Noradrenaline secretion by the human kidney


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Summary

1. In 20 subjects with uncomplicated essential hypertension, 10 of whom were on propranolol treatment, several blood samples were drawn simultaneously from the renal artery and vein after angiographic studies. In these samples we determined concentrations of noradrenaline, active renin, aldosterone and cortisol.

2. Renal blood flow was measured in all patients by Hippuran-clearance and xenon-washout.

3. Despite marked variations in the arteriovenous difference of noradrenaline, it was apparent in both groups that the kidney is able to release noradrenaline.

4. In the propranolol-treated group noradrenaline secretion by the kidney was enhanced when compared with untreated hypertensive patients.

Key words: noradrenaline, kidney.

Introduction

The role of the kidney in the pathogenesis of essential hypertension is still not completely understood. Systemic pressor reactions could originate from the renin–angiotensin system, but there is little evidence that this system is primarily involved in essential hypertension. This study was undertaken to assess release of noradrenaline from the kidney.

Methods

Twenty patients with uncomplicated essential hypertension were studied; ten of them were untreated and the others had received propranolol for two weeks in an average daily dose of 240 mg. The diagnosis of essential hypertension was made after exclusion of known causes of hypertension. In all patients renal arteriography was carried out to exclude renal vascular disease. Patients with diabetes, hyperlipidaemia or other metabolic disorders were excluded.

All subjects were studied under metabolic ward conditions, sodium intake being restricted to 60 mmol per day.

Noradrenaline production by the kidney was assessed after the angiographic studies, but only when the arteriogram failed to reveal abnormalities.

Noradrenaline concentration was measured in at least two blood samples drawn simultaneously from the right renal artery and vein. In the same samples we determined the concentration of active renin, aldosterone and cortisol. The interval between two successive samples was 30 min. At the same time renal plasma flow was measured by the clearance and extraction of $^{125}$I-labelled Hippuran, and intrarenal haemodynamics were assessed by the washout of $^{133}$Xe.

Intra-arterial blood pressure was measured through the arterial catheter, by using a Statham transducer.

Noradrenaline was assayed by a radio-enzymic method (Henry, Starman, Johnson & Williams, 1975) but with several modifications (Falke, Punt & Birkenhager, 1978).

Active renin concentration was measured as described by Skinner, Cran, Gibson, Taylor, Walters & Catt (1975) and Derkx, Wenting, Man in ’t Veld, Van Gool, Verhoeven & Schalekamp (1976).

Aldosterone and cortisol were determined by radioimmunoassay.

Secretion rates were calculated as the product of the arteriovenous concentration difference and renal plasma flow.

The results are expressed as mean ± SEM.
Results

In the untreated group the average noradrenaline concentration in arterial blood was 0.25 ± 0.02 ng/ml and in venous blood 0.27 ± 0.02 ng/ml. Due to the scatter of data this difference was not significant. When the amount of noradrenaline leaving the kidney was expressed as a percentage of the amount entering, there was an increase of 15 ± 2%. Noradrenaline secretion rate on the average was 19 ± 2 ng/min.

Secretion rates of noradrenaline were not related to age, level of blood pressure or intrarenal haemodynamics as assessed with the xenon-washout technique. We also failed to observe a relationship with renin secretion. When all samples were considered separately, it appeared that noradrenaline release by the kidney was erratic. Substantial intraindividual variations were found, the arteriovenous difference ranging from positive to negative. This could not be related to changes in flow or blood pressure. Some patients did not secrete the hormone at all. No arteriovenous concentration gradients were found for either aldosterone or cortisol, confirming that there was no mixing with adrenal venous blood.

In the propranolol-treated group a more consistent pattern of noradrenaline secretion was found. The average renal arterial concentration was 0.26 ± 0.15 ng/ml and the average renal venous concentration was 0.32 ± 0.20 ng/ml. Noradrenaline secretion rate was 26 ± 14 ng/min. As a percentage, noradrenaline rose by 31 ± 16% across the kidney. The difference with the untreated group was however not significant (Fig. 1).

Discussion

We have investigated noradrenaline release by the human kidney. Although the general pattern indicated that there is indeed secretion, there were several exceptions. In some patients no secretion was found, whereas in others there was a changing pattern of secretion and uptake. It could be argued that the results may have been influenced by adrenal release of hormones. However, blood was always drawn from a catheter in the right renal vein, which minimizes the risk of mixing with adrenal venous blood. Furthermore, no arteriovenous concentration differences were found for either aldosterone or cortisol. Therefore our results indicate that the kidney is a source of noradrenaline, although secretion may occur episodically.

Blockade of β-adrenoreceptors appears to enhance secretion, as the secretion rate is slightly but not significantly higher in the propranolol group. The mechanism for this phenomenon is not clear, but may be related to unopposed α-activity. Since the kidney, and its vessels in particular, are densely innervated with sympathetic fibres, it is tempting to infer that the renal noradrenaline release simply reflects overflow from the synaptic clefts.

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References

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