8. N. Fjallbrandt and A. Iggo, J. Physiol. (London), 156, No. 3, 578 (1961).
9. L. S. Goodman and A. Gilman, The Pharmacological Basis of Therapeutics, New York (1980), pp. 91-99.
10. C. A. Keele and D. Armstrong, Substances Producing Pain and Itch, London (1964).
11. V. M. Khayutin, L. A. Baraz, E. V. Lukoshkova, et al., Prog. Brain Res., 43, 291 (1976).
12. B. Lynn, Textbook of Pain, ed. by P. D. Wall and R. Halzack, Edinburgh (1982), pp. 19-33.
13. P. J. Watson, Br. J. Pharmacol., 40, No. 1, 102 (1970).

EFFECT OF PRAZOCIN ON TISSUE OF THE HUMAN PROSTATE WITH BENIGN HYPERTROPHY

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Recent investigations have shown the presence of an adrenergic innervation in tissue of the human prostate [2, 6]. A pharmacological study of the tissue of the prostatic capsule and of benign hypertropy of the prostate (BHP), taken during prostatectomy, showed the presence of humerous α-adrenoreceptors in objects studied in vitro [4]. It is considered that α-adrenoreceptor stimulation may increase the ureteric obstruction caused by HBP [3]. The beneficial effect of certain α-adrenoblockers (prazocin, phentolamine, phenoxybenzamine) on the parameters of micturition in patients with BHP has been described (diminution of the barrier pressure in the prostatic urethra, improvement of the stream of urine, and so on) [1, 3, 5, 7]. Investigations in vitro have confirmed the hypothesis regarding the α-adrenoblocking mechanism of action of prazocin [8] and phentolamine [4] on the tissue of BHP and the prostatic capsule.

The Soviet preparation prazocin, synthesized at the S. Ordzhonikidze All-Union Pharmaceutical Chemical Research Institute, has recently been approved for use as an antihypertensive agent. Information on the use of prazocin in urologic practice is not to be found in the Soviet literature. We have undertaken an experimental study of the effect of prazocin on tissue of BHP.

EXPERIMENTAL METHOD

BHP tissue was obtained during prostatectomy. Immediately after the operation the tissue was placed in Krebs' solution. A strip of BHP 2 cm long, 0.5 cm wide, and 0.2 cm thick, was excised and suspended in a cuvette for isolated organs (a thermostatically controlled bath for Hugo Sachs Elektronik, West Germany). The nutrient solution (37°C) was aerated with carbogen. The period of equilibrium was 60 min. Contractions were recorded under isometric conditions by means of a transducer from Ugo Basile (Italy). The duration of action of prozocin was 3 min.

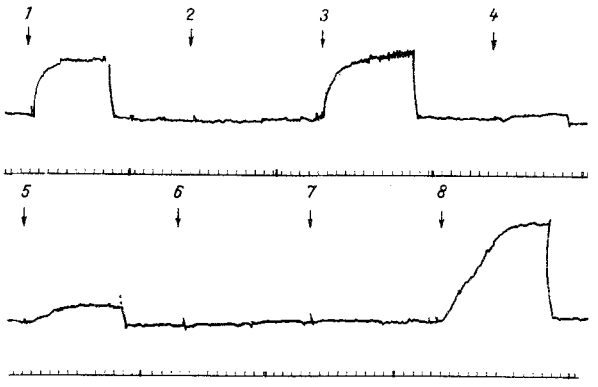

Fig. 1. Effect of different agonists on human BHP tissue. Here and in Figs. 2 and 3: arrows indicate addition of substances to cuvette containing BHP tissue. 1) Adrenalin $1\cdot10^{-5}$ g/ml; 2) acetylcholine $1\cdot10^{-5}$ g/ml; 3) noradrenalin, $2\cdot10^{-5}$ g/ml; 4) histamine, $1\cdot10^{-5}$ g/ml; 5) phenylephrine, $2\cdot10^{-5}$ g/ml; 6) ephedrine, $2\cdot10^{-5}$ g/ml; 7) serotonin, $2\cdot10^{-5}$ g/ml; 8) KCl, $1\cdot10^{-2}$ g/ml.

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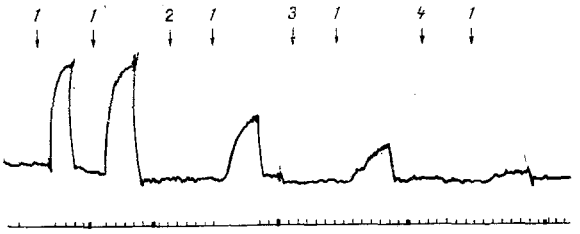

Fig. 2

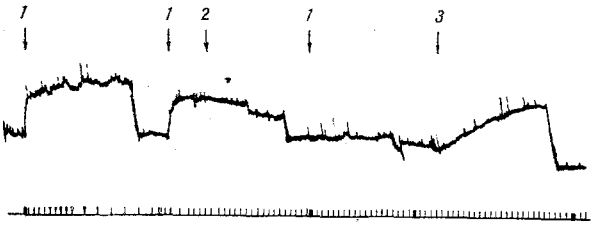

Fig. 3

Fig. 2. Effect of preliminary addition of prazocin on spasm of BHP tissue induced by adrenalin. 1) Adrenalin, $1 \cdot 10^{-5}$ g/ml; 2) prazocin, $1 \cdot 10^{-9}$ g/ml; 3) prazocin, $1 \cdot 10^{-8}$ g/ml; 4) prazocin, $1 \cdot 10^{-7}$ g/ml.

Fig. 3. Effect of prazocin on developed spasm of BHP induced by adrenalin. 1) Adrenalin, $1 \cdot 10^{-5}$ g/ml; 2) prazocin, $1 \cdot 10^{-6}$ g/ml; 3) KCl, $1 \cdot 10^{-2}$ g/ml.

EXPERIMENTAL RESULTS

Experiments were carried out on strips of BHP obtained from nine patients during operation. From each hypertrophied prostate one to three strips were prepared, on which to study the action of the drugs.

It was shown to begin with that adrenalin ($1 \cdot 10^{-5}$ g/ml), noradrenalin ($2 \cdot 10^{-5}$ g/ml), phenylephrine ($2 \cdot 10^{-5}$ g/ml), and ephedrine ($2 \cdot 10^{-5}$ g/ml) as a rule increased the tone of the BHP strip. Adrenalin had the most constant action (Fig. 1). Under the influence of acetylcholine ($1 \cdot 10^{-5}$ g/ml), histamine ($1 \cdot 10^{-5}$ g/ml), and serotonin ($1 \cdot 10^{-5}$ g/ml) the original tone of the BHP tissue was unchanged.

Prazocin in a concentration of 10^{-9}-10^{-5} g/ml has no effect on tone of BHP, but reduced the amplitude of spasm induced by adrenalin to a degree which depended on dose (Fig. 2). In a concentration of $1 \cdot 10^{-9}$ g/ml prazocin reduced the amplitude of spasm by about 30%, in a concentration of $1 \cdot 10^{-8}$ g/ml – by 60%, and in a concentration of $1 \cdot 10^{-7}$ g/ml prazocin completely prevented the spasmogenic action of adrenalin. EC_{50} for prazocin in this particular test was $5 \cdot 10^{-9}$ g/ml, evidence that it is highly effective.

When prazocin ($1 \cdot 10^{-6}$ g/ml) was added at the height of action of adrenalin, tone of the BHP strips was reduced (Fig. 3). Subsequent addition of adrenalin did not cause an increase in tone. The effect of adrenalin was restored by 40-50% 3-4 h after rinsing to remove the prazocin.

Addition of prazocin (10^{-7}-10^{-5} g/ml) in the presence of spasm induced by KCl ($1 \cdot 10^{-2}$ g/ml) did not reduce the spasm.

Prazocin is thus an effective antagonist of the spasmogenic action of adrenalin on BHP tissue. Comparative experiments with adrenalin and KCl demonstrate the specificity of the action of prazocin on adrenoreceptors of BHP. There is reason to consider that the Soviet drug prazocin may be a promising agent for the correction of disturbances of micturition in patients with benign hypertrophy of the prostate.

LITERATURE CITED

1. P. H. Abrams, P. J. R. Sha, R. Stone, and R. G. Choa, Br. J. Urol., 54, 527 (1982).
2. H. G. Baumgarten, B. Flack, and A. F. Holstein, Z. Zellforsch., 90, 81 (1968).
3. C. R. Bouffioux and L. Renders, Eur. Urol., 10, 306 (1984).
4. M. Caine, S. Raz, and M. Zeigler, Br. J. Urol., 47, 193 (1985).
5. M. Caine, S. Perlberg, and S. Meretyk, Br. J. Urol., 50, 551 (1978).
6. J. A. Gosling and S. A. Thompson, Urol. Int., 32, 269 (1977).
7. H. Hedlund and K.-E. Anderson, J. Urol. (Baltimore), 130, 275 (1983).
8. A. Shapiro, B. Mazouz, and M. Caine, Urol. Res., 9, 17 (1981).