SHORT COMMUNICATION

Release by vasopressin of E-type prostaglandins from the rat kidney

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Summary

1. In order to test whether the release of E-type prostaglandins from the kidney by various vasoconstrictor stimuli is related specifically to adrenoreceptor activation, we have compared release of prostaglandin E-like material from perfused rat kidneys during infusion of noradrenaline or vasopressin.

2. Concentrations of noradrenaline or vasopressin that produced comparable rises in renal perfusion pressure also released comparable amounts of prostaglandin E-like material. This effect was abolished by infusion of an inhibitor of prostaglandin synthesis into the kidney.

3. We conclude that liberation of E-type prostaglandins during renal vasoconstriction is probably related to the activation of intrarenal smooth muscle and does not involve any specific hormonal receptor. Stimulation of release of prostaglandin E may explain certain reported renal actions of vasopressin.

Key words: antidiuretic hormone, prostaglandins, renal circulation, vasopressin.

Introduction

Liberation of prostaglandins of the E type into renal venous blood has been shown to occur after stimulation of the renal vasomotor nerves (Durham & Zimmerman, 1970; Davis & Horton, 1972) or intrarenal infusion of noradrenaline (McGiff, Crowshaw, Terragno, Malik & Lonigro, 1972a; Gagnon, Gauthier & Regoli, 1974). Both angiotensin and bradykinin when infused into the renal circulation have a similar effect (McGiff, Crowshaw, Terragno & Lonigro, 1970; McGiff, Terragno, Malik & Lonigro, 1972b; Needleman, Kauffman, Douglas, Johnson & Marshall, 1973; Gagnon et al., 1974). As the capacity to cause or facilitate liberation of catecholamines from nervous stores is a property shared by angiotensin and bradykinin (Feldberg & Lewis, 1964; Bell, 1972) it is possible that the effect of all the above stimuli on liberation of prostaglandin E is secondary to activation of a-adrenoreceptors. It is thus uncertain whether the phenomenon of liberation of prostaglandin E is a general consequence of renal vasoconstriction or is specifically linked to vasoconstriction involving a-adrenoreceptors. The vasoconstrictor activity of vasopressin appears not to be associated with appreciable a-adrenoreceptor-stimulating capacity (Nash, 1965; Supek, Urović, Gjuriš & Marijan, 1962). We have therefore compared the prostaglandin E-releasing capacity of noradrenaline with that of vasopressin, in the rat's isolated perfused kidney.

Methods

Sprague-Dawley rats of either sex weighing 300-400 g were anaesthetized with sodium pentobarbitone intraperitoneally (1.2 x 10^{-4} mol/kg). Tracheostomy was performed and the renal arteries were exposed through a mid-line abdominal incision. The left kidney was prepared for perfusion with physiological solution,
as described by Vandongen, Peart & Boyd (1973), of the following composition (mol/l): NaCl, 0.125; KCl, 0.006; CaCl₂, 0.0025; KH₂PO₄, 0.0016; MgSO₄, 0.0016; NaHCO₃, 0.033; sodium fumarate, 0.007; sodium glutamate, 0.0064; sodium lactate, 0.0064; glucose, 0.0015, gassed with O₂/CO₂ (95:5). The rate of perfusion was constant at 2.5 ml min⁻¹, 100 g⁻¹ body weight and the resting perfusion pressure was 94±9.9 mmHg (n = 9). Over perfusion periods of up to 4 h reproducible responses of the perfused kidney to injected vasoconstrictor agents were obtained and, although considerable oedema of the abdominal cavity occurred, there was less than 5% increase in weight of the perfused kidney compared with that of the contralateral, non-perfused kidney. In some preliminary experiments, addition of dextran (3.6 x 10⁻⁴ mol/l) (mol. wt. 70,000) to the perfusate reduced the generalized oedema seen with prolonged perfusion but did not affect the responses of the kidney to experimental manoeuvres.

Vasoconstrictor drugs used were L-noradrenaline bitartrate (Sigma) and vasopressin (Pitressin; Parke Davis and Co.). Each drug was diluted from stock solution into the physiological solution and infused into the renal perfusion stream at a rate of 0.5 ml/min or less, for a period of 60 s.

The venous effluent from the perfused kidney was allowed to flow into an open reservoir (0.3 ml) and was withdrawn from this via a second channel of the perfusion pump and used to superfuse a bank of isolated tissues chosen for their differential sensitivities to prostaglandins (Vane, 1969; McGiff et al., 1972b): rat stomach strip, rat colon and chick rectum. In order to prevent effects on the assay tissues of noradrenaline added to the renal perfusion stream, pronethalol (0.5-1.0 x 10⁻⁴ mol/l) was infused into the superfusion fluid distal to the kidney. Responses of the assay tissues to renal manoeuvres were compared with those induced by infusions directly into the superfusion stream of pure prostaglandins E₂ and F₂α. When inhibition of production of prostaglandins by the kidney was required, indomethacin (Indocid; Merck, Sharpe and Dohme) was dissolved in ethanol and added to the renal perfusion fluid to produce a final concentration of 2.8 x 10⁻⁶ mol/l. The final concentration of ethanol was less than 100 mg/l.

Results

The superfused assay tissues used were capable of detecting increases in concentration of approximately 0.3 x 10⁻¹¹ mol/ml (1 ng/ml) for prostaglandin E₂ and 1.4 x 10⁻¹¹ mol/ml (5 ng/ml) for prostaglandin F₂α. Activity due to either of these compounds could be differentiated by their relative potency on the tissues used. Both noradrenaline and vasopressin caused a rise in renal perfusion pressure when infused into the renal artery. The threshold concentration of noradrenaline causing a pressor response (≥5 mmHg) during infusion varied in different experiments between 6 x 10⁻¹¹ mol/ml (0.02 μg/ml) and 6 x 10⁻¹⁰ mol/ml (0.2 μg/ml). That of vasopressin was more constant at about 1 minuit/ml.

Doses of either vasoconstrictor that produced a pressor response also caused appearance in the renal venous effluent of prostaglandin E-like material. Detectable release of this material was never observed in association with infusion of either vasopressin or noradrenaline at concentrations that did not produce an increased perfusion pressure.

Within any one preparation an increased pressor response due to increasing the concentration of either vasopressin or noradrenaline infused was associated with an increased concentration of prostaglandin E-like material in the venous effluent. However, pooling of data from the series of experiments performed was impossible because the concentration of vasoconstrictors required to produce a given increase in perfusion pressure varied between individual kidneys (Table 1). From the results obtained it was nevertheless clear that vasopressin was at least as effective in causing liberation of prostaglandin E-like material from the kidney as was an equipressor concentration of noradrenaline (Table 1). Indeed, in some of the experiments performed vasopressin appeared to release more prostaglandin E-like material than noradrenaline at equipressor concentrations. This may have been related to the fact that the time-course of recovery of normal perfusion pressure after infusion of vasopressin was somewhat longer than that after infusion of noradrenaline at concentrations producing equivalent peak increments in perfusion pressure.

After addition of the inhibitor of prosta-
Prostaglandin E release by vasopressin

Table 1. Release of prostaglandin-like activity into renal venous effluent of isolated, perfused rat kidneys by infusions of noradrenaline and vasopressin

<table>
<thead>
<tr>
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<th>Noradrenaline</th>
<th>Vasopressin</th>
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<tbody>
<tr>
<td>Expt. no.</td>
<td>Dose (µg/min)</td>
<td>Pressor effect (mmHg)</td>
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<td>0.2</td>
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<td>2</td>
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glandin synthesis (Vane, 1971), indomethacin, to the renal perfusion fluid, renal constrictor responses to noradrenaline and to vasopressin and responses of the assay tissues to prostaglandins were unaffected or enhanced. However, neither constrictor agent was then effective in releasing detectable amounts of prostaglandin E-like material into the venous effluent, confirming the identity of this material with a prostaglandin.

On the basis of biological activity, no evidence was obtained in the present experiments to suggest that appreciable amounts of prostaglandin F₂-like material were liberated in association with the prostaglandin E-like material.

Discussion

In the isolated, perfused rat kidney similar amounts of prostaglandin E-like material are released by short periods of vasoconstriction induced by either noradrenaline or vasopressin. In sub-pressor concentrations, however, neither of these vasoconstrictors liberates prostaglandin E-like substances at concentrations detectable by our assay system. It appears therefore that the previously well-documented release of prostaglandins from the kidney by noradrenaline and by renal nerve stimulation (see the Introduction for references) is a response to the increased renal vascular resistance per se rather than being specifically linked to β-adrenoreceptor activation.

In our experiments the kidney was perfused at constant rate with a highly oxygenated medium. It is therefore likely that the release of prostaglandin-like material was a consequence of the process of smooth muscle cell contraction, rather than being due to intrarenal hypoxia. It is known that mechanical distortion of cell membranes can cause release of prostaglandin (Piper & Vane, 1971). However, involvement of altered preferential perfusion characteristics within the kidney even in the face of constant total perfusion must be considered possible.

It has been reported that vasopressin depresses renin release from the perfused rat kidney (Vandongen, 1975) and that the anti-diuretic action of vasopressin in the dog is enhanced by inhibition of prostaglandin synthesis (Anderson, Berl, McDonald & Schrier, 1975). Both these observations may be attributable to the intrarenal release of prostaglandins by vasopressin.
Acknowledgments

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References


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