SHORT COMMUNICATION

The mechanism of urinary kallikrein excretion in the rat

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Summary

1. In male Wistar rats urinary kallikrein excretion was positively correlated with urinary flow and glomerular filtration rate (GFR).
2. Osmotic diuresis produced by a 30% (w/v) glucose solution increased urinary kallikrein, and a positive correlation between this variable and urine flow was observed. No correlation was observed with GFR.
3. The mechanism of urinary kallikrein excretion is interpreted as a wash-out effect of renal kallikrein.

Key words: kallikrein, kidney.

Introduction

Urinary kallikrein is biochemically indistinguishable from renal kallikrein. Four types of kallikrein were isolated from urine and rat kidney with similar molecular weight, pH optimum and ability to liberate bradykinin from kininogen [1, 2]. Renal kallikrein is principally located at the level of the distal nephron tubule [3]. The distal tubular cells release the enzyme into the tubular fluid, without important modification, by an unknown mechanism.

Our purpose was to study the effect of urine flow on urinary kallikrein excretion under physiological conditions.

Materials and methods

Male Wistar rats each weighing approximately 250 g were used. In one group of rats, 24 h urine samples were collected in plastic beakers by placing the rats in individual metabolic cages.

The experimental conditions of the other group of animals have been described elsewhere [4]. Briefly, the animals were anaesthetized with 1 g of urethane/kg body weight intraperitoneally, and a constant infusion of 30% glucose in water was started through the jugular vein at a rate of 0.103 ml/min. After 30 min equilibration, urine was collected during 1 h. Blood was obtained by cardiac puncture at the end of the period. Urinary kallikrein was measured by either the direct oxytocic activity on rat uterus [5, 6] or by the hydrolysis of α-N-benzoyl-L-arginine ethyl ester (BAEE) [7]. One esterase unit (EU) was defined as the amount of enzyme that hydrolysed 1 μmol of ester/min under the conditions of the assay. As we obtained good correlation between values by both methods \((r = 0.70, P < 0.001)\), only the results obtained with the BAEE method were reported. Creatinine was determined in plasma and urine by the method of Hare [8] and glomerular filtration rate (GFR) was calculated from creatinine clearance by a standard formula.

All results were expressed as the means ± SEM and compared by Student’s \(t\)-test. To establish the existence of correlation between the different variables studied, linear regression analysis was used. The 5% probability level was used as a criterion for significance.

Results

Table 1 summarizes the results obtained. Urine flow and kallikrein excretion increased significantly in the group that received glucose infusion without change in the GFR. In the control rats, urinary kallikrein excretion was positively correlated with urine flow \((r = 0.86, P < 0.001)\) and with GFR \((r = 0.87, P < 0.001)\). In the rats given glucose there was only a positive correlation between kallikrein excretion and urine flow \((r = 0.77, P < 0.01)\).
Discussion

An increase in urine flow rate has been reported to be associated with a concomitant increase in urinary kallikrein excretion [9–12]. This suggests that, in some conditions, the urinary kallikrein excretion could be a wash-out effect on renal kallikrein. The results observed in control animals, in which kallikrein excretion was positively correlated with the urine flow and the GFR, are in agreement with this hypothesis.

The principal site of action of an osmotic diuretic within the nephron is at the proximal tubule. In our experimental animals glucose infusion did not modify the GFR. In keeping with the wash-out hypothesis glucose infusion should increase urinary kallikrein excretion. Also, a positive correlation with urine flow and no correlation with GFR should be observed, since the presumed site of kallikrein formation is the distal tubule. These suggested effects are in fact those observed in our experiments.

Recently, Bönner et al. [13] reported that mannitol solution increased kallikrein excretion without correlation with urine flow. The lack of correlation in their study does not agree with our results. A possible explanation of the discrepancy is that the number of animals used in their study was small (six).

In conclusion, we think that at least under the conditions of our experiments the principal mechanism regulating kallikrein excretion into the renal tubule is a wash-out effect on renal kallikrein.

References