.4 Exclusion criteria

a) Age less than 20 years and more than 60 years.
b) Hypothyroid patients.
c) Subclinical hyperthyroid patients.
d) Thyroid malignancy associated with hyperthyroidism.
e) Transient thyrotoxicosis of thyroiditis.
f) Hyperthyroidism associated with comorbid condition like diabetes mellitus (DM), hypertension (HTN), ischemic heart disease (IHD), chronic obstructive pulmonary disease (COPD) and chronic renal failure (CRF).

3. Statistical Methods

All the statistical calculation (frequencies, chi square test, cross tabs) were performed using the software SPSS for windows (statistical presentation system software, SPSS Inc, 1999, New York) version 10.

4. Results

4.1 Age and Gender Distribution

In our study, out of 75 patients, 35 (46.7%) patients were in the age group of 31-40 years followed by 21 (28%) patients were in the age group of 20-30 years. 61 (81.3%) patients were females and 14 (18.7%) were males, female to male ratio of approximately 4.35:1.

4.2 Type of Hyperthyroidism

In our study, out of 75 patients, 57 (76%) patients had Graves’ disease (GD), 14 (18.7%) patients had toxic multinodular goiter (T MNG) and 4 (5.3%) patients had toxic adenoma (T A).

4.3 Response Following Treatment

4.3.1 75 cases treatment response

All 75 cases were followed up for 6 months in both drug therapy group and radioiodine therapy group. At the end of 6th month, in drug therapy group 34 (46.7%) patients were euthyroid, 13 (26.0%) patients were hyperthyroid and 3 (6.0%) patients were hypothyroid. In radioiodine therapy group 16 (64.0%) patient were hypothyroid, 5 (20.0%) patients were euthyroid, and 4 (16.0%) patients were hyperthyroid as shown in table 2.

4.3.2 50 cases treatment response

50 cases were followed up for 12 months in both drug therapy group and radioiodine therapy group. At the end of 3rd month, in drug therapy group 21 (63.6%) patients were hyperthyroid, 11 (33.3%) patients were euthyroid and 1 (3.0%) patient was hypothyroid. In radioiodine therapy group 8 (47.1%) patients were hyperthyroid, 4 (23.5%) patients were euthyroid and 5 (29.4%) patients were hypothyroid as shown in table 3.
At the end of 9th month, in drug therapy group 26(78.8%) patients were euthyroid, 6(18.2%) patients were hyperthyroid and 1(3.0%) patient was hypothyroid. In radioiodine therapy group 12(70.6%) patient were hypothyroid, 3(17.6%) patients were hyperthyroid and 1(5.6%) patient was hypothyroid as shown in table 5.

At the end of 12th month, in drug therapy group 30(90.9%) patients were euthyroid, 2(6.1%) patients were hyperthyroid and 1(3.0%) patient was hypothyroid. In radioiodine therapy group 13(76.5%) patient were hypothyroid, 3(17.6%) patients were hyperthyroid and 1(5.6%) patient was euthyroid as shown in table 6.

All 75 cases were followed up for 6 months in both drug therapy group and radioiodine therapy group. At the end of 3rd month, in drug therapy group 22(44.0%) patients were euthyroid, 27(54.0%) patients were hyperthyroid, and 1(2.0%) patient was hypothyroid. In radioiodine therapy group 9(36.0%) patients were euthyroid, 9(36.0%) patients were hyperthyroid and 7(28.0%) patients were hypothyroid. At the end of 6th month, in drug therapy group 34(68.0%) patients were euthyroid, 13(26.0%) patients were hyperthyroid and 3(6.0%) patient were hypothyroid. In radioiodine therapy group 16(64.0%) patient were hypothyroid, 5(20.0%) patients were euthyroid, and 4 (16.0%) patients were hyperthyroid. 50 cases were followed up for 12 months in both drug therapy group and radioiodine therapy group. At the end of 12th month, in drug therapy group 30(90.9%) patients were euthyroid, 2(6.1%) patients were hyperthyroid and 1(3.0%) patient was hypothyroid. In radioiodine therapy group 13(76.5%) patient were hypothyroid, 3(17.6%) patients were hyperthyroid and 1(5.6%) patient was euthyroid.

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4.3.3 25 cases treatment response

25 cases were followed up for 18 months in both drug therapy group and radioiodine therapy group. At the end of 15th month, in drug therapy group 16(88.9%) patients were euthyroid, 1(5.6%) patients were hyperthyroid and 1(5.6%) patient was hypothyroid. In radioiodine therapy group 4(57.1%) patient were hypothyroid, 2(28.6%) patients were euthyroid and 1(14.3%) patient was hyperthyroid as shown in table 7.

At the end of 18th month, in drug therapy group 16(88.9%) patients were euthyroid, 1(5.6%) patient was hyperthyroid and 1(5.6%) patient was hypothyroid. In radioiodine therapy group 4(57.1%) patients were hypothyroid, 2(28.6%) patients were euthyroid and 1(14.3%) patient was hyperthyroid as shown in table 9.
At the end of 6 hyperthyroid patients were euthyroid, 13 (26.0%) patients were persistent group 9 (36.0%) patients were euthyroid, 9 (36.0%) patients were hypothyroid, 2 (28.6%) patients tolerated the drug treatment without any side effects. Cooper D S et al [5] reported that the agranulocytosis following drug treatment occurs in approximately 1 out of every 200 patients (0.5%) and it almost invariably occurs within first 3 months of therapy.

Table 9: Summary of Treatment Response

<table>
<thead>
<tr>
<th>Duration of follow-up (n)</th>
<th>Treatment response</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Drug therapy</td>
</tr>
<tr>
<td></td>
<td>Euthyroid</td>
</tr>
<tr>
<td>3 months(75)</td>
<td>22(44.0%)</td>
</tr>
<tr>
<td>6 months(75)</td>
<td>34(68.0%)</td>
</tr>
<tr>
<td>9 months(50)</td>
<td>26(78.8%)</td>
</tr>
<tr>
<td>12 months(50)</td>
<td>30(90.9%)</td>
</tr>
<tr>
<td>15 months(25)</td>
<td>16(88.9%)</td>
</tr>
<tr>
<td>18 months(25)</td>
<td>16(88.9%)</td>
</tr>
</tbody>
</table>

n – Number of cases

5. Discussion

In our study, a total of 75 patients in which 50 patients were in drug therapy group and received 10mg of carbimazole thrice daily followed by maintenance dose of 10mg twice daily once patients achieved euthyroid. 25 patients were in radioiodine therapy group and received 10-15 mCi of radioiodine 131.

All 75 cases were followed up for 6 months in both drug therapy group and radioiodine therapy group. At the end of 3rd month, in drug therapy group 27(54.0%) patients were hyperthyroid, 22(44.0%) patients were euthyroid and 1(2.0%) patient was hypothyroid. In radioiodine therapy group 9(36.0%) patients were euthyroid, 9(36.0%) patients were hyperthyroid and 7(28.0%) patients were hypothyroid. At the end of 6th month, in drug therapy group 34(68.0%) patients were euthyroid, 13(26.0%) patients were persistent hyperthyroid and 3(6.0%) patients were hypothyroid. In radioiodine therapy group 16(64.0%) patients were hypothyroid, 5(20.0%) patients were euthyroid and 4(16.0%) patients were persistent hyperthyroid.

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No patients developed agranulocytosis. All the patients tolerated the drug treatment without any side effects. Cooper D S et al [5] reported that the agranulocytosis following drug treatment occurs in approximately 1 out of every 200 patients (0.5%) and it almost invariably occurs within first 3 months of therapy.

Macfarlane IA et al [6] in this study, 21 patients treated with carbimazole 30 mg daily and followed-up for more than 1 year (median 77 weeks). All patients became euthyroid with normal serum thyroxine (T4) levels, usually within 1-3 months.

D Reinwein et al [7] in this study, 309 patients of Graves’ hyperthyroidism in which 153 patients received 10 mg of methimazole (MMI), 156 patients received 40 mg of MMI and followed up for 12 months. With 10 mg of MMI daily, 68.4% of the patients were euthyroid after 3 weeks and 84.9% after 6 weeks compared to 83.1% and 91.6% respectively with the use of 40 mg MMI daily.

Mayuree Homsanit et al [8] in this study, 71 patients of Graves’ disease received 15 mg of methimazole or 150mg of propylthiouracil (PTU) and followed up for 12 weeks. More patients achieved euthyroidism at 12 weeks, almost one-third of patients were biochemically hypothyroid at 12 weeks.

Antony P W [9] mentioned that after radioiodine therapy, 70% of patients became euthyroid in 4 to 8 weeks, 5 to 20% of patients had persistent hyperthyroidism and 10 to 30% of patients became hypothyroid during first 2 years after treatment and 5% per year thereafter.

Stanley E et al [10] in this study, 48 patients received 10mCi radioiodine and followed up for 12 months. 24(50%) patients became hypothyroid at 3 months of therapy, 33(69%) patients became hypothyroid within 12 months of therapy. 6(12%) patients became euthyroid, 9(19%) patients were persistent hyperthyroidism requiring retreatment.

Amit A et al [11] in this study, 813 patients received 5 and 10 mCi radioiodine and followed up for 1 year. At the end of 1 year, 370 patients received 10 mCi in which 60.8% patients were hypothyroid, 23.8% patients were euthyroid and 15.4% patients were persisting hyperthyroidism requiring second dose of radioiodine.

R Shankar et al [12] in this study, 174 patients received 2 to 15 mCi radioiodine and followed up for 12 months. After 12 months following therapy, 29(16.7%) subjects were euthyroid, 51(29.3%) were hypothyroid and 94(54%) had persisting hyperthyroidism.

GE Ratcliffe et al [13] in this study, 93 patients of Graves’ disease received 550MBq radioiodine and followed up for
mean duration of 37 months. 45(48.38%) patients became hypothyroid, 30(32.26%) patients were euthyroid and 18(19.36%) patients had persistent thyrotoxicosis requiring further radioiodine ¹³¹I therapy.


Carbimazole: Indications: Treatment of hyperthyroidism (long-term treatment may lead to remission of the disease), to reduce the degree of hyperthyroidism in preparation for subtotal thyroidectomy or radioiodine therapy, used when thyroidectomy is contraindicated or is not advisable. Contraindications: pregnancy & nursing mothers - carbimazole is found in breast milk & is contraindicated in nursing mothers, can cause fetal harm when administered to a pregnant woman.

Advantages and disadvantages of treatments for hyperthyroidism [15]

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Advantages</th>
<th>Disadvantages</th>
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<tbody>
<tr>
<td>Antithyroid drugs</td>
<td>-Conservative treatment</td>
<td>-High relapse rate</td>
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<td></td>
<td>-No hospitalization required</td>
<td>-Requires frequent clinic visits for monitoring</td>
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<td></td>
<td>-Low risk of subsequent hypothyroidism</td>
<td>-Poor adherence</td>
</tr>
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<td></td>
<td>-No radiation exposure</td>
<td>-Adverse events (rarely major)</td>
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<td></td>
<td>-No adverse effect on Graves ophthalmopathy</td>
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<tr>
<td></td>
<td>-Safe to use during pregnancy and breastfeeding</td>
<td></td>
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<tr>
<td>Radio iodine ¹³¹I-(radiotherapy)</td>
<td>-Definitive treatment</td>
<td>-Lifelong hypothyroidism</td>
</tr>
<tr>
<td></td>
<td>-Low cost</td>
<td>-Radiation exposure</td>
</tr>
<tr>
<td></td>
<td>-No hospitalization required</td>
<td>-Slow control of hyperthyroidism</td>
</tr>
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<td></td>
<td>-No need for surgery or anaesthetic</td>
<td>-Possible progression or de novo occurrence of Graves ophthalmopathy</td>
</tr>
<tr>
<td>Thyroidectomy</td>
<td>-Definitive treatment</td>
<td>-Lifelong hypothyroidism</td>
</tr>
<tr>
<td></td>
<td>-No radiation exposure</td>
<td>-Adverse events related to surgical procedure and anaesthesia</td>
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<tr>
<td></td>
<td>-Prompt control of hyperthyroidism</td>
<td>-Hospitalization</td>
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<td>-High cost</td>
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<td></td>
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<td>-Permanent scar</td>
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</table>

6. Conclusion

Hyperthyroidism is a common clinical disorder all over the world. Even though diagnosis in hyperthyroidism is generally straightforward, its prevalence varies among population. Although effective treatments for hyperthyroidism are available, none is perfect. In our study, hyperthyroidism patients with antithyroid drug, 90.9% of patients became euthyroid in 12 months, 5.6% of patients remained hyperthyroid at the end of 18th month. 5.6% of patients developed hypothyroidism at the end of 18th month and there was no incidence of adverse side effects with antithyroid drug. Hyperthyroidism patients with radioiodine therapy, 36% of patients were euthyroid after 3 months, 76.5% of patients developed hypothyroidism at the end of 12th month. 14.3% of patients remained hyperthyroid at the end of 18th month. Among the available treatments for hyperthyroidism, radioiodine is the most effective treatment for controlling the hyperthyroidism but hypothyroidism is a common complication. There was a good response to antithyroid drug with lesser side effect of hypothyroidism.

References


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