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Influence of Antihypertensive Drugs on Left Ventricular Hypertrophy Regression in Hypertensive Patients

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ABSTRACT

Background: Hypertension and its effect on heart in the form of left ventricular hypertrophy are the important predictors of heart failure. Hypertension treatment and left ventricular hypertrophy regression is crucial in the prevention of cardiovascular disease. However, the impact of antihypertensive treatment on left ventricular hypertrophy is less studied and which particular class of antihypertensive medicine is more effective is largely unexplored in our population. We designed this study to explore this issue in subjects taking treatment by evaluation initial and after six months echocardiography findings.

Methods: One hundred fifty subjects aged 25-75 years, taking antihypertensive medicine were enrolled in the study. Along with basic demographic and epidemiological data, initial and after 6 months echocardiographic findings were analyzed for the presence of LV hypertrophy regression. Choice of medicine and necessary changes for the achievement of blood pressure targets were done on treating physician's discretion.

Results: Out of 150 subjects, data for 130 subjects were available for final analysis. Mean age was 54.4 years with standard deviation of 12.3 years. Apart from age, smoking, overweight and obesity, dyslipidemia, and diabetes were the important risk factors with a prevalence of 28%, 26%, 22% and 20% respectively. Although the decrease in rates of LV hypertrophy over the duration of 6 months were not significant in overall and in subjects treated with various antihypertensive medicines, the reductions in LV mass index (108.76±11.3 to 98.46±11.23) in overall and in different antihypertensives were significant ($p<0.001$). The decrease in LV mass index was statistically significant in subjects taking angiotensin converting enzyme inhibitors or angiotensin receptor blockers when compared to subjects taking calcium channel blockers ($p<0.05$). This decrease in LV mass index was not significant when compared between CCBs and mixed drugs.

Conclusion: There was regression in LV hypertrophy among subjects taking antihypertensive treatment. It was more obvious in subjects taking angiotensin converting enzyme inhibitors/angiotensin receptor blockers when compared with subjects taking calcium channel blockers or both.

Keywords: LV mass regression; LV hypertrophy; antihypertensive medicine; hypertension.

INTRODUCTION

Hypertension is an important cardiovascular risk factor.[1] It is multifactorial itself in etiology and it has multidimensional effects on cardiovascular morbidity and mortality. Left ventricular hypertrophy is one of the important mechanisms through which hypertension leads to end stage cardiovascular diseases.[2] Left ventricular (LV) hypertrophy, a marker of cardiac end-organ damage, is associated with an increased risk of cardiovascular morbidity and mortality.[3] LV Hypertrophy, a pathologic thickening of the left ventricular myocardium, is a well-established consequence of chronic hypertension. It is an important predictor of cardiovascular morbidity and mortality, often serving as an intermediary step between hypertension and heart failure.[4] Antihypertensive medications have long been the cornerstone of hypertensive management, and they

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play a crucial role in mitigating the progression of LVH.[3,5] The benefits of antihypertensive treatment are not limited only to the achievement of blood pressure targets, but also to the regression in LV hypertrophy. In recent years, there has been a growing body of evidences indicating that antihypertensive drugs, through various mechanisms, can contribute to the regression of LV hypertrophy.[6,7] Regression of LV hypertrophy is supposed to be beneficial in the prevention major cardiovascular diseases including heart failure and coronary artery disease. This intricate relationship between antihypertensive medications and the reversal of LV hypertrophy provides an in-depth knowledge in the management of hypertension. Among currently available antihypertensive medicines, Angiotensin Converting Enzyme (ACE) inhibitors or Angiotensin Receptor Blockers (ARB) and Calcium Channel blockers (CCB) are the most commonly prescribed medicine. Apart from these, there are Betablockers, Alpha blockers, Thiazide diuretics, Aldesterone antagonist and others.[3,5] But the impact of these various antihypertensive medicines in LVH regression differs widely and the cardiovascular outcome might also differ in these cases.[7,8,9] We have designed a descriptive study to evaluate the evidences of LV hypertrophy regression among subjects taking antihypertensives. In addition, we compared these outcomes among various groups of antihypertensive medicines namely, ACE inhibitors or ARB, CCB and their combinations with an aim to record any differences between them.

METHODS

A prospective observational study was conducted at Bharatpur Hospital from January to December 2022. Ethical approval was taken from Bharatpur Hospital. Participants were recruited from the outpatient department and echocardiography room and were eligible if they met the following inclusion criteria: adults aged 25-75 years with a diagnosis of hypertension; no prior history of cardiovascular events, such as rheumatic heart disease, myocardial infarction or stroke; willingness to provide informed consent for participation; taking any antihypertensive medicines. After obtaining informed consent before data collection. These subjects were followed monthly for the blood pressure control and follow up echocardiography was performed after 6 months. Comparison was made between initial and after six months echocardiographic findings, mainly focused to LV hypertrophy regression or LV mass index regression. In a subgroup analysis, comparison was also made between the subjects grouped as below.

Group 1: Participants taking antihypertensive medicine including any ACE inhibitors or ARBs but not CCBs.

Group 2: Participants taking antihypertensive medicine including any CCBs but not ACE inhibitors or ARBs.

Group 3: Participants taking antihypertensive medicines including both ACEIs/ARBs and CCBs.

Baseline data collection included demographic information, medical history, and baseline echocardiography findings, particularly the presence of left ventricular hypertrophy and LV mass. Follow-up visits were scheduled monthly, and participants underwent blood pressure and heart rate measurement. Adverse events were recorded at each visit and medicine or its dose adjustment were carried. Drug adjustment and dose adjustment were made as required on the discretion of treating physicians. Changes made during each visit were recorded. Echocardiography was performed by experienced cardiologists using a Vivid 9 (GE Echocardiography machine). The presence of left ventricular hypertrophy including Left Ventricular Mass Index (LVMI) and other relevant parameters were measured according to the American Society of Echocardiography guidelines.[10]Echocardiograms were interpreted without knowing the treatment group. Follow up echocardiographic assessment of LV hypertrophy and LV mass was conducted after 6 months of initial study. Change in LV hypertrophy including changes in Left Ventricular Mass (ΔLVM) from baseline to the final visit were recorded. Similarly other parameters such as control of BP, and the incidence of adverse events in each treatment group were also recorded. For the final analysis three groups of subjects were

included; subjects taking antihypertensives including or only ACE Inhibitors or ARBs except calcium channel blockers; subjects taking antihypertensives including or only calcium channel blockers but not ACE Inhibitors or ARBs. Subjects taking both CCBs and ACEI/ARBs at the time of enrollment or later in the due course during drug adjustment were grouped separately. Data analysis was conducted using SPSS software. Descriptive statistics were used to summarize baseline characteristics of the study groups. Changes in Left ventricular mass index and the presence or absence of LV hypertrophy was compared between initial findings and after 6 months findings in the same group. Similarly intergroup comparison was also made to calculate any significance. P-value < 0.05 was considered as statistically significant. A convenient sampling technique was adopted. Only 150 subjects were enrolled in the study, among them 62 participants in group 1, 48 participants in the group 2 and 40 subjects in group 3 at the beginning of the study.

RESULTS

In this study, we investigated the impact of various antihypertensive medication on left ventricular mass regression in a cohort of subjects taking antihypertensive. In overall 150 subjects were enrolled in the study at the beginning, there were 62 subjects in ACEI/ARB group, 48 subjects in CCB group and 40 subjects in mixed group. Over the six months observation period 10, 8 subjects were excluded from the study in first and second groups respectively. Similarly, there were 38 subjects in the mixed group at the end of the study period. So, at

Table 1. The baseline characteristics of the subjects at the time of enrollment.

Particulars	Total (n=150)	Group 1 (n=62)	Group 2 (n=48)	Group 3 (n=40)
Age (years)	54.4±12.3	52.1±12.2	56.4±10.2	54.2±12.6
M:F Ratio	82:68	34:28:00	26:20:00	22:20
Smoking	42 (28)	16 (25.8)	14 (29.16)	12(30)
Overweight and Obesity	39 (26)	14 (22.58)	13 (27.08)	12(30)
Dyslipidemia	33 (22)	12 (19.35)	11 (22.91)	10(25)
Diabetes	30 (20)	15 (24.19)	5 (10.41)	10(25)

Table 2. Comparison of Echocardiographic parameters in group 1, 2 and 3 at the end of the study

Particulars	Total(n=130)	Group 1(n=52)	Group 2(n=40)	Group 3(n=38)
Left Ventricular Hypertrophy (%)	85 (65.38)	32 (61.53)	28 (70)	25 (65.79)
Mean LV Mass (g/m^2)	98.46±11.23	95.4±10.5	101.2±11.2	98.48±10.3
Decrease in LV Mass (%)	112 (86.15)	48 (92.3)	32 (80)	32 (84.21)
LV Diastolic Dysfunction (%)	70 (53.84)	25 (48.07)	25 (62.5)	20 (52.63)

Table 3. Comparison of initial and after 6 months Echocardiographic parameters.

Particulars	At the time of Enrollment	After 6 months	P values
LVH (%)	114 (76)	85 (65.38)	0.05
Mean LV Mass (g/m^2)	108.86±11.3	98.46±11.23	0.0001
LV Diastolic Dysfunction (%)	105 (70)	70 (53.84)	0.005

Table 4. Comparison of initial after 6 months findings og Group 1

Particulars	Initial finding (n=62)	After 6 months findings(n=52)	P values
Left Ventricular Hypertrophy (%)	48 (77.41)	32 (61.53)	0.06
Mean LV Mass (g/m^2)	108.76±11.4	95.4±10.5	0.0001
LV Diastolic Dysfunction (%)	43 (69.35)	25 (48.07)	0.02

Table 5. Comparison of initial after 6 months parameters in group 2.

Particulars	Initial findings (n=48)	After 6 months findings (n=40)	P values
Left Ventricular Hypertrophy (%)	36 (75)	28 (70)	0.59
Mean LV Mass (g/m^2)	109.8±10.9	101.2±11.2	0.0005
LV Diastolic Dysfunction (%)	34 (70.83)	25 (62.5)	0.4

Table 6. Comparison of initial and after 6 parameters in group 3

Particulars	Initial findings (n=40)	After 6 month findings (n=38)	P values
Left Ventricular Hypertrophy (%)	30 (75)	25 (65.79)	0.37
Mean LV Mass (g/m^2)	107.8±11.4	98.48±10.3	0.0003

the end of the study period, there were 52, 40 and 38 subjects in groups 1, 2 and 3 respectively (Table 1). Baseline characteristics of the subjects is given in table 1, mean age and various CV risk factors rates were similar in these groups, except for diabetes; its rate was low (10.41%) in CCBs group. Table 2 summarizes echocardiographic findings in these subjects at the end of the study period. Table 3 to 6 compares the findings at the beginning and after 6 months of study period in overall, and groups 1-3 respectively. LV hypertrophy rate was 76% in overall with almost similar rates among study groups in the beginning of the study (Table 2). Table 4 shows the major indicators related to LV mass at the beginning and after 6 months of study periods in subjects treated with ACE inhibitors or ARBs. The differences in rates of LV hypertrophy is not significant, but the reduction in LV mass index is very prominent and statistically significant ($p<0.001$). Table 5 displays the major findings in group 2; subjects taking calcium channel blockers. In this table also, the reduction in LV mass index is significant but other findings are not. Table 6 displays the comparison of major findings at the beginning and at the end of the study period in subjects on mixed antihypertensives. In this group, there are similar reduction in LV mass indexes among study subjects. When comparison was made between these three groups regarding the reduction in LV mass index, the differences between group 1 and 2 were statistically significant. Other intergroup differences were statistically not significant. In overall, there was significant reduction in LV mass indexes in subjects taking various antihypertensive medicines. The reduction in LV mass index after 6 months treatment was more prominent with ACE inhibitors or ARBs when compared between these various drugs.

DISCUSSION

The findings of our study shed light on the intricate relationship between anti-hypertensive drugs and left ventricular hypertrophy (LVH) regression in hypertensive patients. Our investigation revealed a notable presence of left ventricular mass regression and reduction in left ventricular hypertrophy in subjects getting antihypertensive treatment. These findings were particularly more evident among subjects prescribed Angiotensin-Converting Enzyme (ACE) inhibitors or Angiotensin II Receptor Blockers (ARBs). The robust statistical significance observed in this subgroup suggests a distinctive influence of these medications on the regression of LVH. The mechanisms underlying this phenomenon warrant further exploration. It is plausible that the renin-angiotensin-aldosterone system (RAAS) modulation plays a pivotal role in the observed regression. Both ACE inhibitors and ARBs target key components of the RAAS pathway, potentially mitigating the hypertrophic processes in the left ventricle. Additionally, the vasodilatory and anti-inflammatory effects associated with these drug classes may contribute to the observed regression, emphasizing the multifaceted impact of these medications on cardiac remodeling. Our findings align with previous research highlighting the cardiovascular benefits of antihypertensive drugs.[9,11,12] In addition, our secondary findings showing more prominent LV mass reduction in subjects taking ACE inhibitors or ARBs is also in accordance with similar findings established in some metaanalysis.[12,13] The preferential impact on LVH regression underscores the clinical relevance of these drug classes in managing hypertensive patients at risk of adverse cardiac remodeling. Importantly, this study emphasizes the need for personalized therapeutic approaches, considering not only blood pressure control but also the specific effects on cardiac structure. In contrast to our studies, some studies were unable to show LV mass regression in subjects taking antihypertensives. Gerard et all studied LV mass regression in LIFE study and found no LV Mass regression.[14] In multivariable regression analysis, controlling for age, sex, blood pressure, body mass index, and indices of pump and myocardial function, prior antihypertensive treatment was not associated with either greater LV mass or relative wall thickness on the baseline study. In follow up echocardiography done after one year of antihypertensive treatment, they were unable to record LV mass regression. They proposed that this absence of LV mass regression could be because of previous treatment in study subjects and recommended to include only newly diagnosed fresh cases for the study purpose to record LV mass regression. Lennebakken et al [15] studied patients from the Campania Salute Network. The subjects were free from cardiovascular disease, but had LV hypertrophy based on initial echocardiography. During a median follow-up of 67 months, authors had recorded clear-cut regression of LVH in 14% patients

and additional 9% also had significant reduction in LVMI who had reduction of LVMI ≥5 g/m^2. In their study, nonrespondent with persistent LV Hypertrophy were subjects with older age and longer duration of hypertension, subjects having suboptimal blood pressure (BP) control, subjects with larger body mass index, LV mass, and carotid intima-media thickness. Similarly, women and subjects with diabetes mellitus, isolated systolic hypertension, and metabolic syndrome were common among non-respondents. In multiple logistic regression analysis, older age, female sex, obesity, higher baseline LVMI and carotid intima-media thickness, and suboptimal BP control were significant covariates of persistent LV hypertrophy, independent of diabetes, duration of hypertension, isolated systolic hypertension, follow-up time and number and class of antihypertensive drugs. In our study also the prevalence of LV hypertrophy had fallen from 76% at the beginning to 65% at the end of the study with absolute reduction of 11%. In addition, our study also showed some degree of LV mass index reduction in 86.15% subjects. Agabiti-Rosei et al 16 conducted a study to evaluate long term effect of antihypertensive treatment on left ventricular mass index and other parameters. They measured blood pressure, LVMI, forearm blood flow, plasma renin activity, plasma catecholamines and aldosterone before and after 6 and 12 months of antihypertensive treatment. After 6 months of treatment, they noted a significant reduction in blood pressure, LVMI and minimal vascular resistance and then after 12 months these parameters were further reduced. The LVMI was normalized in 9 out of 14 cases. They concluded that the long-term treatment in essential hypertension can induce normalization of LVMI even before complete regression of arterial structural changes in the forearm. Similar to this study, we have also recorded significant reduction in LVMI in subjects on antihypertensive treatment. Moreover, our study was successful to show some differences among antihypertensive medicines showing higher efficacy of ACEIs/ARBs in reducing LVMI. Nevertheless, the study has its limitations. The descriptive nature and the potential confounding variables necessitate cautious interpretation of the results. Small sample size and diverse groups of subjects included in the study could be another limitation inherent to our study. Similarly, the measurement of echo-based LVMI is not an easy task, chances of errors are very high. Its reproducibility, intra and inter echocardiographer variation in findings were not studied in this study. Therefore, a well-designed prospective, randomized interventional trials are warranted to validate our findings and elucidate the causal relationship between various antihypertensive medicine and LV mass regression including ACE inhibitors, ARBs, and calcium channel blockers.

CONCLUSIONS

This study provides compelling evidence of the influence of anti-hypertensive drugs in overall and especially ACE inhibitors and ARBs, on left ventricular hypertrophy regression in hypertensive patients. These findings contribute to the growing body of knowledge guiding clinicians in optimizing therapeutic strategies for hypertensive individuals, with a focus on mitigating adverse cardiac outcomes through targeted pharmaceutical interventions.

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REFERENCES

1. Yusuf S, Reddy S, Ôunpuu S, Anand S. Global burden of cardiovascular diseases, part I: general considerations, the epidemiologic transition, risk factors, and impact of urbanization. Circulation. 2001; 104: 2746-53.
2. Frohlich ED, Apstein C, Chobanian AV, Devereux RB, Dustan HP, Dzau V, Fauad-Tarazi F, Horan MJ, Marcus M, Massie B. The heart in hypertension. N Engl J Med. 1992; 327: 998–1008.
3. William JE. Systemic Hypertension. Current Problems in Cardiology. 2007:32(40:201-59.
4. Vakili BA, Okin PM, Devereux RB. Prognostic implications of left ventricular hypertrophy. Am Heart J. 2001;141:334–41.
5. Jekell A, Nilsson PM, Kahan T. Treatment of Hypertensive Left Ventricular Hypertrophy. Curr Pharm Des. 2018;24(37):4391-6.
6. Solomon SD, Appelbaum E, Manning WJ, Verma

A, Berglund T, Lukashevich V, et al. Aliskiren in Left Ventricular Hypertrophy (ALLAY) Trial Investigators. Effect of the direct Renin inhibitor aliskiren, the Angiotensin receptor blocker losartan, or both on left ventricular mass in patients with hypertension and left ventricular hypertrophy. Circulation. 2009;119(4):530-7.

7. Liebson PR. Clinical Studies of drug reversal of hypertensive left ventricular hypertrophy. Am J hypertens. 1990;3:512-7.
8. Schulman B, Weiss J, Becker L, Gottlieb S, Woodruff K, Weisfeldt M, Gerstenblith G. The effects of antihypertensive therapy on left ventricular mass in elderly patients. N Engl J Med. 1990;322:1350-6.
9. Dahlof B, Pennert K, Hansson L. Reversal of left ventricular hypertrophy in hypertensive patients: a metaanalysis of 109 treatment studies. Am J Hypertens. 1992;5:95-110.
10. Marwick TH, Gillebert TC, Aurigemma G, Chirinos J, Derumeaux G, Galderisi M, et al. Recommendations on the use of echocardiography in adult hypertension: a report from the European Association of Cardiovascular Imaging (EACVI) and the American Society of Echocardiography (ASE). Eur Heart J Cardiovasc Imaging. 2015 Jun;16(6):577-605.
11. Cruickshank JM, Lewis J, Moore V, Dodd C. Reversibility of left ventricular hypertrophy by differing types of antihypertensive therapy. J Hum Hypertens. 1992; 6: 85–90.
12. Schmieder RE, Martus P, Klingbeil A. Reversal of left ventricular hypertrophy in essential hypertension: a meta-analysis of randomized double-blind studies. JAMA. 1996; 275: 1507–13.
13. Klingbeil AU, Schneider M, Martus P, Messerli FH, Schmieder RE. A meta-analysis of the effects of treatment on left ventricular mass in essential hypertension. Am J Med. 2003; 115: 41–6.
14. Aurigemma GP, Devereux RB, Wachtell K, Palmieri V, Boman K, Gerdts E, et al. Left ventricular mass regression in the LIFE study: effect of previous antihypertensive treatment. Am J Hypertens. 2003 Mar;16(3):180-6..
15. Lennebakken MT, Izzo R, Mancusi C, Gerdts E, Losi MA, Canciello G, et al. Left Ventricular Hypertrophy Regression During Antihypertensive Treatment in an Outpatient Clinic (the Campania Salute Network). J Am Heart Assoc. 2017 Mar 8;6(3):e004152.
16. Agabiti-Rosei E, Muiesan ML, Geri A, Romanell G, Beschi M, Castellano M, Muiesan G. Long-term antihypertensive treatment may induce normalization of left ventricular mass before complete regression of vascular structural changes: consequences for cardiac function at rest and during stress. Journal of Hypertension 1988;6(4):p S94-96.

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