Effects of aprotinin on renal function and urinary prostaglandin excretion in conscious rats after acute salt loading

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Summary

1. Aprotinin, a potent kallikrein inhibitor, was given to conscious rats with and without expansion of the extracellular fluid volume with isotonic saline.

2. In non-expanded rats aprotinin had no effect on arterial pressure, glomerular filtration rate (GFR), hippuran clearance, urinary flow rate, absolute sodium and potassium excretion or free-water clearance.

3. In volume-expanded rats aprotinin significantly reduced GFR, hippuran clearance, urine volume \( V \), \( U_{Na}V \), \( U_KV \) and \( C_{water}/GFR \) without effect on systemic arterial pressure.

4. Urinary immunoreactive prostaglandin \( E_2 \) excretion significantly increased during the expansion phase but returned to below the control range during stable extracellular fluid volume expansion.

5. Aprotinin significantly suppressed urinary immunoreactive prostaglandin \( E_2 \) excretion in non-expanded rats and in volume-expanded rats during the expansion phase, but not during stable expansion.

6. The results suggest that the kallikrein–kinin system may contribute to changes in renal function during extracellular volume expansion. This action may not necessarily be associated with changes in renal prostaglandin \( E_2 \) activity.

Key words: aprotinin, kinin synthesis, prostaglandins, renal function, salt loading.

Abbreviations: ECF, extracellular fluid; GFR, glomerular filtration rate.

Introduction

Expansion of the extracellular fluid (ECF) volume with saline (sodium chloride solution, 154 mmol/l) is associated with a marked natriuresis, which may occur in the absence of changes in glomerular filtration rate or the level of circulating mineralocorticoid activity (DeWardener, Mills, Clapham & Hayter, 1961). Intrarenal physical factors (Rector, van Giesen, Kiil & Seldin, 1964) as well as a 'natriuretic hormone' (DeWardener et al., 1961; Gonick, Kramer, Paul & Lu, 1977; Kramer, Bäcker & Krück, 1977; Kramer, Gonick & Krück, 1972; Kramer & Gonick 1974) have been implicated as factors regulating renal sodium excretion under these circumstances. The role of the renal prostaglandin system in the regulation of renal sodium excretion is still controversial (for review see Düsing & Kramer, 1978). Recent studies from our laboratory have demonstrated that renal prostaglandins, in addition, may significantly contribute to the diuresis and natriuresis after acute salt-loading in the conscious rat by affecting tubular sodium absorption (Düsing, Opitz & Kramer, 1977b) probably through alterations in intrarenal
haemodynamics (Düsing, Melder & Kramer, 1977a). Finally, several studies suggest an intimate link between the renal kinin and prostaglandin systems. Thus, in the isolated kidney, the release of intrarenal prostaglandin is stimulated in the presence of bradykinin (McGiff, Itskovitz & Terragno, 1975; Terragno, Longiro, Malik & McGiff, 1972) and can be blocked by inhibition of kinin synthesis with aprotinin (Colina-Chourio, McGiff, Miller & Nasjletti, 1976). Hence both systems may contribute to the regulation of systemic arterial blood pressure, renal blood flow, and renal sodium and water excretion (Nasjletti, Colina-Chourio & McGiff, 1975). The present experiments were therefore performed to investigate the potential contribution of the renal kallikrein–kinin system to the natriuresis after acute salt-loading in conscious rats as well as its possible mediation by renal prostaglandins. This question was indirectly approached by the use of aprotinin, a potent inhibitor of kallikrein, which therefore blocks kinin generation. To explore a possible direct action of bradykinin on tubular absorption via inhibition of active transport processes, experiments were carried out in vitro to determine the effects of this peptide on renal Na⁺,K⁺-dependent ATPase (EC 3.6.1.3), an enzyme system considered to represent the biochemical basis for active transepithelial sodium transport (Skou, 1965).

Methods

Female Sprague-Dawley rats weighing 190–269 g were fed with a normal rat diet (0·72% K; 0·46% Na) with free access to water. The animals were anaesthetized with methohexitol (50 mg/kg body weight intraperitoneally) and polyethylene catheters were inserted into the carotid artery, the jugular vein (PE 50) and transabdominally into the bladder (PE 90). Two hours after recovery from anaesthesia and surgery the animals were placed in individual restraining cages. In 28 conscious rats infusion of sodium chloride solution (154 mmol/l: saline) was started at a rate of 0·5 ml/min until a 10% increase in body weight was achieved within 1 h (Kramer & Gonick, 1974). At this time a priming dose of either 51Cr-labelled EDTA or 125I-labelled hippuran was given, followed by a sustaining infusion of saline containing 51Cr-labelled EDTA or 125I-labelled hippuran to maintain body weight constant. After an additional equilibration period of 45 min, when steady state was reached, as documented by stable body weight and urinary sodium excretion equalling the amount of sodium infused (Kramer & Gonick, 1974), urine was collected during three 15 min periods. Before ECF volume expansion, 14 animals received an initial dose of 50 000 kallikrein-inhibiting units of aprotinin (Trasylo)/kg body weight, intravenously, followed by a continuous infusion of 100 kallikrein-inhibiting units min⁻¹ kg⁻¹ body weight. At the end of the experiments animals were bled by aortic puncture. Arterial blood pressure was monitored throughout the experiments by using a Statham transducer. Fourteen non-expanded rats, of which seven animals received aprotinin at the above dose, served as controls and were treated in the same manner except that body weight was kept constant by infusion of 2·5% sucrose throughout the experiments. In each group of non-expanded and expanded rats, control and experimental animals were run simultaneously. GFR was measured as 51Cr-labelled EDTA clearance and renal plasma flow was estimated as 125I-labelled hippuran clearance in 14 non-expanded and 14 expanded animals.

Serum and urinary activities of 51Cr-labelled EDTA and 125I-labelled hippuran were measured in an automatic gamma counting system (Nuclear-Chicago). Concentrations of sodium and potassium in serum and urine were determined by flame photometry. Fractional excretion (%) of electrolytes (X) was calculated as 100(Cx/GFR). Serum and urinary osmolalities were determined with a Knauer osmometer to calculate osmolar and free-water clearance. Urinary prostaglandin E₂ concentrations in 24 animals were determined by radioimmunoassay, a highly specific prostaglandin E₂ antibody (Institut Pasteur, Paris, France) being used. Extraction and chromatographic separation were performed by the method described by Auletta, Zusman, Caldwell, Behrman, Kirton, Levitt & Russell (1974). Urinary excretion of prostaglandin E₂ was expressed as ng of immunoreactive prostaglandin E₂/min.

A direct effect of bradykinin on renal Na⁺,K⁺-ATPase was investigated in crude homogenates of rat renal cortical tissue prepared in sucrose/Tris/HCl buffer (pH 6·8). Aliquots of 1·50 (w/v) diluted tissue homogenates were preincubated for 1 h at 4°C with equal volumes of buffer containing bradykinin in amounts giving concentrations of 10⁻⁸, 10⁻⁶ and 10⁻⁴ mol/l in the final incubate.

To study the specificity of possible effects of bradykinin on Na⁺,K⁺-ATPase, assays were repeated with bradykinin previously digested enzymatically with chymotrypsin. Buffer solution
(10 ml) containing bradykinin (1 mmol/l) was incubated with 0.28 unit of α-chymotrypsin from bovine pancreas (EC 3.4.21.1; Serva, Heidelberg, F.R.G.) for 2 h at 25°C. The reaction was stopped by removing the enzyme by filtration (filter paper no. 595; C. Schleicher and Schüll, F.R.G.). Aliquots of filtrate were then preincubated with equal volumes of ATPase enzyme preparation as described above.

Total ATPase, Mg²⁺-ATPase and Na⁺,K⁺-ATPase activities were determined as previously described (Kramer & Gonick, 1970). All analyses were performed in duplicate. Statistical evaluation of results was performed with a double-tail Student’s t-test. Data are presented as means ± SEM.

**Results**

**Effects of aprotinin on systemic arterial blood pressure**

Mean arterial blood pressure in non-expanded control rats was 134.0 ± 1.5 mmHg and was unaffected by administration of aprotinin (135.2 ± 1.8 mmHg). In ECF volume-expanded rats, arterial blood pressure during the expansion phase was 133.2 ± 0.8 mmHg in the absence and 132.8 ± 0.4 mmHg in the presence of aprotinin. During urine collection periods at stable ECF volume expansion, the respective blood pressure values were 130.0 ± 0.5 and 129.6 ± 0.2 mmHg.

**Effects of aprotinin on renal function**

Glomerular filtration rate and ¹²⁵I-labelled hippuran clearance in non-expanded rats remained unaltered in animals given aprotinin (Table 1). However, in expanded rats aprotinin significantly decreased GFR and ¹²⁵I-labelled hippuran clearance by 25% from 12.6 ± 0.4 to 9.5 ± 0.8 ml min⁻¹ kg⁻¹ body weight and by 26% from 37.2 ± 3.6 to 27.5 ± 1.8 ml min⁻¹ kg⁻¹ body weight respectively (Table 2); thus the filtration fraction of 34% remained unaltered.

In non-expanded rats no effects of aprotinin on urinary flow rate and absolute sodium and potassium excretion were noted (Table 1). However, in ECF volume-expanded rats mean urinary flow rate and sodium excretion during the three clearance periods of stable ECF volume expansion decreased by 60% from 3.30 ± 0.12 to 1.32 ± 0.05 ml min⁻¹ kg⁻¹ body weight and by 68% from 475 ± 10 to 153 ± 8 μmol min⁻¹ kg⁻¹ body weight respectively, with a fall in urinary sodium concentration from 133.3 ± 0.7 to 117.4 ± 1.8 mmol/l (P < 0.001). Fractional sodium excretion thus decreased from 27% in non-pretreated expanded rats to 11.5% in aprotinin-treated ECF volume-expanded animals. Mean urinary potassium excretion decreased to a lesser degree, by 34% from 26.8 ± 0.8 to 17.6 ± 1.1 μmol min⁻¹ kg⁻¹ body weight (Table 2).

Osmolar and free-water clearance in non-expanded animals were unaffected by aprotinin (Table 1). In contrast, in aprotinin-treated expanded rats mean U_{osm} increased from 298.4 ± 2.1 to 332.5 ± 5.8 mosmol/l (P < 0.001) and C_{osm} was significantly reduced by 59% from 3.72 ± 0.06 to 1.52 ± 0.06 ml min⁻¹ kg⁻¹ body weight in parallel to the decrease in urinary sodium excretion (Table 2). Thus, C_{osm}/GFR decreased from 29.5 to 16.0%. In ECF volume-expanded animals, the negative C_{water} (−0.15 ± 0.02 ml min⁻¹ kg⁻¹ body weight) was further reduced by

**Table 1. Effects of aprotinin on renal function in conscious non-expanded rats**

Mean results ± SEM (n = 7) are shown. * P < 0.01. RPF, Renal plasma flow.

<table>
<thead>
<tr>
<th></th>
<th>Without aprotinin</th>
<th>With aprotinin</th>
</tr>
</thead>
<tbody>
<tr>
<td>GFR (ml min⁻¹ kg⁻¹ body wt.)</td>
<td>7.32 ± 0.38</td>
<td>6.76 ± 0.32</td>
</tr>
<tr>
<td>RPF (ml min⁻¹ kg⁻¹ body wt.)</td>
<td>34.5 ± 0.4</td>
<td>35.4 ± 0.5</td>
</tr>
<tr>
<td>V (μl min⁻¹ kg⁻¹ body wt.)</td>
<td>80 ± 7</td>
<td>66 ± 2</td>
</tr>
<tr>
<td>U_{net}V (μmol min⁻¹ kg⁻¹ body wt.)</td>
<td>1.5 ± 0.1</td>
<td>1.6 ± 0.1</td>
</tr>
<tr>
<td>U_{net}V (μmol min⁻¹ kg⁻¹ body wt.)</td>
<td>3.9 ± 0.2</td>
<td>4.1 ± 0.2</td>
</tr>
<tr>
<td>C_{osm} (μl min⁻¹ kg⁻¹ body wt.)</td>
<td>147.4 ± 11.4</td>
<td>127.1 ± 5.2</td>
</tr>
<tr>
<td>C_{water} (μl min⁻¹ kg⁻¹ body wt.)</td>
<td>−67.2 ± 5.9</td>
<td>−61.0 ± 3.4</td>
</tr>
<tr>
<td>C_{net}/GFR (%)</td>
<td>0.14 ± 0.01</td>
<td>0.17 ± 0.01*</td>
</tr>
<tr>
<td>C_{net}/GFR (%)</td>
<td>10.63 ± 0.48</td>
<td>12.05 ± 0.45*</td>
</tr>
<tr>
<td>C_{osm}/GFR (%)</td>
<td>2.06 ± 0.24</td>
<td>1.88 ± 0.07</td>
</tr>
<tr>
<td>C_{water}/GFR (%)</td>
<td>−0.94 ± 0.11</td>
<td>−0.90 ± 0.04</td>
</tr>
</tbody>
</table>

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TABLE 2. Effects of aprotinin on renal function in conscious rats acutely extracellular fluid volume expanded with saline

Mean values ± SEM are shown with the numbers of animals used in parentheses.

RPF, Renal plasma flow; N.S., not significant.

<table>
<thead>
<tr>
<th></th>
<th>Without aprotinin</th>
<th>With aprotinin</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>GFR (ml min⁻¹ kg⁻¹ body wt.)</td>
<td>12.6 ± 0.4 (7)</td>
<td>9.5 ± 0.8 (7)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>RPF (ml min⁻¹ kg⁻¹ body wt.)</td>
<td>37.2 ± 3.6 (7)</td>
<td>27.5 ± 1.8 (7)</td>
<td>&lt;0.02</td>
</tr>
<tr>
<td>V (ml min⁻¹ kg⁻¹ body wt.)</td>
<td>3.30 ± 0.12 (14)</td>
<td>1.32 ± 0.05 (14)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>U\textsubscript{Na}V (μmol min⁻¹ kg⁻¹ body wt.)</td>
<td>457 ± 10 (14)</td>
<td>153 ± 8 (14)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>U\textsubscript{K}V (μmol min⁻¹ kg⁻¹ body wt.)</td>
<td>26.8 ± 0.8 (14)</td>
<td>17.6 ± 1.1 (14)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>C\textsubscript{osm} (ml min⁻¹ kg⁻¹ body wt.)</td>
<td>3.72 ± 0.06 (14)</td>
<td>1.52 ± 0.06 (14)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>C\textsubscript{water} (ml min⁻¹ kg⁻¹ body wt.)</td>
<td>0.0 - 0.15 (14)</td>
<td>-0.23 ± 0.02 (14)</td>
<td>&lt;0.02</td>
</tr>
<tr>
<td>C\textsubscript{Na}/GFR (%)</td>
<td>26.95 ± 0.61 (7)</td>
<td>11.51 ± 0.63 (7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>C\textsubscript{K}/GFR (%)</td>
<td>42.57 ± 1.45 (7)</td>
<td>37.09 ± 2.23 (7)</td>
<td>N.S.</td>
</tr>
<tr>
<td>C\textsubscript{osm}/GFR (%)</td>
<td>29.54 ± 0.58 (7)</td>
<td>16.03 ± 0.66 (7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>C\textsubscript{water}/GFR (%)</td>
<td>-1.16 ± 0.09 (7)</td>
<td>-2.38 ± 0.24 (7)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Effects of aprotinin on urinary immunoreactive prostaglandin E₂ excretion

Mean urinary immunoreactive prostaglandin E₂ excretion in six non-expanded rats was 0.60 ± 0.10 ng/min. In six ECF volume-expanded rats immunoreactive prostaglandin E₂ excretion was significantly increased to 1.14 ± 0.22 ng/min during the expansion phase (P < 0.05) and returned to 0.32 ± 0.02 ng/min during stable ECF volume expansion, a value significantly lower (P < 0.02) than that of non-expanded control rats. Aprotinin reduced urinary immunoreactive prostaglandin E₂ excretion in six non-expanded rats to 0.22 ± 0.09 ng/min (P < 0.02). Similarly, in six expanded rats aprotinin decreased immunoreactive prostaglandin E₂ excretion to 0.38 ± 0.07 ng/min (P < 0.05) during the expansion phase, but was without effect during stable ECF volume expansion (0.33 ± 0.08 ng/min; Fig. 1).

Effects of bradykinin in vitro on renal cortical Na⁺,K⁺-ATPase

Bradykinin at concentrations of 10⁻⁸ and 10⁻⁶ mol/l in vitro failed to reveal significant effects on renal cortical ATPase activity. Only at a concentration of 10⁻⁴ mol/l was an inhibition of enzyme activity of 15% (P < 0.05) noted in the presence of bradykinin. This effect was blunted when bradykinin was inactivated by chymotrypsin digestion before incubation with the enzyme preparation (Table 3).

Discussion

Bradykinin has recently been incriminated as a natriuretic factor which promotes sodium excretion by the kidney, together with marked vasodilatation (Barroclough & Mills, 1965; Gill, Melmon, Gillespie & Bartter, 1965; Willis, Ludens, Hook & Williamson, 1969). Although a decrease in plasma bradykinin concentrations was found in sodium-depleted healthy subjects after saline infusion (Wong, Talamo, Williams & Colman, 1975), a decrease in plasma kininogen in rats on high sodium intake (Nasjletti & Azzam, 1970) and a significant increase in circulating kinins in salt-loaded dogs...
were observed in the presence of intact kidneys (Marin-Grez, Cottone & Carretero, 1972). Thus activation of renal kallikrein may have mediated enhanced sodium excretion through the release of kinins. Such activation of kallikrein was also observed in man (Adetuyibi & Mills, 1972) and rat (Geller, Margolius, Pisano & Keiser, 1972) during chronic fludrocortisone (Adetuyibi & Mills, 1972; Margolius, Horwitz, Geller, Alexander, Gill, Pisano & Keiser, 1974) and deoxycorticosterone treatment (Geller et al., 1972) respectively, or in patients with primary aldosteronism (Margolius, Horwitz, Pisano & Keiser, 1974) with a significant correlation between urinary kallikrein and sodium excretion (Barroclough & Mills, 1965; Carretero & Scicli, 1976). It was further suggested that some effects ascribed to the renal kinin system may be mediated by intrarenal prostaglandins (Colina-Chourio et al., 1976; McGiff et al., 1975; Terragno et al., 1972; Zusman & Keiser, 1976).

In the present study the possible participation of the kinin system in the natriuretic response to an acute salt load was investigated. Based on the experimental design of Colina-Chourio et al. (1976) and on evidence presented by Nustad (1970) this approach was indirectly made by the use of aprotinin, an inhibitor of conversion of inactive prekallikrein into kallikrein; aprotinin therefore suppresses kinin generation. Aprotinin is a polypeptide with a molecular weight of approximately 6500, which also inhibits the proteolytic actions of trypsin, chymotrypsin, plasmin and other proteolytic enzymes, which are presumably not related to the regulation of systemic or renal haemodynamics. In fact no effects of aprotinin on systemic arterial blood pressure were observed in the present study. Although urinary kallikrein excretion was not measured in this study, suppression of kinin synthesis at the dose of aprotinin employed can be assumed on the basis of previous experimental work.

In non-expanded animals no effects of aprotinin on arterial pressure or renal function were observed, although urinary immunoreactive prostaglandin E₂ excretion was significantly reduced after kallikrein inhibition. Although urinary prostaglandin E₂ excretion significantly rose during acute saline loading, prostaglandin E₂ excretion after 60–90 min of stable ECF volume expansion was below normal limits. Administration of aprotinin significantly reduced urinary prostaglandin E₂ excretion during rapid saline infusion. Although this drug had no effect on immunoreactive prostaglandin E₂ excretion during stable ECF volume expansion, both GFR and renal plasma flow were significantly reduced to the same degree after inhibition of kinin synthesis. Thus the total filtration fraction of 34% remained unaltered. Although hippuran clearance without determination of renal hippuran extraction may not accurately reflect renal plasma flow, the significant decrease in hippuran clearance after aprotinin in the absence of changes in systemic arterial pressure as observed in the present study suggests an increase in renal vascular resistance. Thus the vasodilator action of bradykinin may be important not only at the level of efferent but also of afferent arterioles. In addition, the natriuresis of ECF volume expansion markedly decreased after administration of aprotinin, accompanied by a decrease in potassium and free-water excretion. This suggests enhanced proximal tubular sodium and water absorption and/or enhanced water absorption in collecting tubules respectively.

Qualitatively similar kinin inhibition was previously reported by Marin-Grez (1974) in rats moderately expanded with saline equal to a 4.5% increase in body weight. In these studies, kinin activity was suppressed by administration of a

<table>
<thead>
<tr>
<th>Enzyme control (n = 10)</th>
<th>Total ATPase</th>
<th>Mg²⁺-ATPase</th>
<th>Na⁺,K⁺-ATPase</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1.75 ± 0.03</td>
<td>1.35 ± 0.03</td>
<td>0.40 ± 0.01</td>
</tr>
<tr>
<td>Enzyme + bradykinin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10⁻⁶ mol/l (n = 7)</td>
<td>1.72 ± 0.04</td>
<td>1.36 ± 0.04</td>
<td>0.36 ± 0.01</td>
</tr>
<tr>
<td>10⁻⁵ mol/l (n = 7)</td>
<td>1.67 ± 0.04</td>
<td>1.34 ± 0.03</td>
<td>0.33 ± 0.03</td>
</tr>
<tr>
<td>10⁻⁴ mol/l (n = 7)</td>
<td>1.64 ± 0.02</td>
<td>1.30 ± 0.02</td>
<td>0.34 ± 0.01*</td>
</tr>
<tr>
<td>Enzyme + bradykinin (10⁻⁴ mol/l) + chymotrypsin (n = 3)</td>
<td>1.67 ± 0.10</td>
<td>1.26 ± 0.05</td>
<td>0.41 ± 0.05</td>
</tr>
</tbody>
</table>
bradykinin-binding antibody. Treatment with this antibody resulted in a significantly smaller response of absolute and fractional excretion of sodium and water to ECF volume expansion than in untreated rats, and no effect on systemic arterial blood pressure was noted. In contrast to the results of the present study, no significant differences in potassium excretion and p-aminohippurate or insulin clearances were observed between control and expanded animals given this antibody. From these results it was concluded that bradykinin participates in the regulation of sodium excretion during ECF volume expansion probably by preferential distribution of blood flow to the inner cortex and by inhibition of proximal tubular absorption in juxtamedullary nephrons. No measurements of intracortical blood flow distribution, however, were performed. The discrepancy between the findings of unaltered p-aminohippurate and insulin clearances in the study by Marín-Grez (1974) and our present observations may be explained either by differences in the magnitude of blockade of kinin activity or, more likely, by the fact that the former experiments were performed in animals anesthetized with pentobarbital, whereas conscious rats were utilized in the present study. Since the reduction of filtered sodium does not appear to be of sufficient magnitude to explain the decrease in sodium excretion after administration of aprotinin in the present study a direct inhibitory action of kinins on tubular absorptive capacity may be considered. Since total filtration fraction remained unaltered after aprotinin there is no evidence for changes in peritubular oncotic pressure (Windhager, Lewy & Spitzer, 1969) in the present results. Effects of bradykinin on active transepithelial transport mediated by the Na+, K+-ATPase enzyme system are unlikely, since we found that only very high concentrations of bradykinin inhibit this enzyme in vitro. However, bradykinin at concentrations of 10^{-10} to 10^{-12} mol/l was shown to inhibit transepithelial transfer of sodium and water of everted sacs of rat jejunum when basal transfer was high, an effect possibly related to cyclic AMP activity (Crocker & Willaivos, 1975). By analogy, the natriferic action of vasopressin in the toad bladder was also shown to be affected by this peptide (Furtado & Machado, 1966). Thus direct effects of bradykinin on epithelial electrolyte transport and water permeability cannot be excluded.

The observed decrease in urinary immunoreactive prostaglandin E2 excretion after aprotinin in non-expanded rats and in ECF volume-expanded animals during acute saline infusion is in agreement with previous studies utilizing an isolated kidney preparation (Colina-Chourio et al., 1976; McGiff et al., 1975) or tissue cultures (Zusman & Keiser, 1976), in which bradykinin was shown to stimulate renal prostaglandin synthesis. Furthermore, the results obtained during stable ECF volume expansion do not exclude an inter-relation-ship between the kinin and prostaglandin systems, e.g. an effect of bradykinin on prostaglandin E9-ketoreductase activity to increase conversion of prostaglandin E2 into prostaglandin F2α (Wong, Terragno, Terragno & McGiff, 1977). However, they also raise the possibility of independent roles of both the kinin and prostaglandin systems with respect to renal function during stable ECFV expansion. Thus suppression of kinin synthesis does not necessarily result in decreased urinary prostaglandin E excretion.

In summary, the present results suggest that in addition to a yet unidentified natriuretic hormone (DeWardener et al., 1961; Gonick et al., 1977; Kramer et al., 1977; Kramer et al., 1972; Kramer & Gonick, 1974) and a possible role for renal prostaglandins (Düsing et al., 1977a,b), the kinin system may represent an additional humoral system contributing to the adaptation of renal function to an acute saline load.

Acknowledgments

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References


Aprotinin and renal function in salt-loaded rats

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