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Effect of Vasoactive Intestinal Peptide on the Contractility of the Rabbit Urinary Bladder

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Summary. Vasoactive intestinal peptide (V. I. P.) has been demonstrated in neuronal elements of smooth muscle organs including the urinary bladder, thus indicating that this peptide may be a neurohumoral transmitter. In isolated strips of rabbit urinary bladder we have demonstrated that V. I. P. causes relaxation. Unlike the relaxant effect of the beta agonist isoproterenol, the inhibition produced by V. I. P. could not be blocked by propranolol.

These studies indicate that V. I. P. may play a role in the regulation of bladder contractility.

Key words: Vasoactive intestinal polypeptide, Urinary bladder, Contractility.

INTRODUCTION

Recent reports indicate that vasoactive intestinal polypeptide (V. I. P.) may be a neurohumoral transmitter in certain areas of the gastrointestinal tract (1-3). The demonstration by Alm et al. (1) that V. I. P. is also present in neuronal elements of the feline urinary bladder led us to investigate the response to V. I. P. of isolated smooth muscle strips from the rabbit urinary bladder.

MATERIALS AND METHODS

Urinary bladders of 4 adult, white, female New Zealand rabbits were removed under light sodium pentobarbital anaesthesia. The bladders were dissected free of fat and serosa and separated into base and body at the level of the ureteric orifices. Smooth muscle strips (1 cm x 0.5 cm) from the bladder base and body were mounted in a 30 ml glass chamber containing Tyrodes solution (125 mM NaCl; 2.7 mM KCl; 0.4 mM $NaHPO_4$; 1.8 mM $CaCl_2$; 0.9 mM MgCl2; 23.8 mM $NaHCO_3$ and 0.2 glucose) equilibrated with a gas mixture of 95% O_2, 5% CO_2 and maintained at 37°C. Contractility was monitored using a Grass force displacement transducer connected to a 4-channel Beckman recorder.

A tension of 1 g was placed on each strip and the tissue was allowed to equilibrate for approximately 1 h. Pharmacological agents were dissolved in de-ionized water and added in 50 µl aliquots. Dose response curves were performed by the sequential addition of drug (in a cumulative manner) at 5 min intervals. Drug concentrations shown represent the total concentrations in the bath. A minimum of 6 different concentrations of drug were used for each curve. Following the completion of each dose response curve the tissues were washed 4 times with 30 ml fresh oxygenated buffer (at 37°C) and allowed to recover for 30 min.

RESULTS

The addition of V. I. P. to rabbit urinary bladder strips produced a consistent decrease in bladder contractility (Fig. 1). The response to V. I. P. was approximately the same for strips isolated from both the bladder body and bladder base. Since response of the bladder to V. I. P. was similar to that of a beta adrenergic agonist such as isoproterenol, we performed dose response studies of the bladder strips to V. I. P. in the presence of the beta-adrenergic blocker propranolol. The decrease in contractility observed following V. I. P. administration was not altered by the prior administration of 50 µM propranolol.

To determine whether the tissue remained viable following V. I. P. administration, dose response curves to bethanechol were performed

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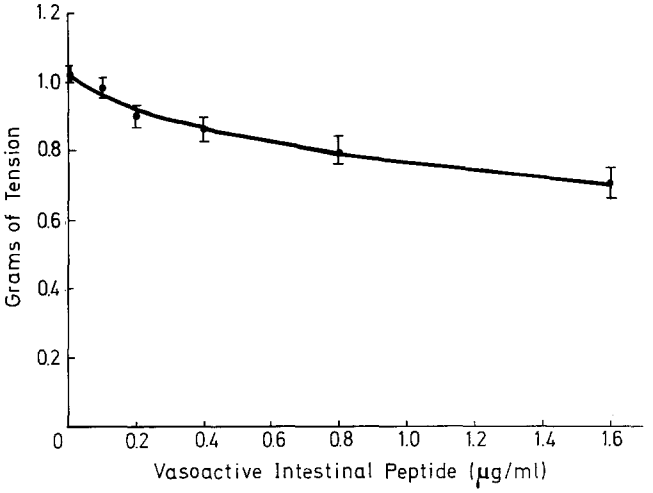

Fig. 1. The effect of V. I. P. on the contractility of the rabbit urinary bladder

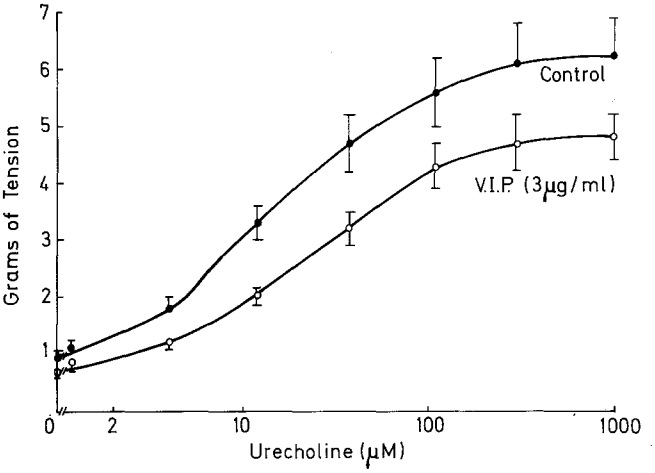

Fig. 2. The effect of urecholine on the contractility of the rabbit urinary bladder in the presence and absence of V. I. P.

prior to and following V. I. P. administration (Fig. 2). V. I. P. (3 mg/ml) produced a decrease of approximately 30% in contractility in the absence of bethanechol. The magnitude of the response of the bladder strips to bethanechol in the presence of V. I. P. was decreased by approximately 30% at all concentrations of bethanechol.

DISCUSSION

These studies demonstrate that V. I. P. has a direct effect on bladder contractility. The response of isolated urinary bladder strips to V. I. P. is similar to the response to isoproterenol (β-adrenergic stimulation), that is, relaxation. Unlike the response to isoproterenol, the decrease in contractility following V. I. P. administration could not be blocked by the β-adrenergic blocker propranolol.

In previous studies we have demonstrated that the response of the urinary bladder body to both adrenergic and cholinergic agents is considerably different from the response of the bladder base, although both tissues respond to all agonists. The bladder body responds preferentially to β-adrenergic stimulation (relaxation) and muscarinic stimulation (contraction), whereas the bladder base responds preferentially to alpha-adrenergic stimulation (contraction) (4). Unlike the response to these autonomic agents, the response of both bladder base and bladder dome was approximately equal.

Although these studies do not establish V. I. P. as a neurohumoral agent, our demonstration that V. I. P. has a direct effect on muscular contraction supports the findings by Alm et al. (1) that this peptide may potentially play a role in the regulation of bladder contractility.

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