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Comparative study on the efficacy of Angiotensin II Receptor Blockers and Calcium channel blockers as antihypertensive in hypertensive post menopausal women

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ABSTRACT
Angiotensin Receptor Blockers and Calcium Channel Blockers are suitable for the initiation of antihypertensive treatment in postmenopausal women, studies investigating efficacy between this two drugs are limited. Our study was aimed to compare the efficacy of ARB or CCB in postmenopausal women with hypertension. A prospective observational study was conducted in the Department of General Medicine at Karuna Medical College Hospital, Palakkad for a period of one year (October 2019 to September 2020). Post menopausal hypertensive women with self reported cessation of menstruation for >12 consecutive months with or without co morbid diseases, Patients with HT in stage I/ stage II, Newly diagnosed and old patients of hypertension. Hypertensive postmenopausal women prescribed with combination therapies of beta blokers, ACE inhibitors, Diuretics were excluded, only monotherapies with ARB or CCB included. In the CCB-treated group (n=56), the mean SBP prior to treatment was 151.07±15.41mmHg. After 12 and 24 weeks of therapy, the mean SBP was 146.92±12.73 and 144.78±10.61mmHg and the mean DBP was 87.03±9.29, and 85.12±7.80mmHg, respectively. There was statistically significant reduction in SBP and DBPafter 12 and 24 weeks of therapy in CCB group (p<0.05) when compared with the baseline readings. But there was no statistically significant reduction of SBP in ARB treated group (n=54) (p=0.103). CCB and ARB both are equally prescribed antihypertensive drugs for postmenopausal women with hypertension. In efficacy wise CCB was given better reduction of SBP and DBP compare than the ARB.
Key words: Postmenopausal women, Hypertension, Angiotensin Receptor Blockers, Calcium Channel Blockers.

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INTRODUCTION

Hypertension is one of the leading cause of global burden of disease and it is one of the major cause of cardiovascular mortality, which is estimated to be 1.5 million deaths per year in India [1]. Menopause is a physiological state with cessation of menstrual cycles due to loss of ovarian function and is an important phase in woman's life associated with physiological, psychological, cultural and social changes with a wide range of symptoms [2]. It is accompanied by unfavorable levels of cardiovascular risk factors like changes in body fat, distribution from gynoid to android pattern, abnormal plasma lipids, increased sympathetic tone, endothelial dysfunction, vascular inflammation, and increased blood pressure [3].

Hypertensive women need more stringent efforts to achieve therapeutic BP goals than the hypertensive men and they are significantly more likely to receive antihypertensive therapy (61.4% in women as compared to 56.8% in men), only 44.8% of these women were likely to achieve target BP control as compared to 51.1% of treated men [4]. Antihypertensive treatments are similar in men and women, and women are more likely to have their BP measured, hypertension appears to be less well-controlled in women. This suggests that women may not be as aggressively treated for their hypertension as men and/or that the mechanisms responsible for hypertension in aging women may differ from those in men [5].

The two thirds of older hypertensive women, who are most at risk for stroke and cardiovascular events, do not have their hypertension adequately controlled, either because they are not on drug treatment or because in spite of taking antihypertensive drugs, their blood pressure is still above recommended levels. In the WHI, monotherapy with diuretics was more strongly associated with good control of blood

pressure than was monotherapy with b-blockers, calcium channel blockers, ACE inhibitors, or the use of multiple drugs [6]. For women in general, and particularly older women, the BP threshold for initiating drug treatment, BP goal, and which drugs and drug combinations are most effective for reducing CV events are not conclusive [7].

Although ARB and CCB are suitable for the initiation of antihypertensive treatment in postmenopausal women, studies investigating efficacy between this two drugs are limited. Our study was aimed to compare the efficacy of ARB or CCB in postmenopausal women with hypertension.

MATERIAL AND METHODS

Study Design & Study settings

A prospective observational study was conducted in the Department of General Medicine at Karuna Medical College Hospital, Palakkad for a period of one year (October 2019 to September 2020). Approval of the Institutional Ethical committee was obtained prior to commencement of the study.

Inclusion criteria: Post menopausal hypertensive women with self reported cessation of menstruation for >12 consecutive months with or without co morbid diseases, Patients with HT in stage I/ stage II, Newly diagnosed and old patients of hypertension.

Exclusion criteria: Post menopausal women who was done hysterectomy, oophorectomy, women with indeterminate menopausal status, Patients with SBP >210 and/or Diastolic Blood Pressure (DBP) >120 mm Hg requiring emergency care. Hypertensive postmenopausal women prescribed with combination therapies of beta blockers, ACE inhibitors, Diuretics were excluded, only monotherapies with ARB or CCB included.

Study Procedure

Patients were assessed for the changes in the BP with a follow-up of over a period of 24-weeks. Patients were assessed at the time of screening (baseline), then after the 12 weeks run-in period (follow up 1) and then after 6 months (follow up 2). In each assessment visits, both SBP and DBP were measured in the sitting, standing, and lying position using a standardized procedure. Patients were subjected to thorough history, clinical examination, and biochemical investigations. During screening at first visit, patients were examined completely with due consideration to medical history, family history, socioeconomic history, past history, and addiction history. Patients were examined physically to record the anthropometric measurements, body mass index, and vital signs.

Statistical Analysis

Baseline characteristics of two groups compared using chi square test and Change in blood pressure from baseline to follow ups of both treatment groups were analyzed by one way analysis of variance using SPSS program. Results were expressed as mean ± standard deviation of the mean. The confidence limit of the study was kept at 95%. Hence, a $P < 0.05$ indicated a statistically significant association.

RESULTS

The antihypertensive effect in hypertensive postmenopausal women receiving angiotensin receptor blocker and calcium channel blockers were compared. The baseline characteristics of the study population ARB (n = 54), CCB (n=56) were compared in Table 1. The mean age was ARB in 54.74 ± 10.15 and CCB in 59.60±10.04 years respectively. There is a significant differences were observed. Age groups also compared and prevalence of patients were in 46-50 years age group. Age at menarche and menopause were compared between the two groups.

The mean age of menarche in ARB was 13.92 ± 1.16 and CCB in 13.1±1.6. The mean age of menopause among study population in ARB was 46.79±2.72 and CCB with 46.91±2.18 years. There is no significant difference in both groups according to mean age at menopause. Distribution of comorbid diseases were compared in both groups. Diabetes mellitus is more prone to compare than other diseases. The other comorbid were dyslipidemia, coronary artery disease and asthma. There is no significant difference in both groups according to comorbid diseases.

Table.2 shows that overall mean (SD) reductions in SBP and DBP in patients who received ARB or CCB among study population. In the ARB-treated group, the mean SBP prior to treatment was 147.96±16.29 mmHg and after 12 and 24 weeks of therapy, the mean SBP was 145.74±13.82, and 142.11±12.5 mmHg, respectively. In the CCB-treated group, the mean SBP prior to treatment was 151.07±15.41mmHg. After 12 and 24 weeks of therapy, the mean SBP was 146.92±12.73 and 144.78±10.61mmHg, respectively. There was statistically significant reduction in SBP after 12 and 24 weeks of therapy in CCB group ($p<0.05$) when compared with the baseline readings. But there was no statistically significant reduction of SBP in ARB treated group ($p=0.103$).

In the ARB-treated group, the mean DBP prior to treatment was 89.81±16mmHg. After 12 and 24 weeks of therapy, the mean DBP was 86.07±9.80 and 84.81±7.62mmHg, respectively. In the CCB-treated group, the mean DBP prior to treatment was 90.21±11.41mmHg. After 12 and 24 weeks of therapy, the mean DBP was 87.03±9.29, and 85.12±7.80mmHg. There was statistically significant reduction in DBP after 12 and 24 weeks of therapy in CCB group ($p<0.05$) when compared with the baseline readings. But there was no significant reduction in ARB treated group ($p=0.103$). Blood pressure goal attainment among study population is illustrated in Table.3.

As shown, 57.4% of study patients in ARB group achieved the JNC 8 BP goals after following treatment initiation, in comparison with 67.8% in the CCB group. In this CCB group more patients attained the goal compare than the ARB group. The patients were in stage I hypertension was 27.7% in ARB group and 21.4% in CCB group and stage II hypertension with 14.8% of ARB and 10.7% of CCB. This stage I and II patients were more in ARB compare than CCB.

Table: 1. Baseline characteristic of study population.

S.No	Parameters	ARB (n=54)	CCB (n=56)	P value
1	Age in years (mean±SD)	54.74 ± 10.15	59.60±10.04	0.0130*
2	Age in groups (in years)			
	40-45	2	4	0.0593
	46-50	22	10	
	51-55	4	8	
	56-60	10	8	
	>60	16	26	
3	Age at menarche (mean±SD)	13.92 ± 1.16	13.1±1.6	0.0028*
4	Age at Menopause (mean±SD)	46.79±2.72	46.91±2.18	0.7986
5	Comorbid Disease			
	Diabetes mellitus	21	30	0.4069
	Dyslipidemia	3	6	
	Diabetes mellitus+ Dyslipidemia	11	6	
	Coronary artery disease	2	1	
	Asthma	3	3	

Table: 2. Comparison of SBP and DBP in ARBs and CCBs groups.

S.no	Parameters	Baseline	Follow up 1	Follow up 2	P value
1	ARB (n=54)				
	SBP in mmHg (mean ±SD)	147.96±16.29	145.74±13.82	142.11±12.5	0.103
	DBP in mmHg (mean ±SD)	89.81±16.00	86.07±9.80	84.81±7.62	0.072
2	CCB (n=56)				
	SBP in mmHg (mean ±SD)	151.07±15.41	146.92±12.73	144.78±10.61	0.037*
	DBP in mmHg (mean ±SD)	90.21±11.41	87.03±9.29	85.12±7.80	0.020*

***P<0.05**

Table: 3. Distribution of postmenopausal hypertensive women achieved the goal.

S.No	Parameters	ARB (n=54)	CCB (n=56)
1	Patients attained the goal n (%)	31(57.4%)	38 (67.8%)
2	Patients not attained the goal n (%)	23 (42.5%)	18 (32.1%)
3	Stage I Hypertension n (%)	15 (27.7%)	12 (21.4%)
4	Stage I Hypertension n (%)	8 (14.8%)	6 (10.7%)

DISCUSSION

Hypertension in postmenopausal women depends on age at menopause and postmenopausal period and an absence of female gonadal steroids contributes to an increase in blood pressure in elderly women. With the cessation of ovarian functions, there is an increase in plasma cholesterol and triglycerides, reduction in high-density lipids (HDL), and an increase in low density proteins, which are responsible for an increase in BP [8]. In an Italian cross-sectional study investigated on 22,250 women around the menopause, the postmenopausal status doubled the risk of developing hypertension. Similar results were observed in a study on hypertension prevalence in menopause in the Italian population, a cross-sectional investigation on 18,326 women from 46 to 59 years of age and systolic and diastolic BP were slightly but significantly higher in post- than in pre- and perimenopausal women [9].

Recent hypertension guidelines produced by the European Society of Hypertension and the European Society of Cardiology, state that the primary goal of treatment is to achieve the maximum reduction in

long-term total risk of cardiovascular morbidity and mortality. A reduction in SBP/ DBP to 140/90 mmHg is recommended in all patients with hypertension. More recently, the 2009 reappraisal of the European Society of Hypertension guidelines recommends that reducing blood pressure to within the range of 130–139/80–85 mmHg in all hypertensive patients may be prudent [10].

The results of the present study prove that the rate of persistence on initial antihypertensive treatment is prospectively higher for postmenopausal hypertensive patients treated with ARBs and CCB as first-line drugs. Previous studies showed that the use of CCBs was higher in females than in males (61.9% in males, 67.4% in females, $p<0.05$), while ACEIs and BBs were more commonly prescribed in males than in females ($p<0.05$). Monotherapy with CCBs was more frequently prescribed in females than in males (27.5% in males, 34.3% in females, $p<0.05$) [11]. Evaluating changes in BP during the menopausal transition in female patients and the factors associated with BP change is important because early detection of hypertension and appropriate interventions can prevent its complications, including stroke, myocardial ischemia, and renal dysfunction. Angiotensin receptor blockers (ARBs) may be appropriate as a first-line agent for postmenopausal hypertension and small studies showed the good antihypertensive effect of ACEIs or ARBs in postmenopausal women with hypertension [12].

The overall proportion of women not achieving the BP was less than that of men (57.41% versus 59.59%; $p < 0.05$) at 4 weeks and (22.22% versus 23.78%; $p < 0.05$) at 8 weeks after the CCB or ARB treatment. The proportion of patients not attaining the target SBP increased with age; but, the proportion not achieving the target DBP decreased with age. The analysis showed that the changes in SBP were closely related to gender, indicating that the SBP-lowering effect after CCB or ARB treatment might be better in women and the changes in DBP were closely related to age [13]. The major challenge in the current era of hypertension management among post menopausal women is achieving BP goals. There are several reasons are there for patients not achieve target BP values, including inadequate efficacy with current therapeutic plan.

CONCLUSION

CCB and ARB both are equally prescribed antihypertensive drugs for postmenopausal women with hypertension. In efficacy wise CCB was given better reduction of SBP and DBP compare than the ARB. Studies are needed to find out the rationale behind the greater reduction of SBP and DBP in hypertensive postmenopausal women for prevention of cardiac complications and improving their mortality outcome.

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