Experience with the Once - Daily Calcium Antagonist Amlodipine on 24 - Hour Ambulatory Blood Pressure in Hypertensive Patients

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Abstrak

Telah diteliti efektivitas dan tolerabilitas pemberian dosis tunggal antagonis kalsium amlodipin (5-10 mg) pada 20 penderita hipertensi ringan dan sedang. Untuk menilai efek amlodipin, selain dipakai sfigmomanometer air raksa juga dipergunakan alat pengukur tekanan darah 24 jam ambulatoar. Pengukuran tekanan darah secara ambulatoar selama 24 jam setelah pengobatan amlodipin selama 8 minggu, memperlihatkan bahwa obat ini efektif menurunkan tekanan darah selama 24 jam, tanpa merubah pola normal sirkadian.

Abstract

The antihypertensive efficacy and tolerability of once-daily calcium antagonist amlodipine (5-10 mg) were studied in 20 patients with mild to moderate hypertension. 24-hour ambulatory blood pressure monitoring in conjunction with sphygmomanometric measurement were used to study the effects of amlodipine. 24-hour ambulatory blood pressure monitoring made after 8 weeks of treatment with amlodipine revealed that amlodipine effectively reduced blood pressure throughout the whole 24-h period without altering the normal circadian pattern.

INTRODUCTION

Amlodipine, a structural analog of nifedipine, the first of the 1,4-dihydropyridine calcium antagonists, has been shown to be effective in the treatment of hypertension.[1] The structure of amlodipine is shown in Fig.1.[2] Amlodipine has been shown to have an elimination half-life of 35 h following a single oral dose and to be readily absorbed following oral administration, with peak plasma levels being achieved 6-12 h postdose.[3,4] The pharmacokinetic profile of amlodipine allows once daily administration, which has been shown to reduce blood pressure (BP) measured 24 h postdose.[5] The effective antihypertensive dose appears to be 5 or 10 mg once daily, with simple one-step dose adjustment required to meet individual patient's requirements.[6]

The purpose of this study was to evaluate the antihypertensive efficacy and tolerability of once-daily amlodipine during normal daily activity using 24-h ambulatory BP monitoring and periodic clinic BP measurements.
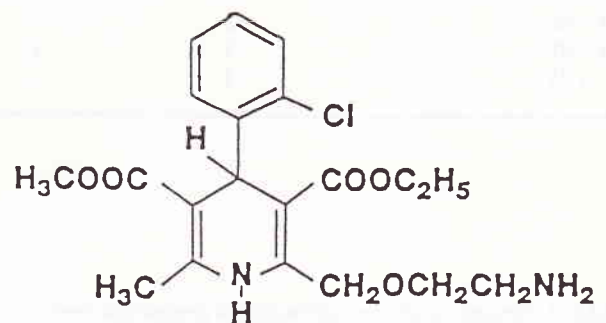

Figure 1. The structure of amlodipine

MATERIALS AND METHODS

Patient selection

Men and women (not of child bearing potential) aged between 21 and 65 years, who had mild to moderate hypertension with supine and standing diastolic BP

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(DBP) of 95-115 mm Hg after a minimum of 2 weeks with no therapy were entered into the study.

Patients with malignant or accelerated hypertension, and/or any other severe concomitant pathologic condition were excluded from the study.

The patients were informed of the nature and purpose of the study and were asked to give their consent to participate.

Study design

A 2-week placebo run-in period was followed by 8 weeks of active treatment with 5-10 mg of amlodipine in a single-blind fashion.

Patients visited the clinic at 2-week intervals. Standing and supine pulse rate and BP were measured in triplicate at each visit. Hematologic and biochemical tests were carried out at the end of the placebo run-in phase, and after 8 weeks of treatment with amlodipine. A 12-lead electrocardiogram (ECG) was obtained on entry to the study and at the end of the treatment with amlodipine.

At the end of the placebo run-in phase and the treatment with amlodipine, ambulatory BP was measured for 24-h period using an automated, noninvasive device (90207 ABP Monitor, Space Labs Inc., Houston, TX, U.S.A.).

A two-tailed t test was used to compare the mean baseline final changes in clinic BP, daytime and nightime 24-h ambulatory BP, heart rate, and ECG parameters. Statistical significance was calculated at 5% level.

RESULTS AND DISCUSSION

Patients

Twenty patients (14 men, 6 women) with a mean age of 47 years (range of 29 to 64 years) were entered into the study.

Three patients failed to fulfill the BP criteria at the end of the placebo phase and were withdrawn. One patient failed to finish the study, because he had to move to another city and so was excluded from the analysis.

Of the remaining 16 patients, seven patients had not received any previous therapy, three patients had received diuretics only, three patients had received beta-blocker, and three patients had received ace-inhibitor. Those drugs were withdrawn before the study.

Eleven patients required an increase in dose to 10 mg of amlodipine once daily and five remained on 5 mg daily.
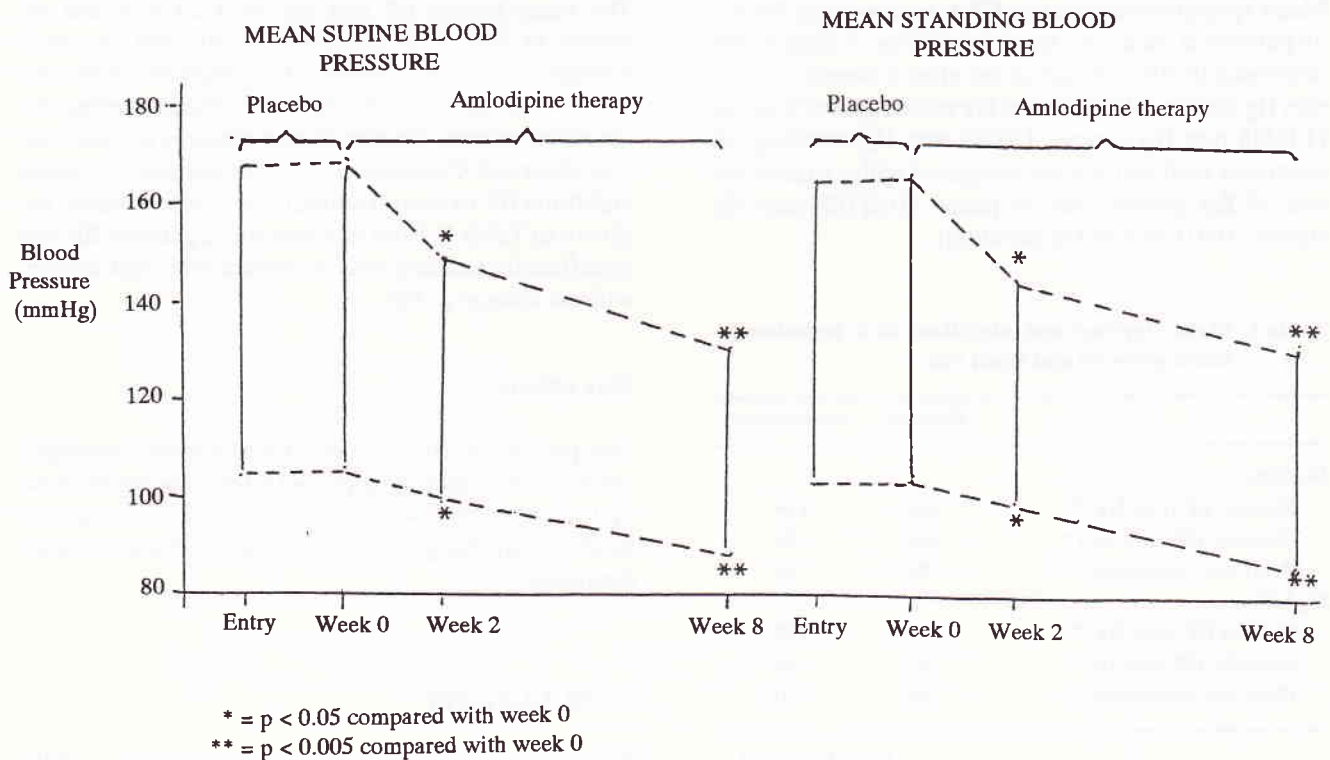

* = p < 0.05 compared with week 0
** = p < 0.005 compared with week 0

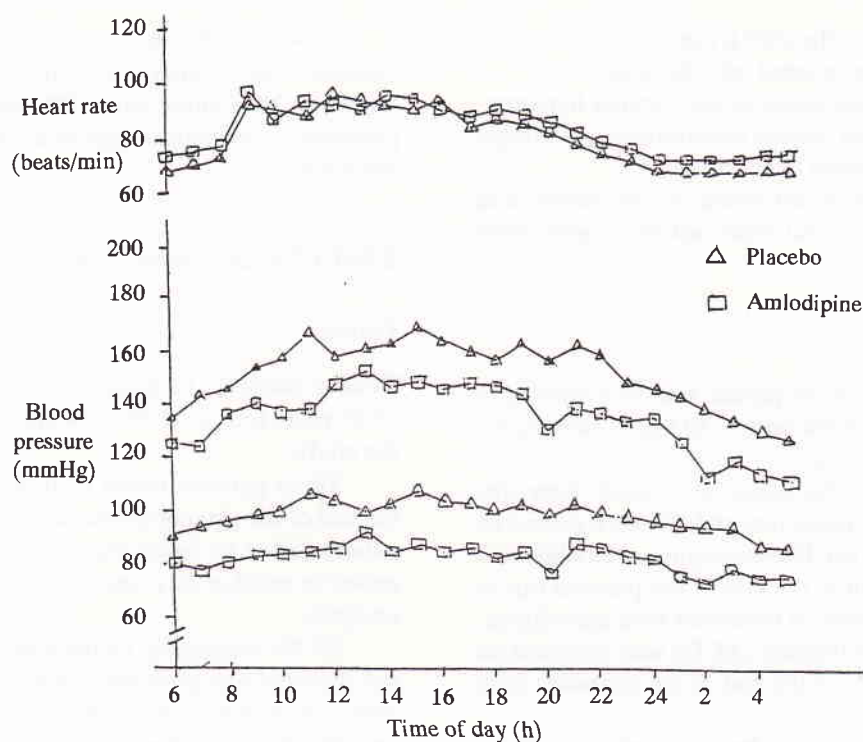*Figure 2. Mean sphygmomanometric blood pressure*

Figure 3. Mean blood pressure and heart rate over a 24-h period using ambulatory monitoring

Sphygmomanometric BP

Mean sphygmomanometric BP measurements for the 16 patients at each visit are shown in Fig. 2. Significant decreases in BP were achieved after 2 weeks (148/96 mm Hg supine, 146/97 mmm Hg standing) and 8 weeks (133/88 mm Hg supine, 133/89 mm Hg standing) of treatment with amlodipine compared with values at the end of the placebo run-in phase (166/105 mm Hg supine, 164/106 mm Hg standing).

Table 1. Mean daytime and nighttime 24-h ambulatory blood pressure and heart rate.

	Placebo	Amlodipine
Daytime		
Systolic BP (mm Hg) *	160	139
Diastolic BP (mm Hg) *	101	89
Heart rate (beats/min) **	88	89
Nighttime		
Systolic BP (mm Hg) *	154	135
Diastolic BP (mm Hg) *	97	84
Heart rate (beats/min) **	68	70

* p value < 0.05
** p value > 0.05

24-h ambulatory BP

The mean hourly BP and HR over 24-h period are shown in Fig. 3. A reduction in BP was observed throughout the 24-h period after treatment with amlodipine compared with placebo without altering the circadian pattern. No significant changes in heart rate was observed. Comparison of mean daytime and mean nighttime BP values on amlodipine and on placebo are shown in Table 1. Both daytime and nighttime BP was significantly reduced after treatment with amlodipine, with no change in HR.

Side effects

One patient on 10 mg dose of amlodipine developed ankle edema which disappeared after reducing the dose up to 5 mg. There were no significant hematologic or biochemical changes and no changes in the electrocardiograms.

CONCLUSIONS

The results of this study clearly show that once daily amlodipine provides 24-h BP control without altering

the physiologic circadian pattern of BP variation. Amlodipine was well tolerated in this study.

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