Treatment of Essential Hypertension: Changes in Blood Pressure Echocardiography and Electrocardiography on Three Therapeutic Regimes


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Summary. Forty-three patients with essential hypertension were randomly allocated to one of the following treatment regimes; - atenolol, atenolol and hydralazine or methyl dopa. Blood pressure fell into the normal range at 3 months and was similar in all 3 groups. Blood pressure remained controlled over the period of study. M-mode echocardiography was assessed initially, at 3, 6 and 12 months. All groups showed a fall in the measured indices towards the normal range with a significant reduction in left ventricular wall thickness at 3 months in the methyl dopa group and left ventricular mass in the atenolol group alone of 6 months. In conclusion, no one treatment regime appeared to have sustained advantages over another and none of the groups showed any deterioration on echocardiographic criteria during the study.

Key words: hypertension; cardiac hypertrophy, echocardiography, therapeutic regimes, beta-receptor blockade, hydralazine, methyl-dopa

Reversal of left ventricular hypertrophy in hypertension was until recently studies mainly in animals. Evidence from this source has suggested that various antihypertensive drugs may have different effects on hypertrophy for the same degree of control of blood pressure. Thus, methyl-dopa was shown to cause regression of hypertrophy whereas vasodilators worsened it [1, 2]. When echocardiography became widely available it allowed for a non-invasive method of assessment of left ventricular dimensions [3, 4] which correlates well with angiographic studies [5, 6]. Studies have shown that left ventricular mass falls with control of blood pressure [7], and that this reversal of hypertrophy can be achieved either with methyl-dopa [8, 9] or beta-adrenoceptor blockers [10]. However, studies with methyl-dopa have indicated that with this drug there is a dissociation between regression of hypertrophy and blood pressure control [9]. The effect of vasodilators has not been investigated in this fashion in essential hypertension. We have conducted the first randomised trial of three different antihypertensive regimes used in essential hypertension and evaluation the changes in left ventricular dimensions by M-mode echocardiography.

Patients and Methods

Forty-nine patients with essential hypertension were entered into the study. All patients had outpatient casual measurements of blood pressure greater than 140/90 mmHg lying and standing on three separate clinic visits. Causes of secondary hypertension were excluded by clinical examination, biochemical investigation and midstream urine examination. Those patients with hypertensive complications (myocardial infarction, cerebrovascular accident, renal failure) or obstructive airways disease were excluded from the study. Although the majority of patients had received no drug therapy, 6 had been treated with a thiazide diuretic and 3 had had other hypotensive drugs (methyl-dopa, guanethidine, acebutolol). All drugs had been discontinued at least 2 months before the study.

After basal studies, including M-mode echocardiography, patients were allocated randomly to one of the following 3 drug regimes: atenolol, atenolol and hydralazine or methyl-dopa. The dosage of drugs was adjusted together with the addition of a diuretic to achieve maximum blood pressure control. Blood pressure and echocardiography were remea-
Results

Forty-three patients were investigated three months after commencing treatment. Six patients of whom four had been allocated to the atenolol and hydralazine regime, did not complete this part of the study (2 through non-compliance, 1 failed to attend again, 1 zine regime, did not complete this part of the study (2 on methyl dopa (1 by his general practitioner, 1 had diarrhoea) and one on atenolol due to poor control. The mean age of the 3 groups were similar (atenolol, 45±3.2 years, atenolol and hydralazine 51±3.2 years, methyl-dopa 49±3.6 years).

Blood Pressure (Table 1)

Initial blood pressures in all three groups, both lying and standing were not significantly different from each other. At 3 months there was a significant fall in lying blood pressure in all 3 groups. A similar fall was seen in standing blood pressure although this did not achieve significance in the systolic pressure of the atenolol and hydralazine group. The fall in blood pressure achieved by the methyl dopa group appeared to be less but analysis of the change in blood pressure at 3 months revealed only a significantly smaller fall in lying systolic pressure in this group. (MD 22±7; A 38±3.5; A + H 45±5.4; F Ratio 4.61; p<0.05). The only group to show a further significant fall in blood pressure between 3 months and 12 months was the one receiving methyl-dopa (lying mean BP 109±5.3 v 96±1.7; p<0.05; standing mean BP 112±4.1 v 102±1.4; p<0.05). Thus, at 12 months the group blood pressures were within the normal range and there was no significant differences between the 3 groups.

Initial pulse rates were comparable between the groups. At 3 months, only the group receiving atenolol alone demonstrated a significant fall in pulse rate (p<0.001) and this was maintained at one year (p<0.05).

Echocardiography (Table 2)

There was no significant difference in left atrial size between the groups (F ration=0.35). In addition there was no change in size in any of the groups over the period of study. Interventricular septal thickness was similar in the three groups and all groups showed a decrease in thickness, although this was not significant. Septal thickness did remain above the upper limit of normal in all groups. In contrast although there was no difference in initial posterior ventricular wall thickness only that of the methyl-dopa group was at the upper limit of the normal range (6–11 mm). This group showed a significant fall at 3 months (p<0.01) although this was not significantly smaller in those studied at 12 months (p>0.05). The atenolol and hydralazine group showed a marked improvement in wall thickness at 12 months although the group was small (n=4, 9.5±0.66 mm v 7.3±0.6 mm; p<0.05).

The initial values for left ventricular mass (LV mass) were similar in all groups (F ratio=0.43). All three groups showed a fall in LV mass this achieving significance in the atenolol group at 3, 6 and 12 months. This was not so in the methyl-dopa group and only seen at 12 months in the small number of patients in the atenolol and hydralazine group.

M-mode echocardiography was performed with in 'Echoline 20A' diagnostic ultrasonoscope (Smith Kline Instruments, Inc., USA) and recorded on ultraviolet paper by a Cambridge Fibroptic Multi-channel Physiological Recorder (Cambridge Medical Instruments Ltd., USA). Patients were investigated lying in the 30° right anterior oblique position reclining at 35° from the horizontal with transducer placement in the third to fifth intercostal space. Simultaneous visualisation of the interventricular septal thickness, left ventricular internal dimension and posterior wall thickness was sought, at just below the mitral valve [4]. Left ventricular mass was calculated as described previously [11]. All echocardiograms were carried out by one technician (J.B) who was not aware of the blood pressure recordings or drug treatment regimes allocated to the patients. The same technician was responsible for all blind measurements. The coefficient of variation for LVID was 1%, septum 7.5% and left ventricular wall was 12%.

Electrocardiographs were standardised so that 1 mV = 10 mm. The sum of the R wave in V2 (right precordial lead) and S wave in V5 (left precordial lead) was recorded for each patient as an electrocardiographic measurement of left ventricular hypertrophy [12]. The height of the T wave was measured in V5.

The results are presented as means±SEM. Statistical analysis was performed using Student's t-test for paired data and one way analysis of variance.