Urinary Endothelin and Sodium Excretion in Essential Hypertension

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used was 250% with ET-2, 14% with human big ET and less than 0.01% with ET-3.

Whereas no significant differences in the plasma irET-1 were observed among the normal-, low- and high-sodium intakes, urinary excretion of irET-1 was 20.1 ± 2.5 (mean $\pm$ SE), 11.8 ± 3.8 and 29.6 ± 3.5 ng/g creatinine with the respective sodium diets. A similar change in fractional excretion of irET-1 (FEET) was observed with these different sodium intakes (1.2 ± 0.2 , 0.7 ± 0.1 and

7.0-

6.0-

5.0

4.0-

Ui

3.0

2.0-

1.0-

Fig. 1. Relationship between

FEET and FENa

of low-, normal- and

high-sodium

intakes.

0.0

0.0

Dear Sir,

Endothelin (ET), a potent vasoconstrictor known today, has been suggested to play multiple roles in cardiovascular diseases. Although ET was first isolated from vascular endothelial cells, recent studies have provided evidence which suggests that ET is widely distributed in renal tissue compatible with important autocrine and paracrine actions in the kidney [1]. Indeed, several reports demonstrated that increased ET production within the kidney may contribute to the intense intrarenal vasoconstriction characteristic of acute renal failure [2], endotoxin shock [3] and cyclosporin nephrotoxicity [4]. However, knowledge concerning the precise role of ET in the kidney tissue is still scanty. We have, therefore, examined the effect of sodium intake on

urinary ET excretion to gain insight into a role of ET in renal handling of sodium in essential hypertensive patients with normal renal function.

After informed consent had been obtained, 12 patients with uncomplicated, untreated essential hypertension were enrolled in this study. These subjects were given a daily diet containing 120 mmol of sodium (normal sodium) for at least 10 days. Then, a diet containing 35 mmol of sodium (low sodium) was given to the subjects for 1 week, after which a diet containing 250 mmol of sodium (high sodium) replaced it and was continued for 1 week. On the final day of each regimen, a 24-hour urine sample was collected at 4°C for determinations of sodium, creatinine, immunoreactive atrial natriuretic peptide and immunoreactive ET-1 (irET-1). Blood was withdrawn on the last morning of each regimen for measurement of sodium and irET-1. irET-1 was determined by radioimmunoassay. The cross-reactivity of the anti-ET-1 antibody (2.5 ± 0.4%, respectively). There was a significant positive correlation between FENa and fractional excretion of sodium (FENa), as a whole group ($r = 0.48$, $p < 0.01$; fig. 1).

Although the origin of urinary ET-1 is not clear at present, our data raise the possibility that a large part of urinary ET-1 is of renal origin since plasma ET-1 levels remained unchanged with different sodium intakes which, in contrast, affected significantly the mode of urinary excretion of ET-1. In support of this

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concept, recent studies have shown that radio-labeled ET infused into the rat vein could not be detected in urine [5]. Further, irET was detected in quantities in cultured inner medullary duct cells, indicating synthesis of ET in those particular cells in the kidney [6].

Of interest in the present study is the finding that FEEj was correlated positively with FENa. It has been shown that exogenous ET reduces glomerular filtration rate concomitantly with increment in FENa [7]. ET has also been shown to inhibit Na⁺-K⁺-ATPase in inner medullary collecting duct cells [8]. In the light of these findings, together with the present results, it seems likely that renal ET increases sodium excretion by suppressing sodium reabsorption in the duct. If this is the

case, our study suggests an important role of ET in the renal handling of sodium in patients with essential hypertension with normal renal function. Apparently, further studies are needed to

elucidate a more precise role of renal ET in sodium homeostasis in diverse physiopathological states.

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153