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Modifications of Ureteric Peristalsis by Local Anaesthetic An Experimental Study in Dogs

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Summary. An in vivo study of the response of the dog ureter to local anaesthetics administered systemically and by ureteric perfusion, revealed that lidocaine, procaine, and mepivacaine, caused hyperperistalsis. The intravenous use of a near toxic dose produced hyperperistalsis of limited duration, whereas, intraureteric administration produced a prolonged and constant response with low dosage. The mode of action of these drugs is unclear as they are generally regarded as being non specific smooth muscle depressants. Continued peristalsis after prolonged exposure to local anaesthetic favours a myogenic rather than neurogenic conduction of the ureteric contraction wave.

Key words: Lidocaine - Mepivacaine - Procaine - Ureteric perfusion - Hyperperistalsis.

The apparent failure of drugs to consistently modify ureteric peristalsis may reflect inadequate ureteric tissue concentrations. As drugs can be absorbed across ureteric epithelium (1) intraluminal perfusion of the ureter might alter ureteric function more predictably than intravenous administration of the drug.

To test this concept, three drugs, lidocaine, procaine and mepivacaine were studied. These drugs have, in addition to a local anaesthetic action, a systemic action which stabilizes excitable membranes and non-specifically depresses smooth muscle. The intraureteric injection of one of these, lidocaine, has been observed to produce a temporary cessation of peristalsis in human ureters (7).

This paper reports the effect on ureteric peristalsis of intravenous and intraureteric administration of these local anaesthetic drugs in dogs which had been prepared with an explanted renal pelvis (8).

MATERIAL AND METHODS

Four female mongrel dogs, Nos. 4, 8, 9 and 10 were used throughout the study.

During each experiment, the conscious dog lay in a padded trough. The ureter was cannulated via the explanted pelvis so that the tip of a 15 cm length of fine polyethylene tubing (Bardic 1817-R) lay in the region of the junction of the middle and lower thirds of the ureter. The ureter was perfused through this tubing with normal saline at 0.5 ml/min, and the pressure in the system recorded with a Statham transducer and Polygraph pen recorder. The bladder was continuously drained by catheter. A venous infusion was maintained with dextrose water, and respiratory movements recorded by a pneumatic chest band.

Stable ureteric recordings were obtained for a minimum period of 15 min before administration of the test drugs.

When the drug was given systemically, it was injected into the intravenous infusion using a Holter pump. Lidocaine was initially injected at a rate of 20 mg/min to a total dose of 100 mg. As each dog tolerated this amount without side effects, the total dose was increased to 120 mg. A 120 mg dose was also used with procaine and mepivacaine.

Intraluminal administration was carried out by substituting the test drug for the saline

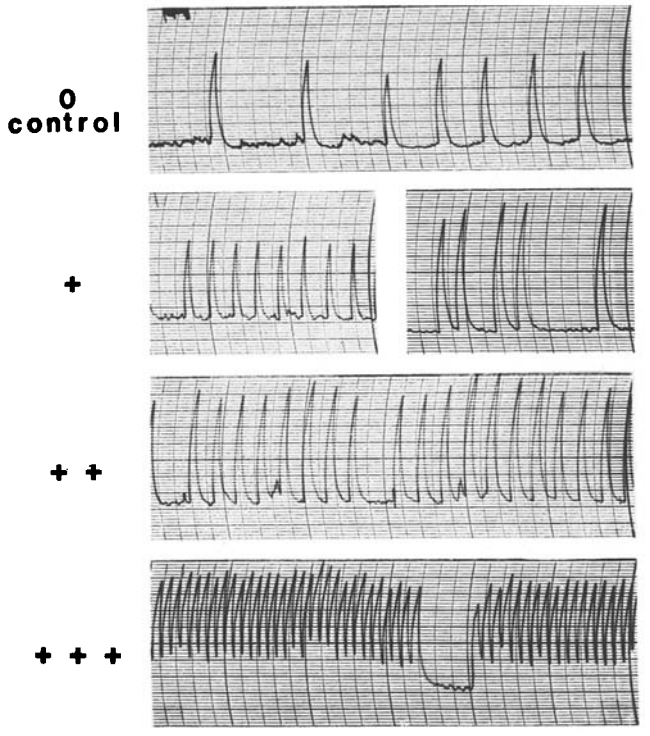

Fig. 1. Grading of hyperperistaltic effect; + sustained increase in either frequency or amplitude; ++ increase in both frequency and amplitude; +++ elevation of baseline ureteric pressure with clonic contraction waves

Table 1. Results of IV administration

Dog	Wt	Lido-caine 100 mg	Lido-caine 120 mg	Pro-caine 120 mg	Mepi-vacaine 120 mg
No. 4	16 KG	0	++	++	++
No. 8	22 Kg	++	++	+	+++
No. 9	23 Kg	+	+	0	+
No. 10	30 Kg	0	+	0	+
Experiments		4	4	4	4

Table 2. Results of topical administration

Dog	Lidocaine 1%	Procaine 1%	Mepi vacaine 1%	Lidocaine 10%
No. 4	++(2), +++	0(2)	++	+++(3)
No. 8	+++(3)	0, +	++	+++(2)
No. 9	++, +++(3)	0, +	+++(2)	+++(2)
No.10	++(2), +++	+(2)	++	+++(2)
Experiments	13	8	5	9

perfusate. The ureter was perfused with a 1% solution of each drug, and, in addition, with a 10% solution of lidocaine. Each experiment was concluded by again perfusing the ureter with saline.

RESULTS

The administration of the three local anaesthetics generally produced a change in ureteric wave pattern characterized by hyperperistalsis. To permit evaluation of the response, the wave pattern was graded empirically as follows: O, where there was no appreciable alteration in the control wave pattern; +, where there was a sustained increase in either frequency or amplitude; ++, where there was an increase in both frequency and amplitude; and +++, where there was an elevation of baseline ureteric pressure with clonic contraction waves (Fig. 1).

The effects of intravenous administration of lidocaine, procaine and mepivacaine on ureteric peristalsis are shown in Table 1. At a dose of 100 mg, lidocaine failed to elicit hyperperistalsis in two dogs, but 120 mg lidocaine produced hyperperistalsis in all four dogs (Fig. 2). Procaine did not effect the ureteric wave pattern in two dogs, and produced hyperperistalsis in two. Mepivacaine produced hyperperistalsis in all experiments. In no instance was there inhibition of peristalsis.

The results of intraluminal perfusion are recorded in Table 2. Both 1% lidocaine and mepivacaine produced hyperperistalsis within a few minutes of commencing infusion, and this reaction persisted for as long as the drug was infused (Fig. 3a). Wash out with saline produced a return to the control wave pattern within 5 to 15 minutes (Fig. 3b). Procaine failed to affect peristalsis in four experiments, but, in four others, a hyperperistaltic effect was apparent (Fig. 4). Lidocaine at a 10% concentration produced marked hyperperistalsis in all experiments (Fig. 5a), and the wave pattern remained abnormal during saline wash out for 20 to 40 minutes (Fig. 5b).

DISCUSSION

The pharmacological effects of local anaesthetics, which include blockade of neural impulse transmission, a blocking action at myoneural

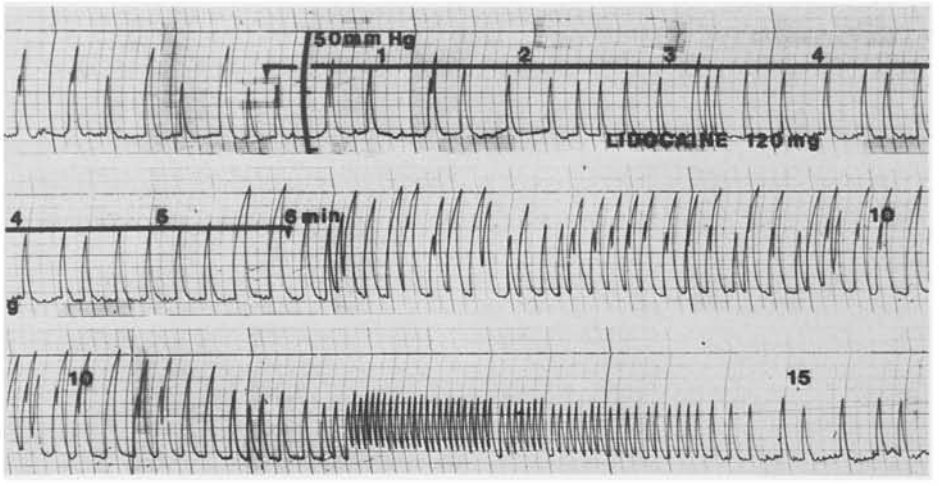

Fig. 2. The intravenous administration of 120 mg. lidocaine produced hyperperistalsis which persisted for 9 min

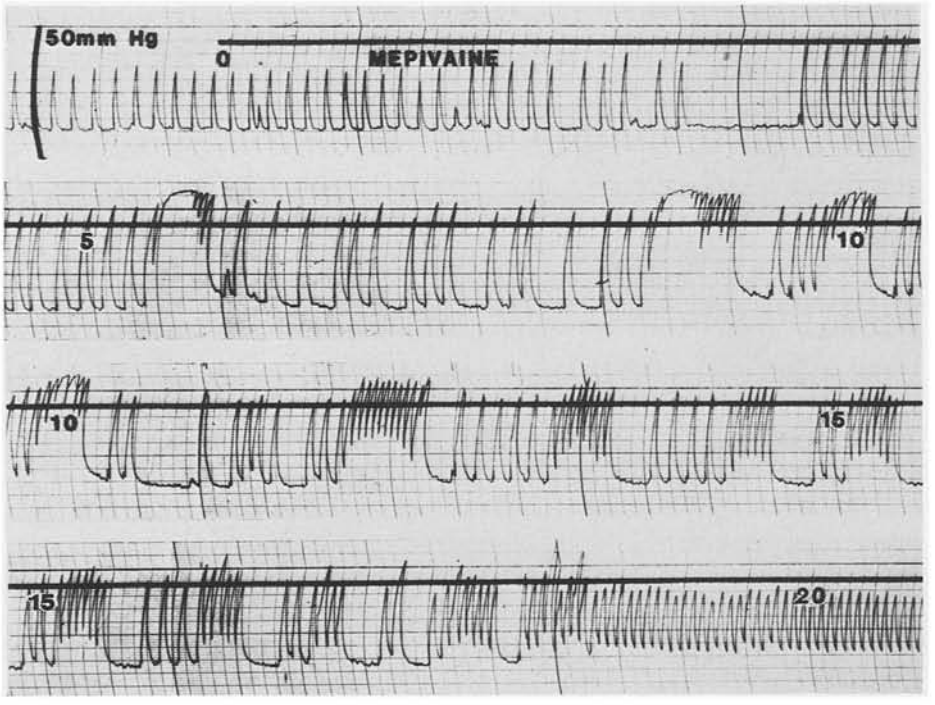

Fig. 3a. Perfusion of the ureter with 1% mepivacaine at 0.5 ml/minute produced hyperperistalsis within 5 min, and this response persisted during perfusion

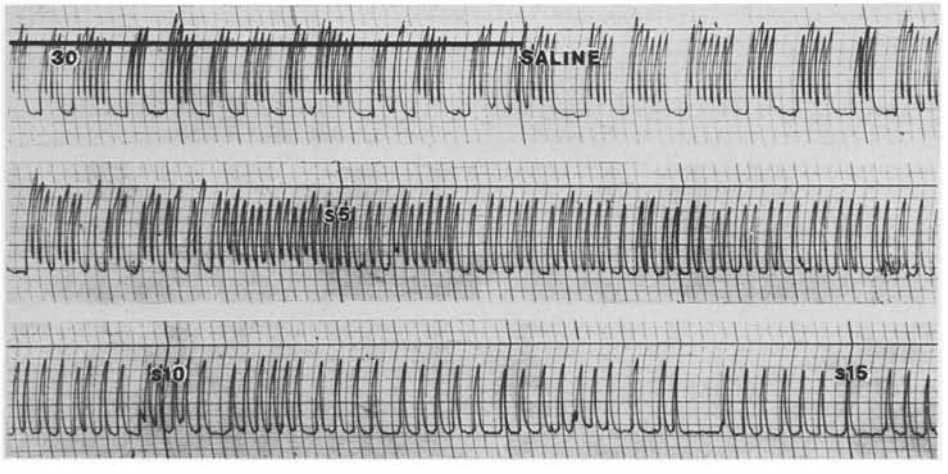

Fig. 3b. Saline wash out following mepivacaine produced return to control wave pattern within 15 minutes

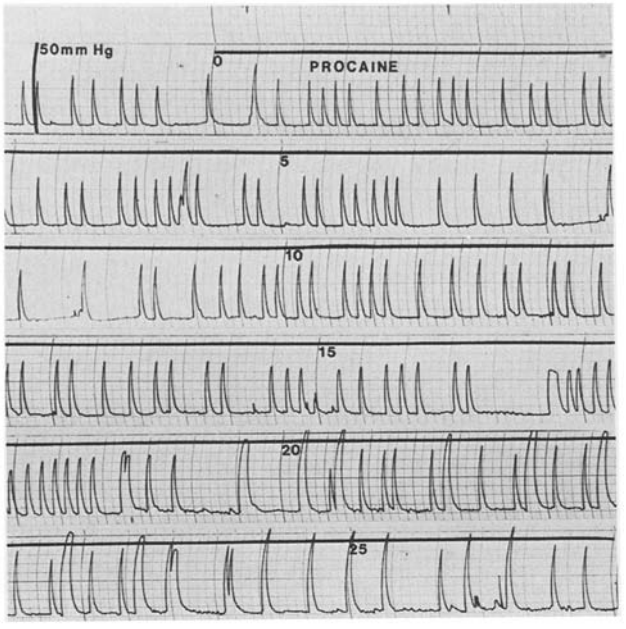

Fig. 4. Limited hyperperistaltic effect produced by perfusion with 1% procaine

junctions (5) and inhibition of smooth muscle contractions (2), suggested that these compounds would have a depressant effect on ureteric peristalsis. This study however found that the dog ureter exhibited marked hyperperistalsis when exposed to these agents.

The mechanism of the hyperperistaltic action is not clear. There is evidence that local anaesthetics can affect smooth muscle alpha and beta receptor systems (3), however in the ureter the alpha adrenergic receptor is considered to have a chronotropic effect, and the beta receptor a negative bathmotropic effect (6), so it is unlikely that the adrenergic receptor mechanism is involved. There appeared to be a correlation with the potency of the local anaesthetic properties of the drug. Procaine, which is two to three times less effective than the other two agents, failed both systemically and topically to consistently produce hyperperistalsis. The rise in contraction frequency on the other hand did not correlate with the topical anaesthetic properties. Mepivacaine, like procaine, is classified as an ineffective

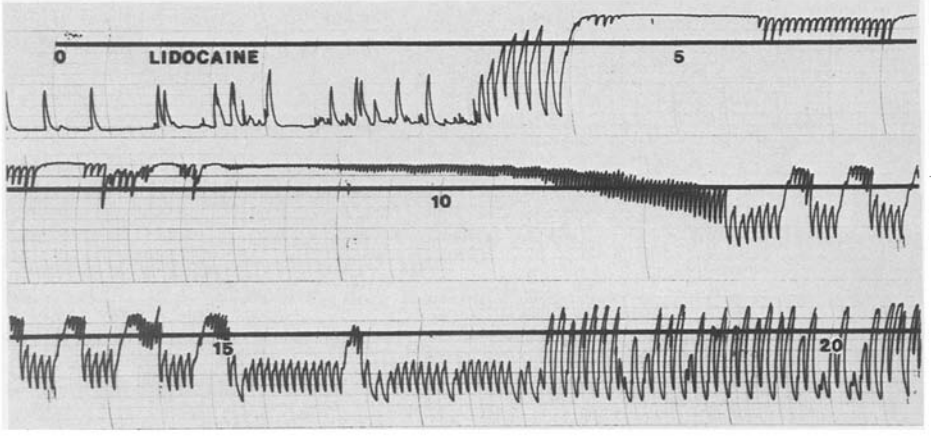

Fig. 5a. 10% lidocaine perfusion produced marked hyperperistalsis

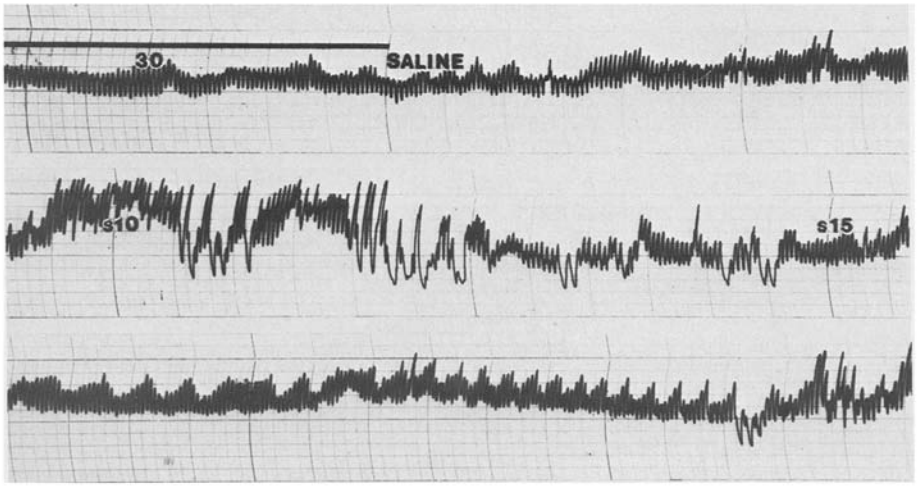

Fig. 5b. Persistence of abnormal wave pattern during 20 minutes of saline wash out following perfusion of the ureter with lidocaine for 32 min

topical anaesthetic (4) but unlike procaine it produced hyperperistalsis in all experiments. With both mepivacaine and lidocaine, hyperperistalsis occurred within a few minutes of the start of perfusion, when the total dose was much less than that required by systemic administration, suggesting that local tissue concentration was important. 10% lidocaine produced maximal peristalsis in all experiments and recovery of normal peristalsis during subsequent wash out with saline was often not apparent by 30 min, whereas, after 1% lidocaine, wash out produced a return to normal peristalsis within 15 min. This persistent effect suggests that hyperperistalsis could be due to blockade of an inhibitor substance rather than an excessive release of a transmitter substance.

As perfusion of the ureter for a prolonged period with a local anaesthetic would be expected to block intrinsic nerves, the continuation of peristalsis under these conditions favours a myogenic rather than a neurogenic conduction of the ureteric contraction wave.

Lidocaine and mepivacaine have been shown to be potent and predictable stimulants of ureteric peristalsis in dogs. Intraureteric perfusion of these local anaesthetic drugs proved to be a more effective method of producing hyperperistalsis than systemic administration, and suggested that perfusion of a dilated ureter with lidocaine or mepivacaine might be a useful test for evaluating residual muscle function.

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