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IMPORTANCE OF INDAPAMIDE ON CONTROL OF BLOOD PRESSURE IN LEFT VENTRICULAR HYPERTROPHY

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Abstract:
Left ventricular hypertrophy (LVH) is a consequence of persistent prolonged systemic hypertension. It is initially a compensatory mechanism, but later, left ventricular hypertrophy carries the risk of arrhythmia, congestive heart failure, angina, systolic and diastolic dysfunction, increased severity and risk of myocardial infarction and heart ruptures. The Framingham Heart Study and other studies have shown that LVH is an independent risk factor for cardiovascular morbidity and mortality. Some classes of drugs regress LVH, e.g., ACE inhibitor, AT1 receptor blockers, calcium channel blockers, B blockers, and methyldopa. The effect of diuretics on regression is inconclusive.

Aim: *To determine the role of indapamide on hypertensive left ventricular hypertrophy.*

Place and Duration: *In the Medicine Unit and Cardiology department of Bahawal Victoria Hospital (BVH) Bahawalpur for one-year duration from March 2019 to March 2020.*

Methods: *We administered indapamide 2.5 mg to 7 patients with echocardiographic evidence of LVH and found that LVID (mm) (mean + SEM) decreased from 50.7+ 1.2 to 50.20 + 1.70, IVST (mean + SEM) decreased from 14.10 + 0.4 to 11.9 + 0.30, PWT (mean + SEM) decreased from 13.0 + 0.3 to 11.2 + 0.2, and LVMI (mean + SEM) decreased from 176.42 + 6.13 to 145.25 + 6.04 g / m2.*

Results: *All patients achieved normal blood pressure, defined as diastolic blood pressure below 90 mmHg. The maximum effect on hypertension was seen within two weeks of treatment. The posterior wall thickness decreased from 13 ± 0.3 (mm) to 11.2 ± 0.2 mm (p <0.001). The interventricular septum thickness decreased from 14.10 ± 0.4 to 11.9 ± 0.3 mm (P <0.001) and the left ventricular mass index decreased from 176.42 ± 6.13 to 145.25 ± 6.04 g / m2 (P <.0001), a mean reduction of 16%. The left ventricular end-diastolic diameter did not decrease significantly (from 50.7 ± 1.2 to 50.20 ± 170). However, there was a significant relationship between ventricular septum thickness and left ventricular mass index.*

Key words: *indapamide, left ventricular hypertrophy, regression, LVMI*

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INTRODUCTION:

Hypertensive patients are prone to left ventricular hypertrophy associated with CCF (Devereux et al., 1982), ischemic heart disease (Kannel et al., 1969), positive systole, paired ventricular tachycardia, and ventricular tachycardia (Mclenachan et al. 1987)[1-2]. The Framingham Heart Study has shown an association between LVH and angina, myocardial infarction, and sudden death (Messerli et al., 1984). Left ventricular hypertrophy is a stronger predictor than age, gender, and ejection fraction, and is as important as the number of constricted coronary arteries[3-4]. When LVH is reversed, ventricular contraction improves and systolic and diastolic functions are improved (Lavie et al., 1992). Antihypertensive drugs that modulate the renin-angiotensin-aldosterone system, sympathetic drive or intracellular free calcium levels include angiotensin converting enzyme inhibitors, beta-blockers, centrally acting adrenergic drugs, and calcium antagonists that lead to regression (Katz, 1998). Diuretics remain the first-line drugs in the treatment of hypertension[5-6]. Not only are they effective in lowering blood pressure, but also cardiovascular morbidity and mortality. Indapamide, an oral once-daily sulphonamide diuretic, is an effective antihypertensive agent and some studies have shown signs of regression of LVH. To see the effect of indapamide on LVH regression, we performed the following study.

SUBJECTS AND METHODS:

Seven patients were selected from the cardiac OPD and written consent was obtained from them. The inclusion criteria were patients with a systolic blood pressure of 180 mm Hg or greater, or a diastolic blood pressure between 95 mm Hg and 115 mm Hg. With echocardiographic evidence of LVH, i.e. LVMI> 130g / m2 in men and> 110g / m2 in women 29-75 years old. Exclusion criteria were secondary arterial hypertension, coronary artery disease, heart failure, cardiac decompensation, patients with concomitant diseases such as renal failure, diabetes or cardiomyopathy. Patients taking drugs such as corticosteroid, digoxin, neuroleptics, and antidepressants were also not taken into account. The M-mode echocardiogram was taken using a standard 3.5 MHz transducer with a Toshiba Sonolayer-LS SAL38 echocardiograph. The patients were held in the left lateral pressure decubitus position, which is a standard echocardiographic technique. The transducer was placed parasternally in the 3rd and 4th intercostal spaces. Airless contact of the transducer with the skin was ensured by using an ultrasonic gel as a coupling medium. The following parameters were obtained from the echocardiogram:

1. Ventricular septum thickness (mm) IVST
2. Posterior wall thickness (mm) of the PWT
3. Left ventricular inside diameter (mm) LVID
4. Left ventricular mass index (LVMI)

RESULTS:

The age of seven patients ranged from 29 to 75 years (mean 54.6 years) and all patients had mild to moderate essential hypertension with mean diastolic blood pressure of 101.5 + 1.2 mmHg and SBP 174.1 + 2.9 mm Hg The mean duration of hypertension was 9.1 + 2.3 years. Indapamide caused a significant reduction in both diastolic and systolic blood pressure. The mean reduction in blood pressure in the supine position was 18.5 mm Hg for diastolic and 28.1 mm Hg for systolic blood pressure. All patients achieved normal blood pressure, defined as diastolic blood pressure below 90 mmHg. The maximum effect on hypertension was seen within two weeks of treatment. The posterior wall thickness decreased from 13 ± 0.3 (mm) to 11.2 ± 0.2 mm (p <0.001). The interventricular septum thickness decreased from 14.10 ± 0.4 to 11.9 ± 0.3 mm (P <0.001) and the left ventricular mass index decreased from 176.42 ± 6.13 to 145.25 ± 6.04 g / m2 (P <.0001), a mean reduction of 16%. The left ventricular end-diastolic diameter did not decrease significantly (from 50.7 ± 1.2 to 50.20 ± 170). However, there was a significant relationship between ventricular septum thickness and left ventricular mass index.

Table-1 Effect of Indapamide on Blood Pressure

	On Day 0	After 6 Months
Systolic BP (mm Hg)	174.1 ± 2.9	146.0 ± 1.7
Diastolic BP (mm of Hg)	101.5 ± 1.2	85. ± 1.5

The echocardiographic parameters and LVMI obtained on day 0 and after 6 months of therapy are:

	On Day 0	After 6 Months
LVID (mm) (mean + SEM)	50.70 ± 1.20	50.20 ± 1.70
IVST (mean + SEM)	14.10 ± .40	11.9 ± 0.30
PWT (mean + SEM)	13.00 ± 0.30	11.2 ± 0.20
LVMI (mean + SEM)	176.42 ± 6.13	145.25 ± 6.04

DISCUSSION:

In our study, the posterior wall thickness (PWT) decreased from 13.00 ± 0.30 to 11.2 ± 0.3 mm (P <0.001). The thickness of the interventricular septum decreased from 14.10 ± 0.40 to 11.9 ± 0.3 mm (P <0.001)[7-8]. The decrease in left ventricular mass index was statistically significant. The LVMI index fell by 16%. Left ventricular end-diastolic diameter decreased from 50.7 1.2 to 50.20 170. The reduction was not significant. A significant relationship was found between the thickness of the interventricular septum and the left ventricular mass index. Sami and Haichin 1991 conducted a study on eleven patients with left ventricular hypertrophy following the use of indapamide. They found that the LVM (mean ± SD) was reduced from 254 ± 47 (g) to 219 ± 46 (g). The reduction was statistically significant (P <0.003). The rear wall thickness decreased from 11.1 (mm) to 10.1 (mm). The internal diameter of the left ventricle in diastole decreased from 51 ± 3 (mm) to 49 ± 5 (mm), the thickness of the interventricular septum decreased from 12 ± 3 to 11 ± 1 (mm) and did not reach statistical significance. LVMI decreased from 146 ± 22 g / m2 to 124 ± 22 g / m2 (P <0.003). The mechanism by which indapamide reduces left ventricular hypertrophy in our patients is unknown. Devereux et al. Have suggested a reduction in peripheral resistance and afterload may be the cause of regression after indapamide use (Komajda and Carey et al., 1996)[9-10]. However, other drugs, such as aspresoline, minoxidil and prazosin, which are known to reduce peripheral resistance and cardiac load post-stress, were not associated with a similar reduction in left ventricular weight in hypertensive patients. Even some studies have found that they can increase left ventricular hypertrophy despite lowering blood pressure[11-12]. These findings have led to other theories of left ventricular mass reduction, such as the reduction of intracellular calcium ions (Homcy, 1998). Indapamide is neutral with respect to the glucose and lipid profile compared to other diuretics. An ideal antihypertensive drug must have beneficial effects on other comorbid factors of cardiovascular morbidity and mortality (Leonetti, 2002)[13-14]. Long-term treatment with indapamide does not alter insulin or glucose metabolism, reducing the risk of hyperglycemia reported with long-term diuretic therapy (Tan et al., 1996). In addition, the metabolic effect of indapamide is also characterized by the absence of deterioration in lipid metabolism, which is an important advantage over other diuretics or B-blockers without ISA (intrinsic sympathetic activity). Indapamide does not worsen and may actually reduce many cardiovascular risk factors, which is an interesting potential for long-term use in hypertensive patients[15]. Indapamide, with its ease of use, its widespread acceptance over many years, and the cardioprotective potential described here, requires further research to see if it can live up to these expectations as an ideal low-cost treatment (Campbell and Brackman, 1990).

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