Captopril + hydrochlorothiazide 24 h ambulatory monitoring effects

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- 1 The purpose of this study was to evaluate over a 24 h period the antihypertensive effect of captopril 50 mg + hydrochlorothiazide (HCTZ) 25 mg once a day in mild to moderate hypertension.
- 2 Ambulatory recordings over 24 h of the blood pressure using the Spacelabs system were performed, at the end of a 15-day placebo period and after giving captopril + HCTZ for 45 days.
- 3 Captopril + HCTZ significantly decreased ($P < 0.001$) systolic and diastolic blood pressures for both the diurnal period (8 h to 22 h) and the nocturnal period (22 h to 8 h). No change in heart rate was observed.
- 4 For further analysis, the mean hour values of blood pressure and heart rate were calculated. A constant decrease of the systolic and diastolic blood pressure throughout the 24 h was obtained after captopril + HCTZ without any change in heart rate and in nyctohemeral variations.
- 5 The study provided evidence that, in patients with mild to moderate essential hypertension, captopril + HCTZ once a day decreased systolic and diastolic blood pressure all day long without any change in the heart rate and the blood pressure nyctohemeral cycle.

Keywords arterial hypertension ambulatory blood pressure captopril hydrochlorothiazide

Introduction

The efficacy of captopril in the treatment of hypertension has been proved in several studies (Richer *et al.*, 1984; Corea *et al.*, 1984; Havelka *et al.*, 1982; Jenkins *et al.*, 1984; Muisan *et al.*, 1984; Simon *et al.*, 1984). Its physiological and synergistic association with hydrochlorothiazide showed a more significant decrease of blood pressure in hypertension (Corea *et al.*, 1984; MacGregor *et al.*, 1985; Weinberger, 1982). This association seems to decrease the incidence of metabolic secondary effects of hydrochlorothiazide when used alone (Veterans Administration Cooperative Study Group, 1982; Weidman *et al.*, 1983; Leary *et al.*, 1985). The purpose

of this study was to evaluate by a non invasive ambulatory blood-pressure monitoring method, the antihypertensive effect of captopril 50 mg + hydrochlorothiazide 25 mg given once a day in mild to moderate hypertension.

Methods

The study was carried out on nine patients (eight males and one female) aged from 33 to 65 years. Mean age was 52 ± 9.1 years ($\pm$ s.e. mean). Mean weight was 77 ± 9 kg. In all patients, therapy was discontinued at least 4 weeks before

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the beginning of the study. Our hypertensive patient population included subjects in whom a supine diastolic blood pressure equal or superior to 95 mm Hg was documented after a 15-day placebo period. Patients with obvious secondary hypertension were excluded on the basis of thorough clinical and biological investigations, as previously described (Safar *et al.*, 1983). From the nine patients, none showed clinical evidence of congestive heart failure, coronary insufficiency, valvular heart disease or cerebrovascular disease.

Study design

After informed consent and a detailed description of the procedure, the patients were investigated as follows: Firstly, ambulatory blood pressure recordings were performed prior to therapy just after the placebo period. Secondly, captopril 50 mg + HCTZ 25 mg was given once daily at 08.00 h by oral administration. Thirdly, at the end of the protocol (after 45 days of treatment) a second ambulatory blood pressure monitoring was performed. Sphygmomanometer blood pressure measurements and side effects have also been studied at the same periods.

Non-invasive nyctohemeral blood pressure measurements

Automated blood pressure monitoring was carried out in each patient with a Spacelabs apparatus to measure and record blood pressure and heart rate as previously described (Harshfield *et al.*, 1983). Recordings were performed throughout a full 24 h period every 15 min from 06.00 h to 24.00 h and every 60 min during the remaining night period. The ambulatory monitoring was undertaken for a full day, the patient working as usual during the day and then going home normally in the evening.

The reliability of this technique was determined previously (Asmar *et al.*, 1985) in 30 patients and was cross-checked with a mercury sphygmomanometer. The microphonic method was tested for accuracy in 15 patients and the oscillometric method in 15 patients, as these two methods are used with the Spacelabs system (Asmar *et al.*, 1985). Table 1 indicates the correlation coefficient of the relationships between blood pressure sphygmomanometer measurements and Spacelabs measurements. Higher correlation coefficients were observed with the microphonic method. For this reason oscillometric recordings were taken into account only if microphonic measurements were not obtained for technical reasons.

Statistical evaluation

Recordings which showed an inconsistent increase or decrease in systolic or diastolic blood pressure of greater than 50 mm Hg, and readings with a calculated pulse pressure of less than 10 mm Hg were deleted prior to further analysis of data. Each full day recording was divided into a day period (from 08.00 h–22.00 h) and a night period (from 22.00 h–08.00 h) based on a patient diary. The means and s.e. mean of systolic and diastolic pressures and of heart rate were calculated by computer for day and night periods separately. For the full 24 h consecutive 1 h periods Student's *t*-test for paired data was used to evaluate the pressure and heart rate changes following captopril + HCTZ administration (Schwartz, 1981).

Results

Figure 1 shows the blood pressure and heart rate changes before and after captopril 50 mg + HCTZ 25 mg for the day, night and full day

Table 1 Values of the linear correlation coefficient between the mercury sphygmomanometer measurement and those by the microphonic and oscillometric method of the Spacelabs monitor

<i>n</i> = 15	Systolic BP (mm Hg)	Diastolic BP (mm Hg)	Heart rate (beats min ⁻¹)
Microphonic method Sphygmomanometer	0.95	0.86	0.98
Oscillometric method Sphygmomanometer	0.82	0.82	0.98

n = number of patients in each method

Figure 1 Mean ($\pm$ s.e. mean) values of blood pressure (BP) measured by the Spacelabs monitor before (■) and after (▢) captopril 50 mg + HCTZ 25 mg: *** $P < 0.001$.

Figure 2 Systolic and diastolic blood pressure (BP) before (●) and after (▲) captopril 50 mg + HCTZ 25 mg mean hour values: * $P < 0.05$, ** $P < 0.01$.

periods. Both systolic and diastolic pressures were significantly decreased ($P < 0.001$) during day and night. No significant change in heart rate was observed.

Figure 2 shows the 24 consecutive 1 h periods before and after captopril 50 mg + HCTZ 25 mg for systolic and diastolic pressures. Significant differences were observed between 06.00 h and 24.00 h while the differences before and after captopril 50 mg + HCTZ 25 mg were not significant between 24.00 and 06.00 h. Similar results were observed for diastolic pressure. Heart rate was unchanged by captopril 50 mg + HCTZ 25 mg throughout the 24 h period. For systolic and diastolic pressures and heart rate, the nyctohemeral cycle was unchanged before and after drug treatment.

Discussion

Based on diurnal and night periods measurements, captopril 50 mg + HCTZ 25 mg was

shown to decrease blood pressure significantly after 45 days of treatment when given once a day (Figure 2). Using 24 h consecutive 1 h periods, blood pressure decreased significantly from 06.00 h–24.00 h but not in the remaining period of the night. The lack of significance during this period may be explained as follows. Firstly, by the number of measurements per hour: as in the latter period, blood pressure was recorded only once per hour whereas four measurements were made hourly in the daily period. Secondly, as is well known (Reeves *et al.*, 1983), the initial level of blood pressure in the night period is lower than that in the daily period, so the decrease in the night is expected to be relatively less than the decrease in the day. Finally, it must be emphasized that captopril 50 mg + HCTZ 25 mg did not impair heart rate throughout the day and did not change the blood pressure nyctohemeral cycle.

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