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Short Report

The Effect of Captopril on Heart Rate in Several Types of Hypertensive Patients

YUTAKA IMAI, KEISHI ABE and KAORU YOSHINAGA
The Second Department of Internal Medicine, Tohoku University School of Medicine, Sendai 980

IMAI, Y., ABE, K. and YOSHINAGA, K. *The Effect of Captopril on Heart Rate in Several Types of Hypertensive Patients.* Tohoku J. exp. Med., 1981, **133** (2), 243-244 —— Captopril, an orally active converting enzyme inhibitor, was administered in a dose of 50 mg to 88 untreated hypertensives (70 essential hypertensives, 8 patients with renal arterial disease, 10 patients with renal parenchymal disease). Captopril caused a decrease in heart rate in 18 patients, but an increase in 2 patients. In the remaining 68, heart rate did not change. As a whole, captopril caused a significant decrease in blood pressure without compensatory increase in heart rate. The change in heart rate caused by captopril in patients with renal arterial disease was significantly higher than that in essential hypertensives. A significant negative correlation was observed between the change in heart rate and plasma renin activity obtained immediately before captopril administration ($n=79$, $r=-0.425$, $p<0.001$). —— captopril; heart rate; blood pressure; plasma renin activity

Captopril has a potent antihypertensive action and, hemodynamically, behaves like a vasodilator (Cody et al. 1978). Several vasodilators have been shown to increase heart rate. Reflex tachycardia is one of undesirable effects of vasodilators when used for the treatment of hypertension. In this study we examined the effect of captopril on blood pressure and heart rate in several types of hypertensive patients.

Studies were performed on 88 untreated hypertensives (70 essential hypertensives, 8 patients with renal arterial disease and 10 patients with renal parenchymal disease). The diagnosis of renal arterial lesion was made angiographically, while that of renal parenchymal disease was made by renal biopsy. The study was started on fasted patients between 9:00 and 9:30 a.m. The subjects were kept in supine position during the study period. After at least 30 min of pre-control period, blood pressure and heart rate were measured every 10 min for 1 hr. The terms used for 30 min, 20 min, 10 min before and immediately before drug administration were expressed as -30 min, -20 min, -10 min and 0 time, respectively. At the end of this control period, blood was collected for the measurement of control plasma renin activity (PRA), after which 50 mg of captopril was administered orally. Blood pressure and heart rate were measured every 30 min with an arteriosonde (Roche) or a mercury sphygmomanometer and a cardiotachometer or palpation of radial pulse. Since the spontaneous change in heart rate measured in each patient during the control period (0, -10, -20, -30 min) was 1.7 ± 1.6 beats/min (mean±S.D.), the change in heart rate above ±4.9 beats/min [$\pm$(mean+2S.D.)] after drug administration was judged as a significant one. PRA was measured using radioimmunoassay of angiotesin I. Results are expressed as mean±S.D. Statistical analysis of the data was performed according to Student's t test.

Captopril decreased mean arterial pressure (MAP) significantly 30 min after the administration. The maximum decrease was reached 1 hr after the drug administration and this level of the MAP was maintained 1 hr thereafter. Despite the marked fall in blood pressure, heart rate exhibited a tendency to decrease. The differences in heart

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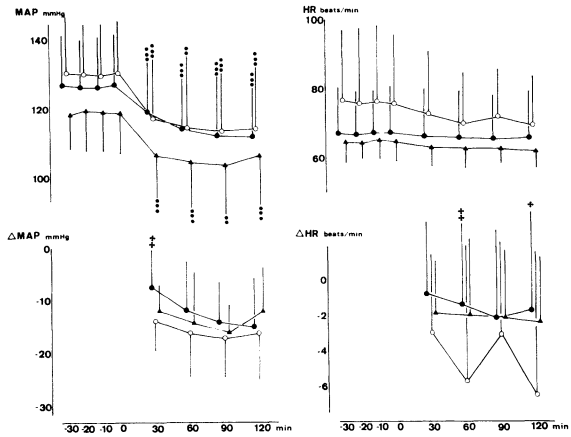

Fig. 1. Difference of effects of captopril on mean arterial pressure (MAP) and heart rate (HR) in 3 groups of hypertension. Essential hypertensives, ●; patients with renal arterial disease, ○; patients with renal parenchymal disease, ▲. The numbers on the bottom line show the times before and after captopril administration. Significant difference from the control period (0): double dots, $p<0.01$; triple dots, $p<0.001$. Significant difference between essential hypertensives and patients with renal arterial disease; single cross, $p<0.05$; double crosses, $p<0.01$.

rate in each patient 30, 60, 90 and 120 min after captopril administration from that of 0 time were averaged and the result was judged on the basis of criteria mentioned above. Heart rate decreased in 18 cases out of 88 patients, while it increased in 2 cases. In the remaining 68 cases, heart rate did not change. As shown in Fig. 1, the change in MAP caused by captopril and its time course were almost identical in the groups of hypertensive patients. Captopril caused a slight decrease in heart rate in all 3 groups, although statistically insignificant. The change in heart rate caused by captopril in patients with renal arterial disease was significantly larger than in essential hypertensives 60 and 120 min after captopril administration. The control PRA in patients with renal arterial disease (30.3 $\pm$17.2 ng/ml per 6 hr) was significantly higher than that in essential hypertensives (7.6$\pm$ 8.8 ng/ml per 6 hr, $p<0.001$) as well as in patients with renal parenchymal disease (10.5$\pm$12 ng/ml per 6 hr, $p<0.001$). The significant negative correlation was observed between the change in heart rate and control PRA ($n=79$, $r=-0.425$, $p<0.001$).

Several vasodilators have been shown to increase heart rate. The increase in heart rate accompanied by an increase in cardiac work and oxygen consumption is undesirable in the treatment of hypertensive patients with coronary insufficiency. Koch-Weser (1974) described that vasodilators occasionally induced angina pectoris in hypertensive patients with coronary insufficiency. We concluded that the absence of compensatory tachycardia and/or bradycardia with captopril is one of its favorable actions. The negative chronotropic effect of captopril is greater in high renin hypertensives. This effect of captopril may be related to the inhibition of angiotensin II through angiotensin converting enzyme inhibition. More detailed study on the mechanism of chronotropic effect is now under progress.

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