The Action of Adrenal Steroids on the Pharmacological Reactivity of the Isolated Vein of the Rabbit Ear*

J. D. HOROWITZ and M. L. MASHFORD
Department of Human Physiology and Pharmacology,
University of Adelaide, South Australia

Received December 19, 1968

Summary. 1. The isolated perfused central vein of the rabbit ear has been used to investigate potentiation by adrenal steroids of the actions of bradykinin, histamine and noradrenaline.

2. Potentiation of all substances occurred when adrenal steroids in large doses were added to the perfusate but was neither large in magnitude nor constant in occurrence. Potentiation was seen with cortisol and dexamethasone and their potency was in the same relationship as their glucocorticoid activity. However aldosterone was roughly equi-potent with dexamethasone.

3. Thus the potentiation by steroids in this preparation is non-specific in that BK and histamine as well as noradrenaline responses are affected. The potency of steroids does not parallel either glucocorticoid or mineralocorticoid activity and so these results do not suggest an effect of steroids on either specific receptors or membrane electrolyte distribution.

Key-Words: Catecholamines — Plasma Kinins — Histamine — Glucocorticoid Aldosterone.


It is well known that the adrenal steroid hormones enhance vascular responses to catecholamines; this has been shown by numerous clinical examples (KURLAND and FREEDBERG, 1951; REIS, 1960; ROSS, 1961 and SCHMID, ECKSTEIN, and ABBOUND, 1966), as well as by studies on adrenalectomised animals (SMALL, WEITZNER, and NAHAS, 1959; D'AGOSTINO and SEGURA, 1964), and on isolated blood vessels (BOHR and CUMMINGS, 1958; BOHR, BRODIE, and CHEU, 1958; SUGIURA, 1954; FOWLER and CHOU, 1961 and BESSE and BASS, 1966). There is, however, no general agreement on the relative potencies of various steroids and little information on the specificity of the phenomenon, since virtually all studies have been concerned with responses to catecholamines.

* Supported in part by Grant G377/206 from National Hearth Foundation of Australia.
It has been found that the central vein of the rabbit ear is only moderately sensitive to catecholamines, but exhibits reproducible and dose-dependent contractions in response to bradykinin (BK) and histamine (Horowitz and Mashford, 1969). This preparation is thus suitable for studies of the effects of adrenal steroids on vasoconstrictors other than catecholamines. Since it shows great differences in pharmacological reactivity from the rabbit aortic strip preparation, which has been used in most in vitro steroid experiments (Bohr and Cummings, 1958; Bohr et al., 1958; Fowler and Chou, 1961 and Besse and Bass, 1966) it is of some use in determining whether steroids potentiate responses in all vascular smooth muscle.

Methods

The preparation used was the isolated perfused central vein of the rabbit ear previously described (Horowitz and Mashford, 1969). The effects of steroids on the responses of the preparation were examined by comparing dose-response curves obtained before and during the addition of steroid to the perfusing fluid; in some cases the comparison was extended to responses after restoration of steroid-free perfusion. The effects of spontaneous sensitivity changes in the preparation were reduced by infusing steroid only after responses had reached a stable level. In addition in most experiments, two vessels, removed from the same animal, were mounted in adjacent perfusion systems; one acted as a control while the other received steroid after the initial determination of dose-response curves. Sensitivity changes were expressed as the ratio of the dose producing equal responses in the vein in the two periods examined (Fig. 1). The

Fig. 1. Shift of bradykinin dose response curves induced by dexamethasone. ••• No dexamethasone in perfusate; ••• 1 µg/ml dexamethasone in perfusate; ••• 3 µg/ml dexamethasone in perfusate. Method of calculating potentiation ratio i.e. ratios of doses giving equal response: in the above figure potentiation ratio for 1 µg/ml dexamethasone B/A = 1.7