EFFICACY OF DIFFERENT DOSAGE REGIMENS OF CARBIMAZOLE IN TREATMENT OF PRIMARY HYPERTHYROIDISM

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ABSTRACT

Objectives: To determine the efficacy of different carbimazole regimens in treatment of primary hyperthyroidism

Methods: This study was conducted at Medical Ward of Mayo Hospital Lahore from September 2023 to March 2024 on 100 patients with primary hyperthyroidism. Patients were assigned to two groups; Group A received carbimazole once a day, whereas Group B were prescribed with divided doses of carbimazole, which were modified based on results of TFTs.

Results: Among 100 patients enrolled (50 in Group A and 50 in Group B), there were no significant differences in baseline levels of TSH and T4, nor in their overall rates of reduction. Additionally, both groups showed comparable rates Of Achieving Euthyroidism During Follow-Up Assessments Conducted At Three-Month Intervals.

Conclusion: When administered in single daily dosing regimen, carbimazole is similarly successful in treatment of hyperthyroidism as daily divided dose regimen. Additionally, it raises the patients' compliance when taken as a single dosage every day.

Keywords: Carbimazole, Hyperthyroidism, regimens

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INTRODUCTION

Hyperthyroidism is clinical condition characterized by excessive production of thyroid hormones, resulting in hypermetabolic state.[1] Common symptoms include weight loss, heat intolerance, palpitations, irritability, and tremors.[2] The most prevalent cause is Graves' disease, an autoimmune disorder that leads to diffuse thyroid hyperactivity.[3] Globally, prevalence of hyperthyroidism is estimated to be around 1–1.5, with women being affected up to ten times more frequently than men. In countries like Pakistan, burden of thyroid disorders is increasing, although exact prevalence remains underreported due to limited nationwide screening programs.[4] Carbimazole, methimazole, and propylthiouracil are primary antithyroid medications used in the management of hyperthyroidism.[5] Owing to their relatively short plasma half-lives, patients are often advised to take these medications in divided doses every 6 to 8 hours.[6] However, recent studies have demonstrated that the antithyroid effects of these drugs correlate more closely with their intrathyroidal retention rather than their plasma half-lives.[7] For example, carbimazole, which has plasma half-life of

approximately 5.3 to 5.4 hours, is converted to its active form methimazole, which itself has plasma half-life of around 6.8 hours. Despite these short half-lives in circulation, methimazole can remain concentrated in thyroid gland for up to 20 hours, allowing sustained pharmacologic action.[8] Traditionally, most hospitals including those in Pakistan follow split-dose regimen for carbimazole. However, emerging evidence supports once-daily dosing, owing to prolonged intrathyroidal activity of methimazole. This shift is being encouraged not only for its pharmacologic rationale but also for improved patient compliance, convenience, and reduced risk of missed doses.[9,10] To determine the most effective and patient-friendly dosing strategy, this study aims to compare the efficacy of different carbimazole regimens in the treatment of primary hyperthyroidism. With growing evidence supporting once-daily dosing due to sustained intrathyroidal drug retention, evaluating its clinical outcomes versus traditional split dosing is essential for optimizing management and adherence.

METHODS

From September 2023 to March 2024, this non-randomized study was done at Mayo Hospital Lahore's Medical Ward. Following Institutional Review Board clearance, total of 100 people were chosen and divided into two groups utilizing reference research population of 60 people divided into three groups.[11] All patients under the age of 16 or above the age of 70 who had painful goiter, were on immunosuppression, had ablative therapy, and were pregnant were eliminated. To balance the clinical effects, all participants in the research were given a constant dose of oral Propranolol 20mg twice day (a beta blocker). Patients were divided into two groups. Group A received carbimazole once/day (OD-CMZ), whereas those in Group B received divided carbimazole doses (DD-CMZ), which were modified based on results of TFTs. Necessity of treatment compliance was stressed to patients who participated in the trial. For 6 months, regular monthly follow-ups were conducted. TFTs were performed at each subsequent visit, and carbimazole dosage was modified as needed. The results were written down on a printed data sheet. SPSS 24 was used for statistical analysis, statistically significant P-value of 0.05 was used. Independent sample t test was used to compare means of two groups. CENUM Centre of Mayo Hospital Lahore supplied cut off values of normal ranges (T4:7–21 pmol/L, TSH: 0.4–4.5 mIU/L) for recording monthly TFT results. These laboratory data were used to determine the number of Euthyroidism obtained at each visit.

RESULTS

There were 100 patients in all, 50 in each group. There was no loss of follow-up, therefore 100 patients were analyzed. Group A has mean age of 41.70 years (SD 6.354), with 20 males. Group B (n=50) had a mean age of 39.59SD 7.25 years. The male to female ratio was 1:1.7, with 25 males. When it came to age, the two groups were nearly identical. (p=0.267). Intergroup comparisons for visit 1 TSH (p=0.257) and T4 (p=0.723) levels are comparable, as indicated in table 1, since there is no significant variation in baseline values between two regimens. Findings revealed substantial fall in blood T4 and TSH levels in both groups. Three Monthly variation in serum T4 levels were not significant between groups at all visits respectively; p-value >0.05 (Visit 1: 31.004±2.88 versus 30.7904±3.01, Visit 2: 19.696±2.03 versus 19.5820±2.24, Visit 3: 15.95±1.06 versus 15.85±1.06). Three Monthly differences in serum TSH levels were also found insignificant between groups in all visits with p-value of >0.05 (visit 1: 0.1156 $\pm$ 0.048 versus 0.126 $\pm$ 0.0459, visit 2: 1.58 $\pm$ 0.5483 versus 1.67 $\pm$ 0.575 and at visit 3: 2.948 $\pm$ 3.3469 versus 2.925 $\pm$ 2.9246).

Table 1: Serum levels of T_4 and TSH at 1st, 2nd and 3rd visit

Follow-up months	1st visit at 0 Month	2nd visit at 3 Month	3rd visit at 6 Month
Serum T4levels			
OD-CMZ (Group A)	31.0004 $\pm$ 2.88	19.6968 $\pm$ 2.03	15.95 $\pm$ 1.06
DD-CMZ (Group B)	30.7904 $\pm$ 3.01	19.5820 $\pm$2.24	15.85 $\pm$ 1.06
p-value	0.723	0.789	0.626
Serum TSH			
OD-CMZ (Group A)	0.1156 $\pm$ 0.048	1.58 $\pm$ 0.5483	2.948 $\pm$ 3.3469
DD-CMZ (Group B)	0.126 $\pm$ 0.0459	1.67 $\pm$ 0.575	2.925 $\pm$ 2.9246
p-value	0.257	0.420	0.971

Table 2: Comparison of thyroid status

Follow-up in months	0 month	3 months	6 months
Hypothyroidism			
OD-CMZ {n (%)}	0 (0)	0 (0)	0 (0)
DD-CMZ {n (%)}	0 (0)	0 (0)	0 (0)
Euthyroidism			
OD-CMZ {n (%)}	0 (0)	48 (96)	50 (100)
DD-CMZ {n (%)}	0 (0)	47 (94)	50 (100)
Hyperthyroidism			
OD-CMZ {n (%)}	50 (100)	2 (4)	0 (0)
DD-CMZ {n (%)}	50 (100)	3(6)	0 (0)

DISCUSSION

In this case study, we included 100 patients with hyperthyroidism between the age of 22- 55 years and compared the efficacy of single dose of carbimazole with a divided dose regime. Lifelong

hormonal treatment is frequently required for patients with primary hyperthyroidism. The half-life of carbimazole is approximately 5.3 hours, typically given in divided doses. On the other hand, single carbimazole dose has been shown in multiple investigations to be as effective at generating euthyroidism.[12] This study found no difference in treatment in efficacy between the two regimens of once daily carbimazole medicine and divided daily carbimazole therapy when generating euthyroid in hyperthyroid patients. Our study's findings are in line with those of other research investigations. In study involving 92 hyperthyroid patients, single daily dose of carbimazole achieved euthyroidism in 100% of cases, while divided doses resulted in 97.8% efficacy, with no significant difference in outcomes.[13] In contrast, Gupta et al found that patients receiving divided doses achieved euthyroidism slightly faster (3.8 weeks) compared to those on single dose (4.6 weeks), but this difference was not statistically significant.[14] Because it affects how easily and effectively patient takes medication, the inquiry into dose regimen efficacy is of fundamental relevance. Drug usage is influenced by various factors, which can be classified. Patient-centered aspects include demographics, psychosocial characteristics (religious views, ambition, mindset), health promotion, patient knowledge, and physician-patient relationship; therapy-related elements include side effects and pharmaceutical taste, administration route, and treatment complexity.[10] However, due to medication non-compliance, the therapy fails to achieve its full potential. Accordingly, many people have taken up the challenge of maintaining drug compliance. We can improve adherence to the medication regimens through various methods, including monitoring for adverse responses, counseling patients on the significance of adherence, and regular follow-up visits.[15] Carbimazole has wide range of side effects, including migraine, dermatitis and fever, urticaria, joint pain, digestive difficulties, and agranulocytosis, in current study side effects were not reviewed.[16,17] There were some limitations to our study, as there were others. The conduction of the trial in minimal setting jeopardized the generalizability of the results. The trial was also not very cost-effective because of the multiple blood sampling of patients over six months. There was no uniformity of carbimazole doses given to patients on the split-dose regimen, based on the patients' TSH and T4 levels at each monthly appointment. However, the study shows that single-dose regimens are effective.

CONCLUSION

When administered in single daily dosing regimen, carbimazole is similarly successful in treatment of hyperthyroidism as daily divided dose regimen. Additionally, it raises the patients' compliance when taken as a single dosage every day.

ETHICAL APPROVAL

Ethical approval was granted by the Institutional Review Board King Edward Medical University; Lahore vide reference No 703/RC/KEMU dated: 29/08/2022

CONFLICT OF INTEREST

Authors declare no conflict of interest.

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AUTHOR'S CONTRIBUTIONS

ND: Manuscript writing, data collection, Topic Selection
MSA: Manuscript writing, data collection
SK: Manuscript writing, data analysis
MK: Critical review, proof reading manuscript writing
UA, AA: Data analysis, review literature
All Authors: Approval of the final version of the manuscript to be published

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