

## Abstract

## Introduction

Angiotensin II (All) plays a major role in regulation of vascular resistance and renal tubular function via its receptor subtypes, AT<sub>1</sub>, AT<sub>2</sub> and non AT<sub>1</sub> non AT<sub>2</sub>. Candesartan, a specific AT<sub>1</sub> antagonist has been used to study the mechanism of action of All in various organs. The purposes of this work were to examine the effects of candesartan on renal proximal tubular reabsorption using lithium clearance technique. The effects on mean arterial blood pressure (MABP), renal plasma flow (RPF), glomerular filtration rate (GFR) and sodium and potassium excretion were also investigated.

## Methods

Male Wistar rat were anaesthetized with Inactin. Clearance markers (8% polyfructosan (PFS), 1% para-aminohippuric acid (PAH) and 4 mmol l<sup>-1</sup> lithium chloride) were given through jugular vein at the rate of 1.6 ml hr<sup>-1</sup> 100 g bw<sup>-1</sup>. Arterial pressure was monitored throughout the experiment. Urine was collected via urinary bladder. Rats were divided into 6 groups (1 control and 5 candesartan treatment; 0.01+0.5, 0.1+5, 0.2+10, 0.5+25 and 1.0+50 mg kg<sup>-1</sup> + µg kg<sup>-1</sup> min<sup>-1</sup>).

## Results

Candesartan caused both unaltered and decreased mean arterial blood pressure (MABP). The nondepressor dose resulted in unaltered renal plasma flow (RPF) and glomerular filtration rate (GFR) while diuresis, natriuresis and kaliuresis observed. Urine flow rate increased by 75% while sodium excretion rate ( $U_{Na}V$ ) and fractional sodium excretion ( $FE_{Na}$ ) increased by 43-75 and 22-85%, respectively. Fractional proximal sodium reabsorption ( $FPR_{Na}$ ) decreased by 7-21%.

The depressor doses of candesartan reduced MABP by 16 mm Hg. Renal plasma flow (RPF) and glomerular filtration rate (GFR) significantly decreased by 13-30 and 12-18%, respectively.

However, diuresis, natriuresis and kaliuresis were still observed. Urine flow rate increased by 32-107% while  $U_{Na}V$  and  $FE_{Na}$  increased by 61-132 and 91-197%, respectively.  $FPR_{Na}$  decreased by 24-30%.

## Conclusions

Intravenous administration of a specific  $AT_1$  antagonist, candesartan, caused both unaltered and decreased mean arterial blood pressure (MABP). Diuresis, natriuresis and kaliuresis were observed independently of an alteration in arterial pressure. The inhibition of sodium reabsorption by candesartan occurred in the proximal nephron segment.