Pharmacology of electrically evoked contractions of human bladder

J.R. HINDMARSH, O.A. IDOWU, W.K. YEATES & M.A. ZAR

Departments of Pharmacological Sciences and Urological Surgery, The Medical School, The University of Newcastle upon Tyne, NE1 7RU

Isolated strips of detrusor muscle from rats, guinea-pigs, rabbits and from other species have been used previously to study the nature of motor transmission in the bladder (Ursillo & Clarke, 1956; Hukovic, Rand & Vanov, 1965; Ambache & Zar, 1970). However, no such comparable investigation has been carried out on human bladder.

A total of 14 experiments were carried out on isolated strips (5 × 0.3 cm) of human bladder, obtained from patients undergoing bladder surgery. The preparations were suspended in 10 ml organ baths between parallel platinum electrodes in Krebs-Henseleit solution at 37°C and contractions were recorded isometrically. For electrical field stimulation, trains of 5–20 pulses (0.5 ms duration, 10 Hz, 12 V) were delivered at 60–90 s intervals. Electrical stimulation resulted in contractions which were abolished by tetrodotoxin (0.2 μg/ml) and which were therefore neurogenic. The electrically induced contraction (EIC) was unaffected by hexamethonium, (0.1 mM) suggesting its post-ganglionic origin. EICs were greatly augmented by eserine (3–6 μM) and were partially antagonized by atropine (0.1 μM); no further antagonism was noticed on increasing the atropine concentration to 1–5 μM. The atropine-resistant component of EIC was not potentiated by eserine.

Noradrenaline (and isoprenaline), 0.01–1 μM inhibited EIC drastically; in contrast, acetylcholine-induced contraction was reduced only slightly or not at all by noradrenaline. The inhibition of EIC by noradrenaline remained unaffected by phentolamine (5 μM) but was antagonized to a variable extent by propranolol (1–5 μM).

Phenylephrine and clinidine (0.01–1 μM), either did not affect the EIC or potentiated it; the potentiation was usually seen with the higher concentrations of these drugs.

EIC, but not the acetylcholine evoked contraction, was potentiated by remarkably low concentrations of 5-hydroxytryptamine (0.1–nM). The potentiating effect of 5-hydroxytryptamine remained unaffected by methysergide (0.5 μM) and by morphine (1 μM). Atropinization did not prevent the potentiating effect of 5-HT on EIC.

The foregoing results provide evidence for the view that

(1) acetylcholine is the predominant, but not the sole, motor transmitter in human bladder. This conclusion contrasts with the findings in isolated strips of guinea-pig, rabbit and cat bladder, when the motor transmission was found to be predominantly non-cholinergic (Ambache & Zar, 1970) and is probably a reflection of species variability.

(2) biogenic amines, noradrenaline and 5-hydroxytryptamine possess the ability to play significant but opposite roles in modulating the motor transmission to the detrusor muscle largely through presynaptic mechanisms.

References

AMBACHE, N. & ZAR, M.A. (1970). Non-cholinergic transmission by post-ganglionic motor neurones in the mammalian bladder. *J. Physiol.*, **210**, 761–783.

HUKOVIC, S., RAND, M.I. & VANOV, S. (1965). Observations on an isolated, innervated preparation of rat urinary bladder. *Br. J. Pharmac. Chemother.*, **24**, 178–188.

URSILLO, R.C. & CLARKE, B.B. (1956). The action of atropine on the urinary bladder of the dog and on the isolated nerve-bladder strip preparation of the rabbit. *J. Pharmac. exp. Ther.*, **118**, 338–347.

Temperature-dependent effects of autonomic drugs on the response of the guinea-pig isolated bladder to parasympathetic nerve stimulation

N. TURNER & D.F. WEETMAN

Department of Pharmacology, School of Pharmacy, Sunderland Polytechnic, Sunderland SR1 3SD

Contractions of the guinea-pig isolated bladder to pelvic nerve stimulation are only partially blocked by hyoscine or ganglion blocking agents (Weetman, 1972; Weetman & Turner, 1973). Whilst continuing this investigation, an experiment was performed at room temperature because a bath heater was inadvertently not switched on. Hyoscine produced no blockade in this case, so the present experiments were performed.

Bladders were taken from female guinea-pigs (250–400 g) and divided longitudinally to provide paired preparations: one, the control, was used at 33°C, the other at a different temperature. Preparations were arranged in 100 ml isolated organ baths filled with McEwen's solution which was gassed