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COMPARATIVE STUDY OF HIGH DOSE MONO-THERAPY OF AMLODIPINE OR TELMISARTAN, AND THEIR LOW DOSE COMBINATION IN MILD TO MODERATE HYPERTENSION, AMONGST OUTDOOR PATIENTS IN A TERTIARY CARE HOSPITAL (N.M.C.H) PATNA

Dr Aman Kishor Post Graduate Trainee, Department Of Pharmacology, NMC, Patna.

Dr Santosh Kumar Post Graduate Trainee, Department Of Pharmacology, NMC, Patna.

Dr Murli Manohar* Assistant Professor, Department Of Pharmacology, NMC, Patna *Correspondng Author

Dr Sanjay Kumar Prof & Head of Department, Department Of Pharmacology, NMC, Patna

ABSTRACT

Introduction: Hypertension is one of the major public health challenges worldwide. Angiotensin receptor blockers (ARBs) and Calcium channel blockers (CCBs) are among the first line antihypertensive drugs. **Materials & Methods:** A total of 60 patients were enrolled in the study after obtaining informed consent.Patients were randomized into three treatment groups i.e. Telmisartan 80 mg, Amlodipine 10 mg and low dose combination of Telmisartan 40 mg + Amlodipine 5 mg once daily for 8 weeks. The systolic BP, Diastolic BP, and ADRs were recorded at 0, 2, 4, 8 weeks. **Results:** In the present study, significant reduction of mean systolic blood pressure (SBP) and mean diastolic blood pressure (DBP) was seen in all the three treatment groups. Low dose combination of Amlodipine 5 mg and Telmisartan 40 mg showed statistically significant reduction in SBP as compared to Telmisartan 80 mg mono-therapy and in DBP as compared to Amlodipine 10 mg mono-therapy. Maximum adverse drug reactions (ADRs) were reported in Amlodipine mono-therapy group, like ankle oedema, constipation, headache and fatigue. **Discussion and Conclusion:** In term of BP control, low-dose combination therapy appears a better therapeutic approach than high-dose mono-therapy.

KEYWORDS : Amlodipine,Hypertension and Telmisartan.

INTRODUCTION

The goal of hypertension treatment is usually to reduce blood pressure to the recommended range. A drug of a different class can be added to antihypertensive for patients who fail to achieve control in blood pressure [1].Angiotensin II receptor blockers (ARBs) are currently the most popular class of drugs used in the treatment of hypertension. ARBs are considered good agents in terms of tolerability, the convenience of a once-daily dose, and efficiency in lowering blood pressure. Telmisartan is an ARB that has high affinity to the AT1 receptor subtype and exhibits a long half-life [2-3]. Fixed-dose combinations (FDCs) containing telmisartan have been developed with the diuretic hydrochlorothiazide (HCTZ) or calcium channel blocker amlodipine as two active pharmaceutical ingredients [4].

A telmisartan-amlodipine combination treatment resulted in clinically relevant blood pressure reduction, and was well tolerated with good compliance [5]. Furthermore, compared with monotherapy in patients with previously uncontrolled blood pressure, the addition of HCTZ to telmisartan has been associated with effective blood pressure reduction, as well as with improved hypertension goal-attainment rates (6).

Amlodipine is an orally active, long-lasting dihydropyridine calcium channel blocker (CCB) used to treat hypertension; the drug works by dilating blood vessels and is available in doses of 5 and 10 mg. Amlodipine is also used to treat certain types of chest pain [7].

MATERIALS AND METHODS

This was a prospective, open label, three arms and randomized study. It was conducted in the Medicine OPD, NMCH , Patna from 16th May 2020 to 15th May 2021. A total of 60 hypertensive patients, aged 18 to 60 years having uncontrolled blood pressure (systolic BP ≥ 140 to 179 mmHg and/or Diastolic BP ≥ 90 to 109 mmHg) on low dose mono-therapy with either Amlodipine (5mg) or Telmisartan (40 mg) were enrolled in the study after obtaining informed consent in writing. Patients with other concomitant medical conditions, alcohol or drug dependence, pregnant and lactating women and cases of secondary hypertension were not included in the study.

Each enrolled patient was subjected to the detailed medical history, demography and physical examination. Measurements of systolic and diastolic BP were performed manually with a calibrated mercury sphygmomanometer in sitting position.Patients satisfying inclusion and exclusion criteria were randomized in three treatment groups as following:

- **Group A:** In this group, patients were put on high dose mono-therapy of Telmisartan 80 mg, once daily for eight weeks.
- **Group B:** In this group, patients received high dose mono-therapy of Amlodipine 10 mg, once daily for eight weeks.
- **Group C:** In this group, patients had fixed dose combination of Telmisartan 40 mg and Amlodipine 5 mg, once daily for eight weeks.

Follow up visits were performed after two weeks, four weeks and eight weeks. At each visit, complete clinical examination was carried out, including a recording of systolic and diastolic blood pressure (BP)

RESULTS

A total of 60 subjects were included for analysis; 20 subjects from group A (Telmisartan 80 mg), 20 subjects from group B (Amlodipine 10 mg) and 20 subjects from group C (fixed dose combination of Telmisartan 40 mg and Amlodipine 5mg). Comparison of blood pressure changes within the group was done by 'ANOVA', comparison of blood pressure changes between various treatment groups was done by 'ANOVA' and 'Post Hoc LSD' and comparisons of adverse drug reactions and effectiveness of eight week treatment on systolic and diastolic BP (characterized by systolic BP ≤ 139 mmHg and diastolic BP ≤ 89 mmHg) in various treatment groups were done by Chi-square test.

Reduction in mean systolic blood pressure (SBP) and mean diastolic blood pressure (DBP) from baseline to end of study visit was statistically highly significant (p-value <0.001) in all treatment groups.

At each study visit, the highest fall in the mean SBP was observed in group C (treated by combination of Telmisartan 40 mg and Amlodipine 5 mg) whereas lowest in group A

(treated by Telmisartan 80 mg), and the difference between group A and C was found statistically significant. Similarly, highest reduction in mean DBP at each study visit was also observed in group C while lowest in group B.

Table 1 :Effect of treatment on mean SBP and DBP in various treatment groups. (*p<0.001, highly significant)**

Follow up visit	Group A (N=20)		Group B (N=20)		Group C (N=20)	
	SBP (mmHg)	DBP (mmHg)	SBP (mmHg)	DBP (mmHg)	SBP (mmHg)	DBP (mmHg)
Baseline	152.6±8.01	92.8±6.12	152.5±8.13	93.02±6.18	153.9±10.02	94.7±5.31
Week 2	142.15±6.19	84.11±5.01	141.7±7.81	86.23±6.73	140.17±9.15	83.01±5.32
Week 4	135.1±6.02	79.09±5.41	132.1±6.02	84.24±6.12	130.21±7.55	78.35±5.41
Week 8	132.25±7.5***	77.5±5.3***	129.7±7.2***	83.44±7.89***	126.42±9.2***	76.45±5.6***

After eight weeks of treatment, SBP target (<139 mm of Hg) was achieved in 85% cases of group A, 90 % cases of group B and 90% cases of group C. But the difference was statistically not significant. DBP target (< 89 mm of Hg) after eight weeks therapy was attained in 90% and 95% cases of group A and group C respectively. While group B was placed in bottom as only 75% cases achieved DBP target. The difference was found statistically highly significant.

Table 2 : Changes in mean SBP & DBP in follow up in various treatment groups

Follow up time	Change in SBP (mmHg) Group A (N=20)	Change in SBP (mmHg) Group B (N=20)	Change in SBP (mmHg) Group C (N=20)	Significant difference among groups
Week 0 to 2	9.00±2.15	11.11±2.72	13.16±4.43	A-C
Week 2 to 4	16.00±4.27	20.02±5.19	23.02±6.13	A-C
Week 4 to 8	21.04±5.09	24.17±6.21	27.01±7.11	A-C
Follow up time	Change in DBP Group A (N=20)	Change in DBP Group B (N=20)	Change in DBP Group C (N=20)	Significant difference among groups
Week 0 to 2	7.763±2.71	6.18±3.12	10.71±3.49	A-B, A-C, B-C
Week 2 to 4	13.89±4.05	9.59±4.23	15.65±6.02	A-B, B-C
Week 4 to 8	16.12±5.91	10.29±5.14	17.39±6.41	A-B, B-C

DISCUSSION

In the present study, low dose combination of Amlodipine 5 mg and Telmisartan 40 mg showed maximum reduction in mean SBP as compared to Telmisartan 80 mg mono-therapy and in mean DBP as compared to Amlodipine 10 mg mono-therapy after two, four &eight weeks treatment.

Ohishi M, Kawai T, Hayashi N, Kitano S, Katsuya T, Nagano M, et al.2013 reported that low dose combination of Telmisartan 40 mg and Amlodipine 5 mg significantly reduced 24h mean and clinical BP in patients whose hypertension was not controlled by 5 mg of Amlodipine [8]. In another study, the addition of Telmisartan 40 mg to Amlodipine 5 mg produced statistically significant reductions in trough seated DBP than Amlodipine 5 mg alone [9]. The Telmisartan–Amlodipine clinical development program included a pivotal eight weeks, randomized, double-blind, placebo-controlled clinical trial to demonstrate the additive nature of combination of Telmisartan and Amlodipine across a wide range of doses. In this study, combination of Telmisartan and Amlodipine significantly lowered the SBP and DBP compared to mono-therapies [10]. Clinical studies suggest that combination drug therapy also results in more rapid BP control in addition to the more patients achieving BP target [11].In a meta-analysis, five times more effective BP control was observed with combination of drugs from different antihypertensive classes than increasing the dose of one drug [12].

In our study, 25% patients from Amlodipine 10 mg mono-therapy group reported ADRs like ankle oedema, constipation, headache and fatigue. All ADRs were of mild nature and did not require discontinuation of therapy.

CONCLUSION-:

In this study, a low dose Telmisartan–Amlodipine combination has demonstrated significantly greater BP reductions for both SBP and DBP compared to high dose mono-therapy of Telmisartan and Amlodipine in the overall study population. This combination is well tolerated with a safety profile consistent with its mono-therapy components. So, in terms of BP control, low-dose combination therapy appears a better therapeutic approach than high-dose mono-therapy for mild to moderate hypertensive patients who failed to achieve BP target on low-dose mono-therapy.

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