Proc EDTA–ERA (1985) Vol 22

ROLE OF ENDOGENOUS PROSTAGLANDINS ON THE RELEASE OF ANTI DIURETIC HORMONE

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Summary

Captopril was administered to normal volunteers before (control study) and after inhibition of prostaglandin synthesis by aspirin (ASA study), to investigate the relationship between endogenous prostaglandins and anti diuretic hormone (ADH) release without the influence of angiotensin II.

Captopril increased significantly the plasma and renal synthesis of PGE_2 and 6-keto-$PGF_{1\alpha}$ in the control study, while these prostaglandins were undetectable in plasma and significantly reduced in urine after aspirin administration.

Plasma renin activity increased and plasma ADH decreased significantly in both studies after captopril. Glomerular filtration rate (GFR) and renal plasma flow (RPF) did not change in either study, urine output and FE_{Na} increased only in the control study after captopril. These results suggest that endogenous prostaglandins do not play an important role in anti diuretic hormone release.

Introduction

The influence of exogenous PGE_2 on ADH release has been studied extensively in hypothalamo-hypophyseal complex in organ culture and in experimental animals [1,2], but the role of endogenous PGE_2 on ADH release is still unknown in normal man. A recent study in man suggests the possibility that PGE_2 stimulates the release of ADH through angiotensin II [3].

Captopril, an angiotensin I converting-enzyme inhibitor, decreases AII formation, meanwhile stimulating prostaglandin synthesis, it thus may be used to study the relationship between endogenous prostaglandins and ADH without the influence of angiotensin II. For this purpose we administered captopril to normal subjects before and after prostaglandin synthesis inhibition by aspirin.

Materials and methods

The effects of captopril alone (control study) and the effects of captopril plus aspirin (ASA study) on plasma ADH, prostaglandin synthesis and renal function have been investigated in six normal volunteers.

Two basal clearance periods of 60 minutes were performed with urine collection by spontaneous voiding; then 100mg of captopril were given and two additional 60 minute clearance periods were carried out with blood samples drawn at 30, 60 and 120 minutes after captopril.

In the ASA study, after the basal period, 500mg of aspirin were given by mouth and a clearance period of 60 minutes was obtained with blood samples drawn 60 minutes after aspirin. Captopril was then given and the study was completed as in the control one. Blood pressure was measured before and every five minutes after captopril. GFR and RPF were determined as inulin and PAH clearances, these were infused in five per cent glucose at a constant rate of 0.5ml/min throughout the study.

Plasma ADH, plasma and urinary PGE_2 and 6-keto-$PGF_{1\alpha}$ were measured by radioimmunoassay [3].

Results

Figure 1 shows the results of the control study. After captopril there was a significant increase in plasma PGE_2 and in the urinary excretion of both PGE_2 and 6-keto-$PGF_{1\alpha}$. PRA also increased following captopril administration; plasma ADH decreased significantly 60 and 120 minutes after captopril. No modifications of GFR and RPF were observed in this study, while urine output, FE_{Na} and osmolar clearance increased significantly after captopril. In the ASA study, plasma PGE_2 were undetectable one hour after aspirin and did not change when captopril was administered (Figure 2); the urinary excretion of prostaglandins was also significantly reduced by aspirin. PRA increased and plasma

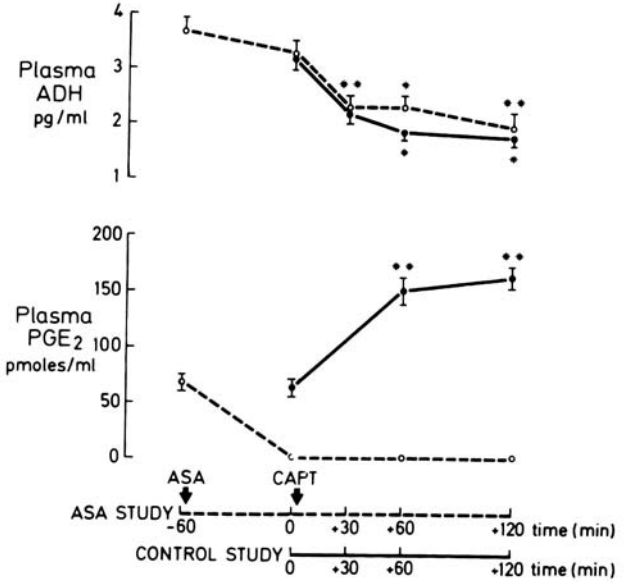

Figure 1

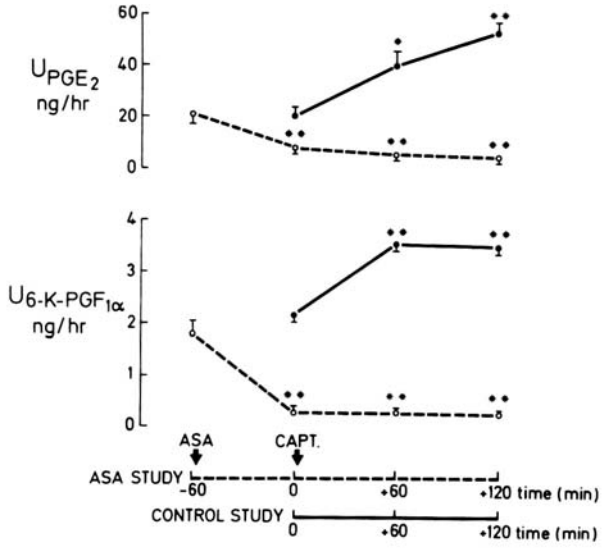

Figure 2

ADH decreased as in the control study. GFR, RPF, urine output, FE_{Na} and osmolar clearance were unmodified after captopril in the ASA study. We did not observe any significant changes of blood pressure after captopril in both studies.

Discussion

Experimental studies have shown that very high doses of exogenous prostaglandin are able to release ADH in anaesthetized dogs and in hypothalamo-neurohypophyseal complex in organ culture [1,2].

On the other hand, the exact role of endogenous prostaglandins on the release of ADH in man is still unknown. Recent studies suggest that, in man, angiotensin II plays an important role in the non-osmotic release of ADH [3]; because prostaglandins, namely PGE_2 and prostacyclin, stimulate AII synthesis [4,5], it is possible that the release of ADH by exogenous PGE_2 reported in experimental animals may be mediated through an increase in AII synthesis. In this study we used captopril to increase prostaglandin synthesis and to decrease angiotensin II production to study the relationship between endogenous prostaglandins and ADH without the influence of angiotensin II in normal man. Our results show a decrease of plasma ADH after captopril, both in the control and in the ASA study (i.e. when prostaglandin synthesis was inhibited by a single dose of aspirin). Plasma angiotensin II has not been measured in this study but it is reasonable to believe that it was reduced as suggested by the significant rise of plasma renin activity observed in both the control and the ASA experiment. These findings strongly suggest that endogenous prostaglandins have little influence on ADH release in man and point to angiotensin II as an important

factor on the non-osmotic control of ADH. Our results also suggest that the diuretic and saluretic effect of captopril is due to prostaglandins. Following captopril, in fact, an increase of urine output and FE_{Na} and C_{osm} was observed only in the control study (i.e. when PGE_2 and 6-keto-$PGF_{1\alpha}$ production increased). Because we did not observe changes in GFR and RPF the increased diuresis and natriuresis were probably due to the inhibitory effect of PGE_2 on sodium transport in the medullary thick ascending limb of Henle's loop [6,7] and on the water permeability of the collecting duct [8,9].

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