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COMPARATIVE STUDY OF EFFECTIVENESS AND TOLERABILITY OF S-AMLODIPINE AND AMLODIPINE (RACEMIC) IN THE TREATMENT OF MILD TO MODERATE HYPERTENSION

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ABSTRACT

OBJECTIVE- To compare the effectiveness and tolerability of S-Amlodipine 2.5 mg and Amlodipine(Racemic) 5 mg in the treatment of mild to moderate hypertension.

MATERIALS AND METHODS - This prospective, randomized, open, comparative, observational study was conducted in the department of pharmacology, NMCH, Patna. This was 8 weeks study between 15 Jan 2019 to 15 March 2019 in 100 mild to moderate hypertensive patients (male 57 and female 43), age ranging between 30 to 70 years visiting outdoor, medicine department, NMCH, Patna.. Patients were randomly distributed into two groups of 50 each. Group A was given 2.5 mg S-Amlodipine and group B was given 5 mg amlodipine (racemic) for duration of 8 weeks. The average systolic and diastolic blood pressures in sitting position of both groups were taken at the start of study (baseline) and 8 weeks. Both the groups were compared and statistical analysis was done by paired student 't' test.

RESULTS - The change in systolic blood pressure (SBP) in Group-A is from 163.84± 10.38 to 142.39 ± 8.42 mmHg and in Group-B from 163.64 ± 10.92 to 142.63 ± 7.82 mmHg. The change in diastolic blood pressure (DBP) in Group-A is from 100.20 ± 7.46 to 86.49 ± 6.34 mmHg and in Group-B from 100.34 ± 7.28 to 86.88 ± 6.26mmHg. Changes in both the groups are statistically significant with p-value < 0.0001. The difference between Group-A and Group-B for reduction in blood pressures (for both systolic and diastolic) is not statistically significant. Incidence of pedal edema was significantly less in S-Amlodipine group.

CONCLUSION - Present study clearly indicates S-Amlodipine 2.5 mg is as effective as racemic Amlodipine 5 mg in control of mild to moderate hypertension with better tolerability.

KEYWORDS : Hypertension, amlodipine, S-amlodipine

INTRODUCTION

Hypertension (HTN) is one of the prevalent health problems worldwide, associated with high morbidity and mortality. Hypertension is defined as systolic blood pressure (SBP) ≥ 140 mmHg and/or diastolic blood pressure (DPB) ≥ 90 mmHg [1]. For treatment of hypertension, calcium channel blockers (CCBs) are the important agents as recommended by Joint National Committee-8 (JNC-8) guidelines [2].

Amlodipine is a calcium channel blocker (CCB), from dihydropyridine group, used for treatment of hypertension [3, 4]. Amlodipine produces significant and persistent reduction of blood pressure (BP). Peripheral edema, mainly pedal edema is a common adverse effect with dihydropyridine CCBs. Amlodipine is a racemic mixture of S and R stereoisomers. S-enantiomer has improved pharmacokinetics (PK) and lesser undesirable adverse events [5]. S-Amlodipine is a chiral amlodipine having greater pharmacological effectiveness due to receptor compatibility than R-isomers. Affinity for receptor is stereo selective, it is 1000 times more for S-enantiomer than R-enantiomer [6]. Pharmacokinetic variability, intrasubject variations are lesser and half-life is longer with S-amlodipine [7]. The primary objective is to compare the effectiveness of chiral S-Amlodipine with racemic amlodipine in the treatment of mild to moderate hypertension. Secondary objective is to compare the tolerability profile.

MATERIALS AND METHODS

This prospective, randomized, open, comparative, observational study was conducted in department of Pharmacology, NMCH, and Patna. This was 8 weeks study between 15 Jan 2019 to 15 March 2019 in 100 mild to moderate hypertensive patients (male 57 and female 43), age ranging between 30 to 70 years visiting outdoor, medicine department, NMCH, Patna. Patients with any co-morbid conditions, pregnancy and lactation, severe hypertension, secondary hypertension were excluded. Written and informed consent form was taken from each patient before the start of study. Patients were randomly distributed into two groups of 50 each. Group A was given 2.5 mg S-Amlodipine and group B was given 5 mg racemic amlodipine for duration of 8 weeks. The average systolic and diastolic blood pressures in sitting position of both groups were taken at baseline and 8 weeks. Both the groups were compared and statistical analysis was done by paired student 't' test. Effectiveness was estimated by measuring the reduction in SBP and DBP before and after the study. Following investigations were performed at start and end of study for fasting plasma glucose, serum total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides, electrolytes, creatinine, blood urea nitrogen, SGOT, SGPT, complete blood count and urinalysis.

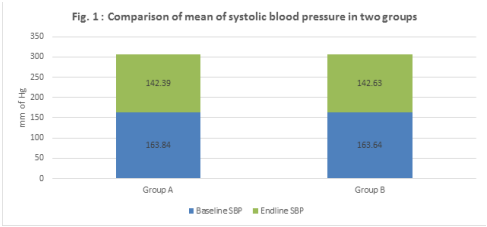
RESULTS

Table 1: Age and Gender distribution of patients in the 2 groups

Characteristics	Group-A	Group-B
Age (years, mean)	51.9	52.1
Gender (numbers)		
Male	31	32
Female	19	18

Table 2: Change in average systolic blood pressure (SBP) values in the 2 groups

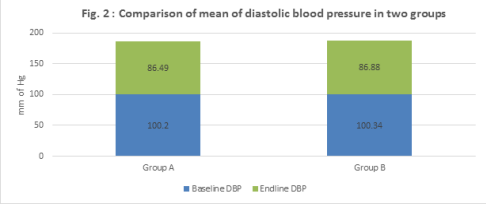
Group	Baseline, mmHg (MeanSD)	8 weeks, mmHg (MeanSD)	Reduction in BP, mmHg, (MeanSD)	P-value
Group A S-Amlodipine 2.5 mg (n = 50)	163.84±10.38	142.39±8.42	21.45±1.98	< 0.0001
Group B Amlodipine (racemic) 5 mg (n = 50)	163.64±10.92	142.63±7.82	21.01±3.1	< 0.0001



The change in systolic blood pressure in Group-A is from 163.84 ± 10.38 to 142.39 ± 8.42 mmHg and in Group-B from 163.64 ± 10.92 to 142.63 ± 7.82 mmHg. Changes in both the groups are statistically significant with p-value < 0.0001, Table 2, Fig. 1.

Table 3: Change in average diastolic blood pressure (DBP) values in the 2 groups

Group	Baseline, mmHg (Mean SD)	8 weeks, mmHg (MeanSD)	Reduction in BP, mmHg (MeanSD)	P- value
Group A S-Amlodipine 2.5 mg (n = 50)	100.20± 7.46	86.49± 6.34	13.71± 1.12	< 0.0001
Group B Amlodipine (racemic) 5 mg (n = 50)	100.34± 7.28	86.88± 6.26	13.46±1.02	< 0.0001



The change in diastolic blood pressure in Group-A is from 100.20 ± 7.46 to 86.49 ± 6.34 mmHg and in Group-B from 100.34 ± 7.28 to 86.88 ± 6.26 mmHg. Changes in both the groups are statistically significant with p-value < 0.0001, Table 3, Fig. 2. The difference between Group-A and Group-B for reduction in blood pressures (for both systolic and diastolic) is not statistically significant.

There was no pedal edema at the start of study in any group. But, after 8 weeks of study, 1 patient in Group-A and 3 patients in Group-B developed pedal edema. Other investigations at start and end of study are nearly similar with no statistically significant difference.

DISCUSSION

This study was to compare the effectiveness and tolerability of chiral S-Amlodipine with racemic Amlodipine in the treatment of mild to moderate hypertension. Both systolic and diastolic blood pressure reductions in the two groups came out statistically significant. Incidence of pedal edema was significantly less in Group-A.

Liu et al., in a meta-analysis of 15 randomized control trials (RCTs), reported similar efficacy of S-Amlodipine 2.5 mg on blood pressure compared to Amlodipine (racemic) 5 mg [8]. The 2 high quality RCTs included in this meta-analysis recorded weighted mean difference [WMD] of SBP and DBP was - 1.13 (95% CI, - 5.29 to 3.03) and -1.34 (95% CI, -2.67 to - 0.01), respectively, at 8 week treatment.

Another multicentric, clinical trial of S-amlodipine 2.5mg and racemic amlodipine 5mg found similar blood pressure lowering activity [9]. Above findings are consistent with the present study, Whereas another meta analysis performed by Zhao and Chen involving 1456 patients concluded that S-amlodipine was efficacious (odds ratio (OR) 2.19, 95% CI 1.61 to 2.97; p < 0.01) and tolerable (OR 0.51, 95% CI 0.34 to 0.77; p < 0.01) than racemic amlodipine [10].

Various studies such as Galappatthy et al. (2016), SESA trial, SESA ll study support lower incidence of pedal edema. The confirmatory evidence came from a meta analysis of 15 RCTs of S-Amlodipine by Liu et al. where it was reported that S-Amlodipine (n=907) has significantly less occurrence of pedal edema than racemic amlodipine (n=897) (test for overall effect: Z = 2.20; p = 0.03; risk difference [RD], - 0.02; 95% CI, - 0.03 to 0.00) [8]. The tolerability and efficacy of S-amlodipine (SESA) trials, reported significant BP lowering activity and significantly less or no incidence of pedal edema in Indian patients with hypertension [11 – 14]. The findings of the present study are consistent with the other studies.

CONCLUSION

Significant reduction in both systolic and diastolic blood pressures was seen in both the groups in the present study. It may be concluded that S-Amlodipine 2.5mg is as effective as Amlodipine (racemic) 5mg for control of mild to moderate hypertension with better tolerability.

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