EFFECT OF THE ACE-INHIBITOR ENALAPRIL ON PLASMA CONCENTRATION OF ATRIAL NATRIURETIC PEPTIDE AND ON GLOMERULAR FILTRATION RATE IN NOR-MOTENSIVE AND HYPERTENSIVE DIABETIC RATS

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ABSTRACT

Earlier experimental data support the hypothesis that the atrial natriuretic peptide (ANP) is a potential mediator of glomerular hyperfiltration in diabetic rats. Several studies have shown that the renal hemodynamic and excretory responses to ANP are modulated by intrarenal angiotensin II. In the present study we investigated the effect of the angiotensin-converting (ACE)-inhibitor enalapril on plasma concentration of ANP and on glomerular filtration rate (GFR) both in normotensive diabetic rats and in diabetic rats with five-sixths renal ablation. We didn't find a significant increase of plasma ANP in rats with moderate hyperglycemia. Treatment with enalapril significantly \((p<0.05)\) decreased GFR both in control rats and in normotensive diabetic rats. Plasma concentration of ANP was significantly \((p<0.001)\) decreased in five-sixths nephrectomized rats with diabetes mellitus by ACE-inhibiton. "Normalization" of plasma ANP in diabetic rats with renal ablation by enalapril treatment was positively correlated with a reduction of systolic blood pressure and with a decrease of body weight, while GFR didn't change under these conditions.

INTRODUCTION

Early stages of Type I diabetes mellitus are characterized by elevation of the glomerular filtration and renal plasma flow rates. Micropuncture studies in streptozotocin-induced diabetic rats demonstrate an increase in the glomerular plasma flow rate and because of a proportionately greater reduction in afferent
than efferent arteriolar resistance, the mean glomerular capillary hydraulic pressure tends to rise (1, 2).

Despite intensive investigation, the mechanisms that underly the hyperfiltration of diabetes is not clear. It has been postulated that one of the factors that contributes to this hyperfiltration is extracellular fluid volume expansion (3).

Atrial natriuretic peptide is a hormone released by atrial myocytes in response to acute and chronic extracellular volume expansion. Experimental data of Ortola and coworkers suggest that diabetic hyperfiltration is associated with elevation of endogenous ANP levels (4). They could demonstrate that antibody-induced blockade of endogenous ANP action reverses this hyperfiltration response in moderately hyperglycemic diabetic rats. These experimental findings but also data of patients with poorly controlled diabetes mellitus (5) point to a role for endogenous ANP in mediating diabetic hyperfiltration.

In many tissues ANP and the renin-angiotensin system appear to be counterbalanced. Several studies have shown that the renal hemodynamic and excretory responses to ANP are modulated by intrarenal angiotensin II (6, 7). There is circumstantial evidence pointing to an interaction between ACE-inhibition and ANP (8, 9, 10).

The aim of the present study was to investigate the effect of the ACE-inhibitor enalapril on plasma concentration of ANP and on glomerular filtration rate both in normotensive and in hypertensive diabetic rats.

MATERIALS AND METHODS

Male Wistar rats with initial weights of 220 - 240 g were used in these studies. The rats were randomly assigned to 6 experimental groups:

Group I: Control rats; normoglycemia, normotensive
Group II: Diabetes mellitus rats; "moderate hyperglycemia"
Group III: Diabetes mellitus rats with renal ablation
Group IV: Control rats with enalapril treatment
Group V: Diabetes mellitus rats with enalapril treatment
Group VI: Diabetes mellitus rats with renal ablation and enalapril treatment.