LEFT VENTRICULAR MASS CHANGES WITH NICARDIPINE THERAPY IN ESSENTIAL HYPERTENSION

Philippe Gosse, Philippe Lacroix, Raymond Roudaut, Modeste Dallocchio
Hôpital Cardiologique du Haut-Lévêque, Centre Hospitalier et Universitaire de Bordeaux, Bordeaux-Pessac, France

SUMMARY. Eighteen hypertensive patients (13 males, 5 females; age 48 ± 13; diastolic blood pressure > 95 mmHg), either previously untreated or who had been off treatment for more than 3 months, underwent M-mode echocardiography before (DO) and after (D90) 3 months of nicardipine therapy (60-90 mg/day). All echocardiograms were read blind, and left ventricular mass (LVM) was calculated (Devereaux’s formula). Blood pressure was significantly reduced after 3 months from 167 ± 15/102 ± 8 mmHg on DO to 152 ± 16/92 ± mmHg on D90 (p < 0.001). The reduction in LVM was not significant: 266 ± 95 g on DO, 247 ± 78 g on D90. There was a trend to a higher (although nonsignificant) LVM reduction in patients with left ventricular hypertrophy at entry (-11%, n = 11) than in patients without left ventricular hypertrophy (-2%), n = 7).

KEY WORDS. left ventricular hypertrophy regression, calcium antagonist, hypertension therapy

Most antihypertensive drugs have been reported to induce regression of left ventricular hypertrophy (LVH) in hypertensive patients, and there are as yet unconfirmed data to suggest that reversal of cardiac hypertrophy is beneficial [1-11].

We have conducted a 3-month survey of the effects of nicardipine, a new calcium antagonist, on left ventricular anatomy assessed by echocardiography in hypertensive patients who were either previously untreated or who had been off treatment for more than 3 months. Our aims were twofold: first, to establish—to our knowledge for the first time in humans—that nicardipine, like other calcium antagonists, has the ability to induce LVH regression; second, to determine whether regression occurs in all hypertensive patients.

Methods

Patients

Eighteen patients (13 men, 5 women; mean age, 48 years; range, 30–75 years) with a diastolic blood pressure (DBP) greater than or equal to 95 mmHg after 10 minutes supine on two occasions were included in the study. The patients had either never been treated with antihypertensive drugs or had discontinued treatment more than 3 months prior to the study. None had a history of ischemic heart disease, cardiac failure, or a DBP greater than or equal to 120 mmHg.

The echocardiograms of all patients were of sufficient quality to allow left ventricular mass (LVM) determination. Secondary causes of hypertension were ruled out by routine screening tests. According to these criteria, most patients were newly recognized hypertensives with mild to moderate hypertension. Their mean BP at entry was 167 ± 14.6/102 ± 7.5 mmHg (mean ± 1 SD).

Trial Course

Fifteen days after initial selection on clinical grounds, BP was redetermined and echocardiography performed. If the patient fulfilled the study criteria, nicardipine (20 mg t.i.d) was started and the efficacy was monitored after 1 month. If the DBP remained greater than or equal to 95 mmHg at the end of the first month, the dose of nicardipine was increased to 30 mg t.i.d. Patients were excluded if their DBP remained greater than or equal to 95 mmHg at the end of the second month, but all patients reached the therapeutic goal. Repeat echocardiography was performed after 3 months.

Echocardiography

All investigations were performed by the same individual. M-mode tracings of the left ventricle, guided by two-dimensional echocardiography, were recorded at the tip of the mitral valve. All recordings were...
coded and read blind at the end of the study, according to the Penn Convention [12]. The measurements of five different cardiac cycles were averaged. LVM was calculated according to Devereux’s formula [12] and indexed for body surface area. The average LVM index of the 18 patients at entry was $146 \pm 44 \text{ g/m}^2$ (range, 97–281 g/m²). LVH, as defined by Devereux’s criteria (LVMI ≥ 135 g/m² in males, ≥ 110 g/m² females [13]), was present in 11 patients.

As an indication of the quality of echocardiograms in this study, 20 sample recordings were reread blind by the same observer after a 1-month interval. The coefficient of variation (standard deviation of the difference between pairs divided by the average of the measurements) with respect to LVM was 4.26%.

**Statistical Analysis**

BP and LVM values before and after 3 months of treatment were compared by a paired t test. The relationship between the change in LVM and the change in BP was studied by linear regression.

**Results**

**Whole Population**

Three months of treatment with nicardipine significantly reduced both systolic and diastolic BP ($152 \pm 16 \text{ vs. } 167 \pm 14.6 \text{ mmHg}$, and $92 \pm 9 \text{ vs. } 102 \pm 7.5 \text{ mmHg}$, respectively; $p < 0.01$). There was no significant change in heart rate ($73.6 \pm 11.7 \text{ vs. } 75.3 \pm 11.6 \text{ beats/min}$).

An overall reduction of 7% in LVM was observed in 18 patients ($246.8 \pm 78 \text{ g vs. } 265.7 \pm 85 \text{ g}$), but not significant ($t = 1.89$). A significant reduction in posterior wall thickness was observed ($10.08 \pm 1.18 \text{ mm vs. } 10.9 \pm 1.6 \text{ mm}; p < 0.05$). There was no significant change in septal thickness ($11.6 \pm 2.9 \text{ mm vs. } 11.4 \pm 3.1 \text{ mm}$) or in end-diastolic diameter ($50.4 \pm 5.0 \text{ mm vs. } 51.3 \pm 4.4 \text{ mm}$).

**Relationship Between LVM Changes And LVH At Entry (Table 1)**

LVH was present in 11 patients at entry according to Devereux’s criteria. These patients were compared to those without LVH using a t test. SBP at entry was significantly higher in the group with LVH ($174 \pm 10 \text{ vs. } 152 \pm 13 \text{ mmHg}$). No other difference was significant. LVM was reduced by an average of 11% in the group with LVH, compared with 2% in the group without LVH. According to our criteria, LVH was no longer present in two patients at the end of the study.

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<th>Table 1. Comparison of patients according to the presence of LVH at entry</th>
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**Correlation Between BP And LVM**

There was a significant correlation between LVM index and SBP at entry ($r = 0.49, p < 0.05$). There was no significant correlation with DBP. There was no correlation between changes in LVM and changes in SBP with treatment ($r = -0.07$). The correlation between changes in the LVM and LVM index at entry did not reach statistical significance ($r = 0.42, t = 1.86$).

**Discussion**

Numerous studies using echocardiography have shown the ability of LVM to regress during anti-hypertensive treatment. This has been well demonstrated with beta blockers [2, 8, 9, 14, 17], converting-enzyme inhibitors [6, 7, 18, 19], and centrally acting drugs [20]. Results with diuretics are still controversial. As in SHR, pure vasodilators such as dihydralazine or minoxidil [3, 7] are unable to induce LVH regression. Few studies have been devoted so far to the effects of calcium antagonists on LVH reversal [4, 5, 10, 21, 22]. This is the first study with nicardipine.

In this study, 3 months of therapy with nicardipine (60–90 mg/day) induced significant lowering of BP, by 10%, without affecting heart rate. LVM was reduced after 3 months of treatment, but the reduction failed to reach statistical significance. The lack of a significant change in LVM in the population as a whole is unlikely to be due to the inability of nicardipine to reverse LVH, since other calcium antagonists from the same group, such as nifedipine [4] and nitrendipine [10], have proved to be effective in this respect. The study may have been too short to demonstrate LVH reversal, though other studies have demonstrated the ability of LVH to regress within 3 months or even less [16]. The statistical power required to demonstrate significant change