Thesis Title The Effects of Indomethacin on Antihypertensive Activity of Captopril and Enalapril in Induced Hypertensive Rats

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Date of Graduation 12 October B.E. 2537 (1994)

ABSTRACT

The concurrent administration of drugs used in treating arthritis and hypertension is considerable, especially in the elderly, and drug interactions may be occurred. The aim of this study was to evaluate the effects of indomethacin on antihypertensive activity of captopril and enalapril in induced hypertensive rats produced by deoxycorticosterone acetate (DOCA)-salt and adrenal compression. In addition, whether the BP lowering effects of captopril and enalapril involve prostaglandin synthesis were also evaluated.

Rats were divided into 5 groups, i.e. DOCA-salt hypertensive, adrenal regeneration hypertensive, nephrectomized control, normal, and salt treated rats. Oral doses of 30 mg/kg/day captopril as well as 10 mg/kg/day enalapril were given to all rats for 2 days. The BP lowering effects of captopril and enalapril found in DOCA-salt hypertensive rats were more effective than those found in other groups. Oral administration of indomethacin 5 mg/kg/day for 2 days increased BP in all experimental groups, particularly DOCA-salt hypertensive and adrenal regeneration hypertensive groups. When

indomethacin could attenuate the BP lowering effect of captopril or enalapril. However, BP of rats in each group was still significantly lower than the pretreated levels. The magnitude of BP lowering effect in any models depended on the pretreatment BP levels, as it was found that the highest effect was detected with DOCA-salt hypertensive rats and on the 1st day of treatment. Intravenous injection of bradykinin at a dose of 5 μg/day induced hypotensive effect in normal and DOCA-salt hypertensive rats. The BP lowering effect of bradykinin found in DOCA-salt hypertensive rats was not significantly different from that found in normal rats. Both captopril and enalapril were significantly enhanced the hypotensive effect of bradykinin. These effects found in DOCA-salt hypertensive rats were significantly greater than those found in normal rats. Indomethacin could reduce the BP lowering effect and duration of action of bradykinin in normal and DOCA-salt hypertensive rats. Both normal and DOCA-salt hypertensive rats were significantly different in BP lowering effect of bradykinin between pretreated with captopril or enalapril and pretreated with indomethacin.

The results showed that indomethacin could attenuate the antihypertensive activity of captopril and enalapril. In addition, captopril and enalapril potentiated, whereas indomethacin attenuated the BP lowering effect of bradykinin. These results could support the suggestion that both prostaglandin and bradykinin might be involved in the antihypertensive mechanisms of captopril and enalapril.