Relationship between Pelviureteral Peristaltic Frequency and Urine Flow Change Evoked by Autonomic Drug Administration

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Although effects of autonomic drugs on ureteral peristaltic function have been extensively investigated by experimental studies in vivo, the views regarding them are still confused. The in vivo studies have not only their limitations of recording procedures but also difficulties in standardizing experimental conditions. In the in vivo experiments, various factors may affect the ureteral peristalsis. The ureteral peristalsis is known to be particularly sensitive to urine flow, and it is virtually impracticable to ascertain whether changes in peristalsis evoked by a drug are due to its direct action on the ureteral smooth muscle or due secondarily to alterations in urine flow.

The present investigation was undertaken to determine whether changes in ureteral peristalsis caused by noradrenaline, isoproterenol or acetylcholine are their direct effects or those secondary to alterations in urine flow, by simultaneous accurate measurements of the urine volume, ureteral electromyogram (EMG) and renal pelvic pressure.
MATERIALS AND METHODS

Fifteen adult mongrel dogs weighing 10-16 kg were used. The animal was laparotomized while being maintained under anesthesia by continuous drip infusion of $\alpha$-chloralose into the right cephalic vein after induction with 15 mg/kg of thymyal sodium. An 18-gauge polyethylene catheter was passed into the renal pelvis through the renal parenchyma in a manner of nephrostomy, and connected to a Statham P-50 pressure transducer to measure the renal pelvic pressure. Simultaneously, ureteral EMGs were recorded from about 10 cm distal to the pelviureteric junction (PUJ) via glass electrodes (Transidyne No. 1317) consisting of a platinum wire sealed in a glass tube 300 $\mu$m in outer diameter. The blood pressure was monitored through a catheter inserted into the left brachial artery and coupled to a Statham P-50 pressure transducer. The ureter was catherized distally to detect and quantitate changes in urine output following drug administration, using a drop counter. Fig. 1 is a schematic illustration of the experimental arrangement.

Drugs were administrated intravenously by single shots in the following doses: Noradrenaline $10^{-6}$ g/kg, isoproterenol $10^{-6}$ g/kg and acetylcholine $10^{-4}$ g/kg.

Values are given in terms of mean $\pm$ S.D.

RESULTS

Representative tracings after noradrenaline administration in dog No. 3 are shown in Fig. 2. In response to an i.v. dose of $10^{-6}$ g/kg noradrenaline, the renal pelvic pressure promptly and briefly became irregular. In about 30 sec after administration, the rhythm of contraction quickened slightly, the intervals being reduced from $3.57 \pm 0.11$ sec (before injection, $n = 28$) to $3.40 \pm 0.08$ sec ($n = 30$), although this difference of the contraction intervals is not significant by t-test ($0.50 > p > 0.25$). The baseline pressure was also elevated by 5 cmH$_2$O. Ureteral peristalsis increased in frequency about 30 sec after injection of $10^{-6}$ g/kg noradrenaline. The frequency of ureteral peristalsis returned to the initial level

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Fig. 1. Experimental model.
almost simultaneously with the restoration of renal pelvic pressure at 3.5 min after injection. The urine volume was 0.32 ± 0.04 and 0.34 ± 0.02 ml/min at 2 and 1 min before injection. It diminished to 0.12 ± 0.02 ml/min at 1 min after injection, and then tended to increase to 0.74 ± 0.05 and 0.90 ± 0.08 ml/min at 2 and 3 min.

Fig. 2 shows representative tracings of blood pressure, renal pelvic pressure and ureteral EMG, and urine output volume following intravenous administration of noradrenaline, 10⁻⁶ g/ml.

Fig. 3 shows representative tracings of blood pressure, renal pelvic pressure and ureteral EMG with urine output volume following intravenous administration of isoproterenol, 10⁻⁶ g/kg.
20 sec after injection, with concurrent lowering of the baseline pressure by about 1.5 cm H₂O. Two min after injection two renal pelvic pressure waves were recorded and the baseline pressure began gradually to rise. The pelvic pressure restored its regular frequency 3 min after injection. The interval of pressure waves was slightly prolonged (4.02±0.06 sec, n=10) at 3 min, compared to a pre-injection value of 3.76±0.16 sec (n=12). Ureteral peristalsis was recorded practically at a pace of 1:1 to the wave of pelvic pressure before injection. It disappeared completely 20 sec after injection and was recovered to a pace of approximately 1:1 3 min after injection when the pelvic pressure was restored. The urine volume was 0.54±0.06 and 0.42±0.03 ml/min at 2 and 1 min prior to i.v. injection of acetylcholine, and decreased to 0.18±0.05 ml/min at 1 min, 0.06±0.02 ml/min at 2 min and 0.12±0.02 ml/min after injection.

Representative tracings from dog No. 13 showing the effects of acetylcholine in an i.v. dose of 10⁻⁴ g/kg are presented in Fig. 4. The blood pressure fell and the pulse became irregular immediately after administration. The renal pelvic baseline pressure was lowered slightly, while the pelvic contraction pressure rose for about 60 sec immediately after injection. Then the pace of pelvic contractions became slow concurrently with a depression of pelvic baseline pressure and an enhancement of pelvic contraction pressure which continued for subsequent 40 sec. The urine volume which was 0.26±0.04 and 0.28±0.03 ml/min at 2 and 1 min, respectively, prior to i.v. injection of acetylcholine did not increase or did somewhat decrease (0.16±0.03 ml/min) for 1 min after injection. Then, it increased to 0.52±0.08 ml/min at 2 min, 0.56±0.09 ml/min at 3 min and 0.56±0.07 ml/min after injection.
at 4 min.

**DISCUSSION**

It is generally known that the ureters possess receptors for catecholamines and acetylcholine, but their physiological implication has been the subject of much controversy. Enhancement of ureteral peristalsis by adrenaline and norepinephrine was demonstrated by Boatman et al. (1967), Kaplan et al. (1968) and Rose and Gillenwater (1974) in their in vivo studies on the ureters of dogs or rats. Weiss et al. (1974), observing a significant increase of ureteral diameter in rabbits administered with reserpine for a long period, reported that catecholamines might play an important role in maintaining the ureteral tone. In 1973, McLeod et al. described that α-adrenoceptor agonists definitely increased the frequency of ureteral peristalsis, but that they evoked no tensiometrically detectable increase in ureteral tension or even reduced the ureteral contractility. According to Wein et al. (1972), it cannot be affirmed that the ureters are innervated by sympathetic nerves simply because they possess α- and β-adrenoceptors. The ureteral response to norepinephrine was scarcely altered even in dogs completely deprived of sympathetic nerve endings by the treatment with 6-hydroxydopamine in their study.

There have been many reports supporting that the reduction in both frequency and contractility of ureteral peristalsis was caused by isoproterenol. Inhibitory effects of β-adrenoceptor agonists on the ureter have been observed in dogs by Wein et al. (1972), McLeod et al. (1973), Hannapel and Golenhofen (1974), Rose and Gillenwater (1974) and Reid et al. (1974) and in rats by Finberg and Peart (1970) and Ancill et al. (1972). However, Boatman et al. (1967) and Kaplan et al. (1968) described that no β-adrenoceptors might exist in the ureter since the ureter did not respond at all to the administration of isoproterenol. Thus, experimental findings concerning the effects on the renal pelvis and ureter of drugs acting on sympathetic nerve-endings have been inconsistent, though all those reports generally agreed in asserting that α-adrenoceptor agonists increase the frequency of ureteral peristalsis while β-adrenoceptor agonists reduce or completely suppress the ureteral peristalsis.

Tsuchida et al. (1971) observed a transitory arrest of urine secretion following administration of isoproterenol in vivo, thus suggesting a possibility that the changes in ureteral peristalsis are evoked secondarily by urine volume alteration. Tsuchida and Sakamoto (1974) examined the effects of drugs under an experimental condition where the renal vein was ligated so as to avoid urine volume changes. In the present study, urine volume changes induced by norepinephrine or isoproterenol coincided with alterations in frequency of ureteral peristalsis. Therefore, it cannot be ascertained whether the changes in ureteral peristalsis are direct or secondary effects of drugs.

It was reported by Butcher et al. (1957) and Finberg and Peart (1970) that
acetylcholine had little or no effect on the calyceopyeloureter system. Gruber (1928) and Deane (1967) noted enhancement of ureteral peristalsis by acetylcholine, whereas Chen et al. (1957) and Borgstedt et al. (1962) described that acetylcholine suppressed peristaltic movement of the ureter. From the present study it seems reasonable to conclude that acetylcholine acts upon the ureter to evoke an increase in frequency of its peristalsis for a short period and suppresses pelviureteral activity subsequently.

In the present experiments where ureteral EMG was recorded outside the ureter using a glass electrode so that urinary stasis could be avoided, it would be certain that urine secretion promptly reflected ureteral peristalsis. Accordingly, the ureteral responses to the administration of noradrenaline or isoproterenol might be caused by secondary changes of urine volume. In contrast with them, acetylcholine reduced the urine excretion during the enhancement of ureteral peristalsis. It may be concluded that acetylcholine acts directly on the ureter to enhance its peristaltic movement though for a brief period. From these experiments, it was impossible to discriminate the direct pharmacological responses of the ureter to noradrenaline or isoproterenol from the secondary responses to changes in urine volume.

References

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