Long-term efficacy and safety of sustained-release diltiazem in the treatment of hypertension

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Summary

The long-term efficacy and safety of sustained-release diltiazem (Tilazem; Parke-Davis) were evaluated. A total of 27 young, physically active patients with hypertension were followed up for 17 months. On a dosage of 90 mg twice daily, adequate blood pressure reduction was obtained in 23 patients (85%). No adverse effects were noted.

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In a previously published double-blind parallel study the short-term antihypertensive efficacy of sustained-release (SR) diltiazem (Tilazem; Parke-Davis) was compared with that of atenolol.[1] The study was extended in order to evaluate the long-term efficacy and safety of the SR formulation of diltiazem.

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Patients and methods

The study comprised 27 patients and the first phase — the comparison of the antihypertensive efficacy of SR diltiazem with that of atenolol[1] — lasted 5 months. On termination of this phase, 14 patients controlled on SR diltiazem were followed up for another 12 months. The 13 patients on atenolol were switched to SR diltiazem 90 mg twice daily and followed up for another 17 months.

The patients were all men and were specifically selected on the basis of youth (mean age 32 ± 2 years) and being physically active.[1]

Patients were evaluated at monthly intervals in the morning 12 - 14 hours after their last dose of SR diltiazem. Blood pressure was measured by conventional mercury sphygmomanometry in triplicate at rest, after 5 minutes in the supine

position, and after 2 minutes of standing. Systolic and diastolic blood pressures were determined by phase I and V Korotkoff sounds, respectively. A resting ECG, chest radiography, body mass determination and laboratory investigations were performed before treatment and after 4, 12 and 17 months of treatment. Laboratory investigations included urinalysis, measurement of haemoglobin concentration, white cell count and differential count, determination of blood glucose and urea value, and serum creatinine, sodium potassium, chloride, aspartate transaminase, alanine transaminase, alkaline phosphatase and uric acid levels.

Untoward effects were evaluated by asking patients at each visit whether they had experienced any problems since their last visit. Significance of difference between values was evaluated using paired and unpaired *t*-tests. Statistical significance was established at the 0,05 confidence level. Values are expressed as mean ± standard error of the mean.

Results

During diltiazem treatment blood pressures decreased significantly ($P < 0{,}0001$). Representative values at 9 months were: systolic blood pressure fell from a mean of 152,5 ± 11,0 mmHg to a mean of 133,3 ± 15,2 mmHg in the supine position and from 144,3 ± 12,1 mmHg to 128,1 ± 13,3 mmHg ($P < 0{,}0001$) in the upright position. Diastolic blood pressure fell from a mean of 105 ± 6,1 mmHg to a mean of 84,7 ± 10,7 mmHg in the supine position and from a mean of 106,5 ± 4,8 mmHg to a mean of 89,2 ± 11,0 mmHg in the standing position (Fig. 1). These reductions were maintained for both systolic and diastolic blood pressures in both supine and standing positions for the duration of the 17 months of observation (Fig. 1).

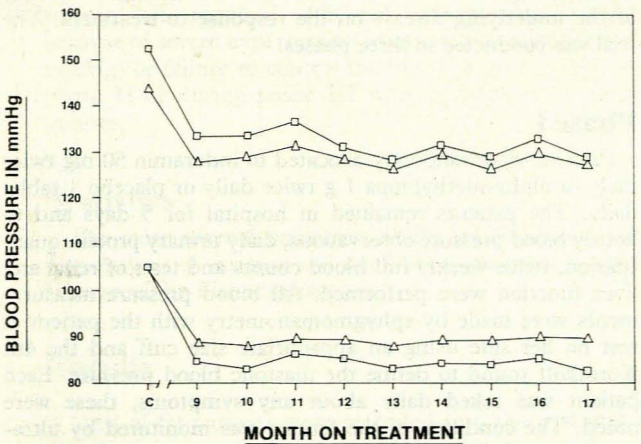

Fig. 1. Supine and erect blood pressure (C = control; □ = supine; Δ = erect).

In 4 patients the supine diastolic blood pressure could not be reduced to < 90 mmHg or by at least 10 mmHg for patients with a baseline value of > 100 mmHg. In 3 of these patients the SR diltiazem had to be increased to 180 mg twice daily and in the fourth patient the blood pressure remained uncontrolled in spite of the double dose and a β-blocker was added in order to achieve adequate control.

No side-effects were noted in any of the patients. No significant changes in the mean values of the laboratory data were noted.

Discussion

In practically all cases of essential hypertension, the increase in blood pressure is due to an elevation of vascular resistance. Vascular resistance is determined by the smooth-muscle tension in the arterioles.[2] The predominant action of calcium antagonists is the dose-dependent inhibition of the slow inward calcium current in the vascular smooth-muscle cells[3] and, as such, they may be potentially useful in the treatment of hypertension. In fact, these agents are now well established as potent antihypertensive agents. The clinical efficacy of the available calcium-channel blockers is, however, hampered by their relatively short half-lives.

In consonance with other studies,[4-7] the present study showed that long-acting SR diltiazem was efficacious and safe. In the majority of patients (23 out of 27) with mild-to-moderate hypertension, adequate blood pressure reduction was obtained with SR diltiazem 90 mg administered twice daily. No side-effects were noted during the 17 months' duration of the study. The simplified administration regimen should improve patient compliance in the long-term treatment of hypertension.

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