The Effect of Autonomic Drugs on Ureteric Peristalsis: A Canine in vivo Study

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Summary. An in vivo canine model was developed in which the renal pelvis was perfused by a cannula nephrostomy and ureteric activity assessed by monitoring bolus volume and interperistaltic interval. The effect of autonomic drugs showed that the ureter contained α-adrenergic receptors which on stimulation caused an increase in ureteric contraction rate and a decrease in bolus volume. With β-adrenergic receptor stimulation, there was complete inhibition of ureteric peristalsis for a variable period and evidence is presented that the β-adrenergic receptors may be β1 rather than β2. Cholinergic stimulation of ureteric rate was observed, but seemed to be mediated indirectly via α-adrenergic receptors. No significant change was seen in ureteric activity with adrenergic blocking agents alone, suggesting that the physiological importance of these receptors in normal activity is questionable.

Key words: Autonomic receptor, Bolus volume, Interperistaltic interval.

INTRODUCTION

The presence of adrenergic receptors (α stimulatory and β inhibitory) have been demonstrated in the ureter (14, 15, 19, 23) and functional innervation has been shown to be present for the α-adrenergic receptors in in vitro ureteric (24) and caliceal (13) preparations. Cholinergic agents have been shown to stimulate peristalsis (2, 8), but Rose and Gillenwater found that this was secondary to catecholamine release (19). Although the ureter can function independently of nerve supply after transplantation (16), denervation (28) and reversal of ureteric segments (26, 27), the autonomic adrenergic nerve supply is thought to have a modulating effect (25). However, this has not yet been clearly demonstrated.

Most in vivo methods used previously to investigate the effects of drugs on ureteric activity have been relatively invasive. Direct cannulation and perfusion of the ureter (18, 20), although separating the indirect effects of urine flow from the direct effect of the drug on peristalsis, excluded the site of the normal pacemaker in the pelvis or calices (4, 6, 7). Measurement of intraluminal pressure with a fluid-filled catheter or other measuring device has been widely used for many years, but Weinberg (21, 22) and Dale et al. (5) clearly demonstrated the problems associated with intraluminal devices. It was found that the size of an intrareteric catheter influenced the amplitude of both the basal and contractile pressures and the presence of a catheter altered the interperistaltic interval which normally had a modal distribution. More recently, less invasive methods have been developed in which the activity of the ureter was monitored in terms of peristaltic rate (or interperistaltic interval) and bolus volume without using intraluminal measuring devices or direct ureteric perfusion (34, 29).

In this study, using similar less invasive techniques, the effects of autonomic drugs on the interperistaltic interval and bolus volume have been determined. Natural urine flow was kept to a minimum and the renal pelvis was perfused via a cannula nephrostomy. Any change in natural urine flow was monitored so that its effects could be separated from those due to the effect of the drug on the ureter.

MATERIALS AND METHODS

Nineteen female adult mongrel dogs, mean weight 19.75 (SE 0.31) kg, were anesthetised with intra-
venous pentobarbitol using an initial dose of 25 mg/kg and anaesthesia was maintained with 60 mg increments. Endotracheal intubation and ventilation with room air were performed when necessary. A mid-line laparotomy incision was made, the bladder opened and a 5 F ureteric catheter inserted transvesically into the lower 2 to 3 cm of each ureter and secured in place with a silk ligature (Fig. 1).

Ureteric flow rate was measured by using an optical reflectance method to count the number of drops from the ureteric catheters per unit time. Each drop was detected by light reflecting from its surface and causing an increase in the voltage of a photosensor. This was converted to a digital signal that produced a step-wise increase in voltage for 9 drops, and with the 10th drop the voltage returned to 0. In this way the pen of the chart recorder traversed the paper once and returned to baseline every 10 drops (Fig. 2). Calibration with various flow rates showed that with a 25-gauge needle drop volume was 0.0105 ml and that flow rates of up to 4 ml/min could be recorded. Drop volume was constant up to rates of 1.5 ml/min, but tended to decrease above this. The sensitivity of this recording method was sufficient to allow the determination of urine bolus volume as well as ureteric flow rates below 1.5 ml/min.

Ureteric peristalsis was monitored with extraluminal optoelectronic sensors. These were originally developed by Halbert et al. (9) for use on the oviducts of experimental animals. For the study of ureteric peristalsis the original configuration of a rigid cuff was modified by separating, physically, the light emitting diode (LED) and phototransistor (PT) thereby permitting the ureter to expand without restriction. The larger LED was placed posteriorly and the smaller PT, weighing approximately 15 mg, was placed anteriorly. Both halves were fixed to the ureteric wall with cyanoacrylate tissue adhesive after making a small incision through the posterior peritoneum. Two sensors were placed at a separation of 2.5 to 5 cm in order to record peristaltic direction.

The optical sensor signal is related to mechanical events in the ureter according to a complex mechanico-optical transfer function. Since this relationship cannot be precisely defined, the device was used as a muscle activity "event" sensor rather than a true mechanical transducer. It is especially sensitive to change in geometry of the wall and lumen, and it was found that with small boluses at low flow rates the bolus was associated usually with a decrease in light transmission while the contraction wave behind the bolus produced an increase in light transmission. Respiration and other artefacts could readily be distinguished from the signal associated with the peristaltic event as with correct positioning of the sensors the signal from the latter was two or three times greater than that produced by respiratory or mechanical artefacts. Cinematographic studies showed that the circumferential and longitudinal wall movements did not appear to be affected significantly by these measuring devices.

A 16-gauge cannula (Angiocath) was inserted into the renal pelvis for the purpose of perfusing the renal pelvis and recording intrapelvic pressure. This was performed by incising the renal capsule and then advancing the cannula without the needle in place until the tip lay in the renal pelvis. It was found that with a 20 kg dog the tip

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**Fig. 1.** Schematic diagram illustrating the position of the sensors and catheters in the experimental preparation.

**Fig. 2.** The experimental ureter output, as measured by the drop counter, with natural urine flow. It can be seen that the number of steps per bolus varies from 3 to 7. (There are 9 steps from baseline to near the top of the chart and one to return the pen to baseline.)