

Compare the Effectiveness of Carbimazole Single Dose and Divided Dose Regimens for Euthyroid Induction in Hyperthyroid Patients

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ABSTRACT

Objective: The purpose of the current study was to examine the effectiveness of carbimazole administered as a single dose with a divided dose regimen for inducing euthyroidism in hyperthyroid patients.

Study Design: Prospective/Randomized study

Place and Duration: This Prospective/Randomized study was conducted at Khyber Teaching Hospital Peshawar in the duration from June, 2022 to November, 2022.

Methods: There were 92 patients of hyperthyroidism were presented in this study. Age, sex, BMI, and residency details for each enrolled case were recorded after receiving informed written consent. Patients were divided into two groups equally. Carbimazole (OD-CMZ) was administered as a single dosage to 46 patients in group I, and as two separate doses to 46 patients in group II (DD-CMZ). For six months, the effectiveness of the treatment was monitored on a regular basis (every four weeks). SPSS 22.0 was used to analyze all data.

Results: There were 54 (58.7%) females and 38 (41.3%) males in this study. In group I mean age was 35.13±6.60 years and in group II mean age was 40.10±8.86 years. Mean duration of disease was 3.6±10.57 months in group I and in group II mean duration was 4.3±8.35 months. There was no discernible difference between the two groups in terms of baseline TSH and T4 concentrations or their cumulative rates of reduction (p-value, 0.014). Frequency of euthyroidism in group I after final follow up was 46 (100%) and in group II found in 45 (97.8%) cases but difference is insignificant.

Conclusion: In this study, we came to the conclusion that a single dosage regimen is a more effective way to treat hyperthyroidism since there is no discernible difference in efficacy and a greater risk of developing hypothyroidism with a split dose strategy.

Keywords: Hyperthyroidism, Drug therapy, Single dose, Carbimazole, Multidose

INTRODUCTION

The preferred medication for treating hyperthyroidism is carbimazole, which is frequently used in medical settings. [1] The majority of users, however, divide their daily dose and take it every 6 to 8 hours due to its short half-life[2]. Most patients would find this schedule inconvenient, and some might not be able to adhere to the dose recommendations exactly. Despite the shorter biological half-life, investigations by Pittman et al. have demonstrated that methimazole selectively binds to thyroid tissue, and findings by Wartofsky and Ingbat' suggest that a single dose of 30 mg of methimazole has an action duration of 24 to 36 hours when measured on blood levels. The usage of methimazole at fewer frequent intervals throughout the day is thus possible. [3,4]

The standard method of administering MMI, known as the divided daily dose regimen (DD-MMI), which calls for two to three divided doses per day, is advised [5]. But, the once daily dose regimen (OD-MMI), which is preferred, calls for just one dose per day, is also acceptable. If OD-MMI and DD-MMI regimens are equally efficient in inducing euthyroidism, it is not entirely obvious from the research, nevertheless. However, only a small number of studies that compared the efficacy of the OD-MMI and DD-MMI regimens using different [6] or high daily doses of MMI served as the basis for the evidence pointing to an equivalent effectiveness of both regimens. Nowadays, the first-line treatment of hyperthyroidism is advised to use low daily doses of MMI, such as 10–20 mg/day, rather than high daily doses, such as 30 mg/day or greater. [7]

As soon as carbimazole is taken orally, it transforms from a prodrug into methimazole (15–30 minutes required). In comparison to its active equivalent, methimazole, carbimazole has a plasma half-life of 5.3–5.4 hours as opposed to 64 hours. [8] A single dose of the prodrug carbimazolein for hyperthyroid individuals is sufficient because the thyroid gland's half-life can be up to 20 hours. The majority of centres around the world, including Pakistan, use the DD-CMZ protocol. [9] Studies have been

published that have shifted the focus to the OD-CMZ regimen, though, because of the lengthy half-life of its metabolite in the body. [10] We chose to conduct a comparison research to determine the efficacy of the OD-CMZ to DD-CMZ regimen because there is a dearth of data locally for OD-CMZ.

MATERIAL AND METHODS

This Prospective/Randomized study was conducted at Khyber Teaching Hospital Peshawar in the duration from June, 2022 to November, 2022 and comprised of 92 patients of hyperthyroidism. After getting informed written consent detailed demographics of enrolled cases included age, sex, BMI and residency were recorded. Patients who had a severe goiter, were on immune suppression, were younger than 18 or older than 65, had received ablative therapy, or were pregnant were all excluded.

All patients in both groups received a constant dosage of an oral beta blocker to balance the clinical effects (Propranolol 20mg twice a day). That was done with informed permission. The random draw number approach was used to split the patients into two groups at random. Patients in group I were provided a single dose of carbimazole (OD-CMZ), whereas those in group II received divided doses of the drug (DD-CMZ), which were modified based on the results of the thyroid function tests (TFTs). The significance of medication compliance was explained to the participants. For a total of six months, regular monthly follow-ups were conducted. TFTs were repeated and the carbimazole dosage was changed suitably at each monthly appointment. A printed datasheet was used to record the values.

SPSS-22 was used for the statistical analysis, and a p-value of 0.05 was regarded as statistically significant. All of the study's continuous variables underwent the Shapiro-Wilk Normality Test to see if they were all normally distributed. The independent sample t test was used to compare the Means. The Hormone Laboratory at the Pathology Department gave the cut off values of normal ranges (T4:7-21 pmol/L, TSH: 0.4-4.5 mIU/L), which were used to record

the monthly values of TFTs. Based on these laboratory results, the percentage of euthyroidism attained at each visit was evaluated.

RESULTS

There were 54 (58.7%) females and 38 (41.3%) males in this study.(figure 1)

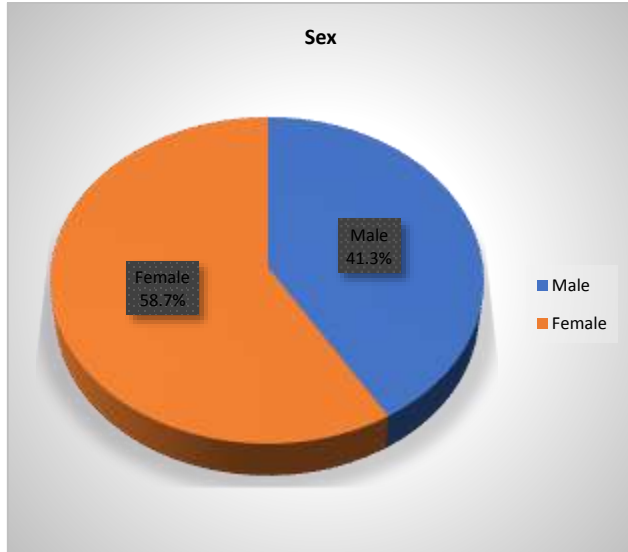


Figure-1: Patients with sex distribution

In group I mean age was 35.13±6.60 years and in group II mean age was 40.10±8.86 years. Mean BMI in group I was 22.7±13.84 kg/m² and in group II mean BMI was 23.4±10.61 kg/m². Mean duration of disease was 3.6±10.57 months in group I and in group II mean duration was 4.3±8.35 months. In group I 26 (56.5%) cases were from rural areas and in group II 24 (52.2%) cases had rural residency.(table 1)

Table-1: Demographics information of both groups

Variables	Group I	Group II
Mean age (years)	35.13±6.60	40.10±8.86
Mean BMI (kg/m ²)	22.7±13.84	23.4±10.61
Mean duration of disease (months)	3.6±10.57	4.3±8.35
Place of Residence		
Rural	26 (56.5%)	24 (52.2%)
Urban	20 (43.5%)	22 (47.8%)

There was no discernible difference between the two groups in terms of baseline TSH and T4 concentrations or their cumulative rates of reduction (p-value, 0.014).(table 2)

Table-2: Analysis of differences in Serum T4 and TSH levels between the OD-CMZ and DD-CMZ groups over the course of therapy

Variables	Group I	Group II
Serum T4 levels (pmol/L)		
At 2months	23.7±9.51	22.88±4.39
At 4months	18.54±12.26	18.37±8.17
At 6 months	15.9±6.46	15.8±5.30
Serum TSH levels ((MIU/L)		
At 2months	1.6±2.40	1.27±1.52
At 4months	2.40±3.11	2.17±6.46
At 6 months	2.49±2.16	2.45±2.44

Frequency of euthyroidism in group I after final follow up was 46 (100%) and in group II found in 45 (97.8%) cases but difference is insignificant. (figure 2)

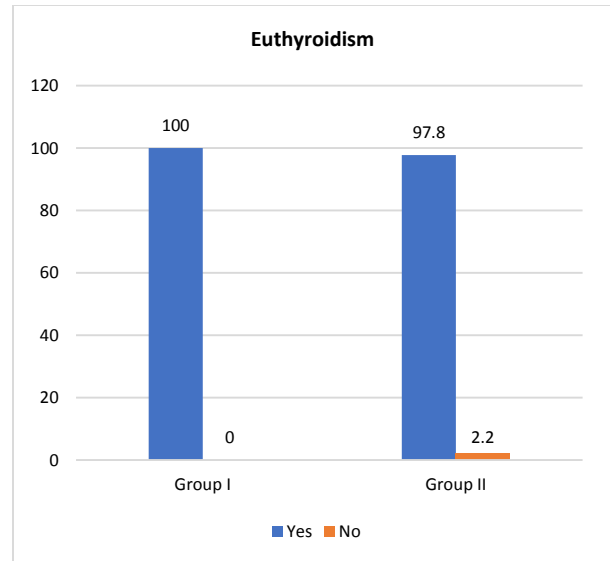


Figure-2: Rate of reaching euthyroidism cumulatively when receiving OD-CMZ and DD-CMZ regimens

DISCUSSION

The two regimens of once-daily carbimazole medication and divided-daily carbimazole therapy for inducing euthyroid in hyperthyroid patients were shown to have similar therapeutic effectiveness in this interventional comparative research. Our study's findings are in line with those of other research that have been done. A few studies merely compared the two groups' differences, while others only employed single dosage regimens..[11,12]

In this study 92 patients of hyperthyroidism were presented. There were 54 (58.7%) females and 38 (41.3%) males in this study. In group I mean age was 35.13±6.60 years and in group II mean age was 40.10±8.86 years. Mean duration of disease was 3.6±10.57 months in group I and in group II mean duration was 4.3±8.35 months. These findings were in line with the previous studies. [13,14] In our research, neither the baseline TSH nor T4 concentrations nor the cumulative rates of decline between the two groups could be clearly distinguished (p-value, 0.014). Twenty-one individuals who received a once-daily carbimazole prescription took part in one particular study. During 1-3 months, everyone's serum T4 levels returned to normal. [15] 50 patients were enrolled in and separated into the two groups for a trial done by Sriussadaporn et al. [14]

Instead, the research population was split into three groups: once daily, twice daily, and three times daily. The blood T3 and T4 levels of the patients in each of these three groups did not significantly differ from one another, although there was a substantial decline in serum T3 and T4 levels relative to the beginning of the treatment. [16]

It is crucial to do research to understand which dosage regimens are more successful because this will affect how easily and consistently patients will take their medications. It is possible to categorise the factors that affect medication compliance. The causes are divided into patient-centered factors, such as demographics (age, ethnicity, gender, education, marital status), psychosocial factors (beliefs, motivation, attitude), forgetfulness, health literacy, patient knowledge, physical difficulties, tobacco use, and patient-prescriber relationships, as well as therapy-related factors, such as side effects and medication taste, administration method, complexity of treatment, and duration.[17] The outcome of the therapy is lacking, nonetheless, as a result of medication non-compliance. As a result, drug compliance is essential and has proven to be difficult for many. Monitoring drug reactions, counselling patients about the value of adherence,

follow-up visits, answering all patient questions, and streamlining dosing regimens are just a few strategies to help patients take their medications more consistently. [18]

However, none of the participants in our research experienced any negative pharmacological side effects. The common adverse effects of carbimazole medication, however, include headache, rash, fever, joint pain, and urticaria, whereas gastrointestinal issues and agranulocytosis are more infrequent. [19] There were various research limitations in our study. Environmental elements like the amount of iodine consumed were not something we could control for. Moreover, there was no uniformity of the dosages supplied as the amount of carbimazole administered changed depending on the patient's TSH and T4 levels at each monthly visit when they were started on the split dose regimen. The study does provide us with a lot of information on the value of a particular dosing regimen, though.

CONCLUSION

In this study, we came to the conclusion that a single dosage regimen is a more effective way to treat hyperthyroidism since there is no discernible difference in efficacy and a greater risk of developing hypothyroidism with a split dose strategy.

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