Reversal of left ventricular hypertrophy after treatment of hypertension by atenolol for one year

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Summary

1. Fifteen patients with essential hypertension, class I, II WHO, nine males and six females, whose mean age was 46 years, were given atenolol, 100 mg a day, for 1 year.

2. After 1 month, compared with control, systolic and diastolic blood pressures, heart rate and cardiac output were reduced, whereas left ventricular end-diastolic dimension and stroke volume were increased and total vascular resistances, wall stress, left ventricular mass and $h/R$ ratio were unchanged.

3. After 1 year, compared with control, systolic and diastolic blood pressures, heart rate and cardiac output were still reduced, total vascular resistance and wall stress were unchanged. End-diastolic dimension and stroke volume reverted to previous values; left ventricular mass and $h/R$ ratio were significantly decreased.

4. These results show that left ventricular hypertrophy in essential hypertension can revert after 1 year of treatment with atenolol, at least in relatively young people. Since the left ventricle wall stress was not changed after atenolol, the regression of left ventricle hypertrophy seems prevalently to be related to the decrease of adrenergic activity of the heart.

Key words: atenolol, essential hypertension, myocardial hypertrophy, ventricular hypertrophy.

Introduction

The left ventricular hypertrophy consequent to arterial hypertension is mainly due to the increase in left ventricular wall tension, which in turn depends upon left ventricular pressure and dimension, according to Laplace's law [1]. Nevertheless, other factors, particularly the adrenergic system, may contribute to myocardial hypertrophy [2].

The reversibility of hypertensive left ventricular hypertrophy with treatment is controversial and the influence of the various antihypertensive drugs is still doubtful.

The aim of this study was to investigate the influence of atenolol, a selective $\beta$-adrenergic blocking agent, on hypertensive left ventricular hypertrophy.

Methods

Fifteen patients (nine males and six females), of mean age $46 \pm 9$ years, with essential arterial hypertension, class I, II WHO, lasting for $4 \pm 3.9$ (0–12) years were investigated after informed consent.

After 15 days of placebo, they received 100 mg of atenolol, once a day, for at least 1 year.

Patients were examined at the end of a period of placebo (control) and after 1, 2, 3, 6, 9 and 12 months of atenolol treatment. Blood pressure was evaluated by sphygmomanometer measurements and heart rate by the electrocardiogram, after 10 min in a supine position and after 3 min standing. An M-mode echocardiogram was recorded after placebo and after 1 and 12 months of treatment. An Organon Teknika ultrasound unit with transducer of 2-25 MHz, $\varnothing 12$ mm, focused at 7.5 cm, was used together with a fibre optic recorder, (Honeywell), paper speed 50 mm/s.

Echocardiogram was recorded in the supine position with the patient lying on the left side in a 'standard area'; by the same investigator. Each echocardiogram was examined in a blind fashion by two observers, and no significant difference was found between their readings.

The following details were obtained from the records: systolic and diastolic arterial pressures
(SBP, DBP) heart rate (HR), left ventricular end-diastolic dimension (EDD) at the peak of the R wave of the simultaneously recorded ECG, end-systolic dimension (ESD), posterior wall thickness (PWT). The fractional shortening (FS%) is EDD−ESD/EDD% and the velocity of circumferential shortening of the left ventricle (mean VCF) is EDD−ESD/EDD × ET (circ./s).

Left ventricle mass (LVM) was calculated by the method of Devereux & Reichek [3] with the formula: LVM = (EDD + IVST + PWT)² − EDD³ × 1.04. The mean wall stress was obtained by the method of Quinones et al. [4]: MWS = SBP × mean radius (R) × mean wall thickness, where mean radius (R) and mean wall thickness represent the average of end-diastolic and end-systolic measurements. h/R is the relationship between LV wall thickness and diastolic radius. Stroke volume (SV) was determined by Theicholz’s method [5]: SV = EDV − ESV, where V = D³ × 7/2 − 4 + D, cardiac output as SV × HR and total vascular resistances as mean arterial pressure (MAP = DBP + 1/2 pulse pressure)/cardiac output, in units × 80 (dynes s⁻¹ cm⁻²).

Results
The body weight was not significantly changed, compared with control (72.8 ± 2.5 kg), after 1 month (72.0 ± 2.4 kg; P > 0.05) or after 1 year (73.0 ± 2.6 kg; P > 0.05) of atenolol treatment.

Haemodynamic and echocardiographic data are reported in Table 1.

Systolic and diastolic blood pressures and heart rate were reduced, in comparison with control, both after 1 month and after 1 year of treatment, without significant differences between these two periods.

The reduction of arterial pressure was mainly due to a decrease in cardiac output; total vascular resistance did not change significantly after 1 month or 1 year of treatment.

The decrease of cardiac output was essentially referable to the reduction of heart rate, as the stroke volume was slightly but significantly increased after 1 month and again was not significantly different from control values after 1 year. The end-diastolic dimension of the left ventricle was increased after 1 month in relation to the heart rate decrease and reverted to pretreatment values after 1 year, in spite of persistent bradycardia.

The left ventricular mass was decreased after 1 year of treatment and this was due to a reduction of both interventricular septum and posterior wall thickness. The mean wall stress was unchanged after 1 month and 1 year of treatment.

The h/R ratio was unchanged after 1 month, and significantly reduced after 1 year, indicating that left ventricular hypertrophy had reversed.

Moreover, the fractional shortening of the left ventricle was normal in the control state (38.2 ± 1.5%) and showed no significant changes after 1 month (37.7 ± 1.7%; P > 0.05) or 1 year of treatment (38.4 ± 1.4%; P > 0.05). Similarly, the mean velocity of circumferential shortening of the left ventricle (mean VCF), was normal at control (1.28 ± 0.6 circ./s) with no significant modifications after 1 month (1.17 ± 0.06 circ./s; P > 0.05) or 1 year of treatment (1.16 ± 0.04 circ./s; P > 0.05). Therefore atenolol seems to have no significant influence on left ventricular performance.

Discussion

Antihypertensive drugs seem to influence hypertensive myocardial hypertrophy differently.

In spontaneously hypertensive rats, the left

<table>
<thead>
<tr>
<th>SBP (mmHg)</th>
<th>DBP (mmHg)</th>
<th>HR (beats/min)</th>
<th>EDD (mm)</th>
<th>IVST (mm)</th>
<th>PWT (mm)</th>
<th>LVM (g/m²)</th>
<th>SV (ml)</th>
<th>CO (l/min)</th>
<th>TVR (dyne s⁻¹ cm⁻²)</th>
<th>MWS (dyne 10⁻¹ cm⁻²)</th>
<th>h/R</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>170-0</td>
<td>109.2</td>
<td>79.2</td>
<td>51.1</td>
<td>11.5</td>
<td>9.9</td>
<td>157</td>
<td>85.1</td>
<td>6.7</td>
<td>1638</td>
<td>343</td>
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<tr>
<td>5-0</td>
<td>2.3</td>
<td>2.8</td>
<td>1.4</td>
<td>0.4</td>
<td>0.4</td>
<td>12</td>
<td>5.3</td>
<td>0.4</td>
<td>102</td>
<td>17</td>
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</tr>
<tr>
<td>After 1 month</td>
<td>148.3**</td>
<td>93.2**</td>
<td>61.5**</td>
<td>53.8</td>
<td>11.8</td>
<td>10.0</td>
<td>167</td>
<td>94.2</td>
<td>5.8*</td>
<td>1645</td>
<td>319</td>
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<tr>
<td>3-8</td>
<td>3.3</td>
<td>2.5</td>
<td>1.6</td>
<td>0.8</td>
<td>0.3</td>
<td>10</td>
<td>5.0</td>
<td>0.4</td>
<td>123</td>
<td>16</td>
<td>0.02</td>
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<tr>
<td>After 1 year</td>
<td>146.2**</td>
<td>93.1**</td>
<td>61.3**</td>
<td>51.9</td>
<td>10.2</td>
<td>8.0**</td>
<td>126</td>
<td>89.3</td>
<td>5.4*</td>
<td>1744</td>
<td>372</td>
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<td>3-1</td>
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<td>2.9</td>
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<td>6.3</td>
<td>0.4</td>
<td>124</td>
<td>28</td>
<td>0.03</td>
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ventricular hypertrophy has been observed to regress after α-methyldopa [6], or a combination of propranolol and hydralazine [7], to remain unchanged after hydralazine [8] and to increase after minoxidil [8]. Myocardial hypertrophy seems to regress after methyldopa, independently of changes in arterial pressure [9, 10] or after high doses of clonidine, in spite of an increase in total vascular resistance due to α-adrenoceptor stimulation [10].

The reduction of left ventricular mass has been documented by echocardiography in man with essential hypertension after multiple antihypertensive therapy (diuretics plus adrenergic β-blocking agents and vasodilators or diuretics plus methyldopa) [11], after sympatholytic drugs alone or in combination with captopril [12] or after diuretics plus other hypertensive agents by reduction of left ventricular dimensions without decrease in the ventricle's thickness [13]. Reduction of left ventricular mass has also been seen after 2 months of atenolol by reduction in left ventricular dimensions and septal thickness, without change of posterior wall thickness [14].

Moreover, the left ventricle's mass was found to be unchanged after diuretics alone or in combination with sympatholytic drugs [12].

This research has shown that atenolol, a β-adrenoceptor blocking agent, reverses hypertensive left ventricle hypertrophy, reducing thickness of the wall of the left ventricle.

The reduction of left ventricular mass did not seem to correlate with the decrease of left ventricular stress, which was unchanged after treatment, in spite of arterial pressure reduction. After 1 month of treatment, the reduction of arterial pressure was counterbalanced by the increase of left ventricular dimension, and after 1 year by the decrease of left ventricular wall thickness.

Therefore the reduction of left ventricular mass could be due mainly to the decrease of adrenergic activity [2, 7].

In conclusion, hypertensive left ventricular hypertrophy can be reversed after long-term antihypertensive treatment, at least in relatively young people. Atenolol, a selective β-adrenergic blocking agent, reduces myocardial mass, decreasing left ventricular wall thickness.

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**References**


