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CAPTOPRIL IN THE TREATMENT OF MILD ESSENTIAL HYPERTENSION

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1 Among 34 patients with mild essential hypertension treated for four weeks with captopril alone the blood pressure of 47% returned to normal. By the end of the fourth week chlorthalidone had been added to captopril in 18 of the patients; 15 then achieved normal blood pressure, and only three failed to achieve diastolic blood pressures of under 100 mm Hg.

2 Among the 16 patients who continued to take captopril alone after the fourth week all achieved a return to normal blood pressure during the next 12 months of treatment.

3 Side effects of captopril were essentially limited to rash, taste alteration, and nausea and vomiting, which were usually mild and transient.

Introduction

Research over the past 20 years has defined the renin–angiotensin–aldosterone control system and defined its involvement in human hypertension. Against this setting, the discovery of a series of drugs, first β-receptor blockers, then saralasin and converting-enzyme inhibitors, whose main action can be traced to suppression of the renin factor, has enabled new understanding and a new era of treatment just as the advent of sodium volume suppressive drugs gave impetus to an earlier advance.

After the discovery of captopril, which inhibits the conversion of angiotensin I to angiotensin II, many investigators provided convincing supportive evidence of the role of captopril in treating severe complicated cases of hypertension.

Figure 1 shows a case that illustrates this first point. This 54-year-old woman, diagnosed as having World Health Organisation stage III essential hypertension, was under a stepped-care treatment protocol. Chlorthalidone and atenolol were then administered up to a dose of 150 mg each. Blood pressure did not return to normal, so hydralazine was added up to 150 mg; 40 mg of guanethidine was then added to the regimen. Her blood pressure still did not return to normal, so we decided to treat the patient with captopril while she was still taking chlorthalidone and atenolol. This proved to be the regimen that allowed us to control blood pressure, indicating the benefits of using captopril in treating severe cases of hypertension.

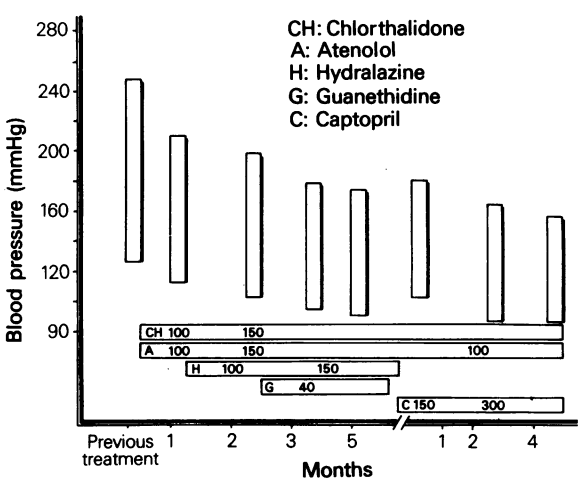

Figure 1 Blood pressure and treatment in a patient with stage III essential hypertension who responded eventually to captopril.

Methods

In the present study we treated several patients with mild essential hypertension with captopril alone or in combination with a diuretic over one year. Thirty-four patients, 12 men and 22 women, were enrolled in this study. They were aged 29–62 years and 15 had stage I hypertension and 19 stage II (WHO classification).

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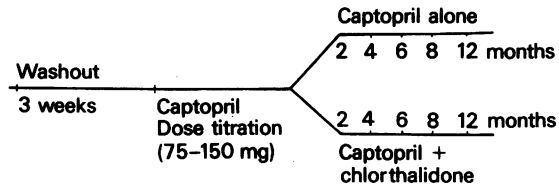

Figure 2 Design of study.

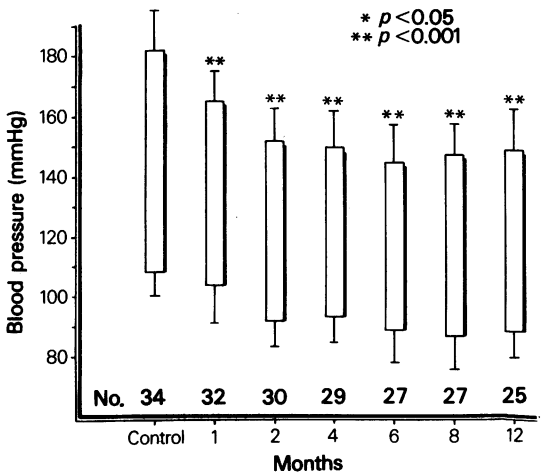

Figure 3 Blood pressure in patients treated with captopril alone.

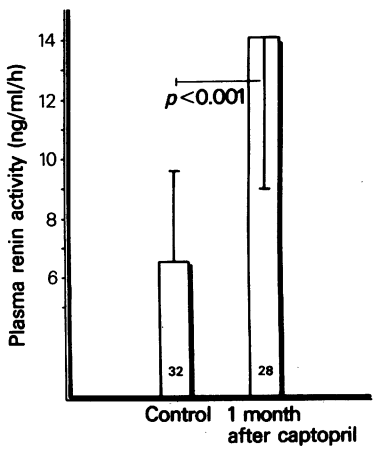

Figure 4 Effect of captopril on plasma renin activity.

The study was divided into three periods (Figure 2). During a wash out period of three weeks the baseline blood pressure was stabilised and the effects of previous antihypertensive medication stopped. In the next four weeks of dose titration the dose of captopril was increased from 25 mg to 150 mg three times a day. After that, patients continued on the appropriate dose of captopril or, if the diastolic blood pressure was not controlled (< 100 mm Hg), chlorthalidone was added at a starting dose of 50 mg and increased up to 100 mg once a day.

Patients visited the clinic every week until the last week of the titration period, when they were seen every four weeks. The blood pressure was recorded with a standard mercury sphygmomanometer and the diastolic pressure was taken at the disappearance of the audible pulse beat. The value recorded was the average of three consecutive readings in which the diastolic pressure did not differ by more than 5 mm Hg. Blood pressure was recorded after 10 minutes of rest.

Results and comment

After treatment for four weeks, the blood pressure of 47% of the patients treated with captopril alone had returned to normal. Over the next 12 months of treatment blood pressure in all the patients taking captopril alone returned to normal (Figure 3).

On the other hand, by the end of the fourth week chlorthalidone had been added to the regimen of 18 (53%) of the patients treated with captopril. Normalisation of the blood pressure was achieved in 15 (82%). Three patients did not complete the study because of adverse reactions, nausea and vomiting in two and a rash in the third. Nevertheless, side effects on captopril were essentially limited to rash, alteration of taste, nausea and vomiting, which were usually mild and transient.

After a month of captopril treatment, plasma renin activity was significantly increased (Figure 4). Figure 5 shows blood pressure, mean arterial pressure, heart rate, and plasma renin activity in a patient with low-renin hypertension. Figure 6 shows the same variables in a patient with high-renin hypertension. As with many other investigators, we observed that the changes in mean blood pressure were to some extent related to the pretreatment levels of plasma renin activity. This suggests that the antihypertensive effect of captopril depends at least partly on its interference with the renin–angiotensin system.

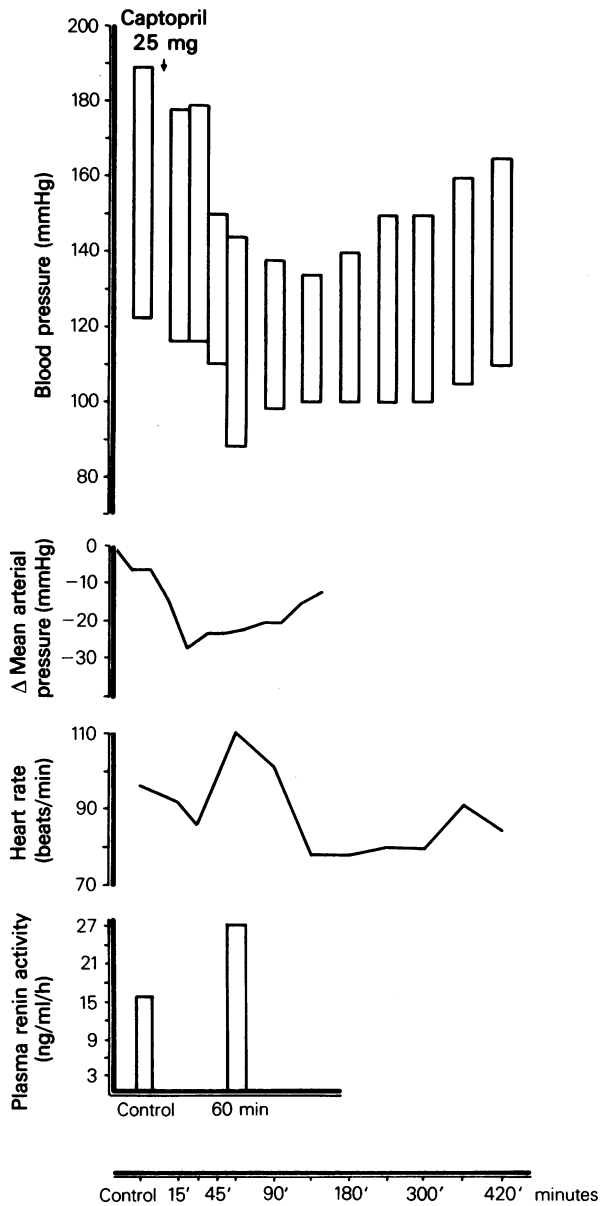

Figure 5 Blood pressure, mean arterial pressure, heart rate, and plasma renin activity in a patient with low-renin hypertension.

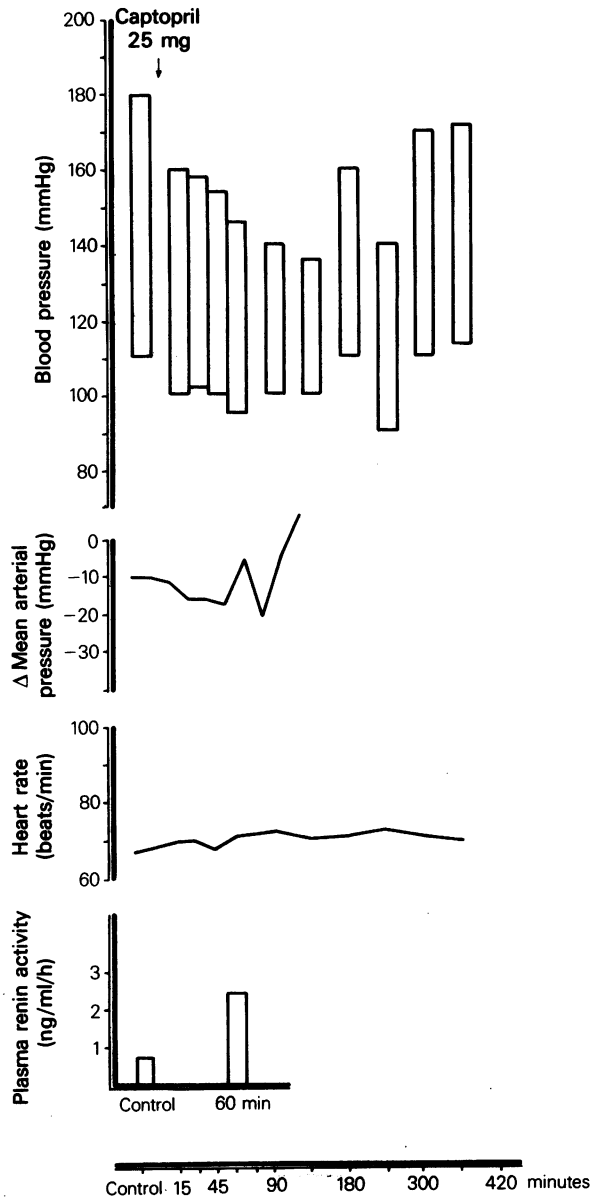

Figure 6 Blood pressure, mean arterial pressure, heart rate, and plasma renin activity in a patient with high-renin hypertension.