Vascular reactivity in 'post-DOCA' hypertension

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Hypertension induced in rats by administration of desoxycorticosterone (DOCA) and saline for several weeks persists when these agents are withdrawn (Friedman & Friedman, 1949). The mechanism responsible for maintaining the high blood-pressure is not known but it may be that changes in arterioles resulting from the initial period of hypertension are responsible. Evidence of functional changes in resistance vessels during post-DOCA hypertension is lacking; however, we have previously shown that peripheral vascular reactivity to noradrenaline is increased while DOCA and saline are being given (Beilin, Wade, Honour & Coles, 1970). This experiment was designed to study vascular reactivity in animals remaining hypertensive when DOCA and saline have been withdrawn.

Twenty male Wistar rats were made hypertensive by removing one kidney and giving 0·9% sodium chloride and 0·2% potassium chloride in tap water, and by injecting DOCA tri-methyl acetate (CIBA) (12·5 mg i.m.) 3 times a week for 4 weeks and 6·25 mg intramuscularly weekly for 3 more weeks. DOCA and saline were then stopped. Twenty control rats studied in parallel were sham operated and subsequently given a normal diet and tap water to drink. Vascular reactivity was assessed in the isolated, perfused tail of the rat (Wade & Beilin, 1970). Tail perfusions were started 5 weeks after stopping DOCA and were completed 5 weeks later. Dose-response curves to bolus injections of noradrenaline (12·5–100 ng) and serotonin (142·5–570·0 ng) were obtained from each preparation, using the increment in pressure in the constant flow perfusion circuit in response to each injection as an estimate of the response of the resistance vessels.

Systolic blood-pressure recorded by tail plethysmography in the conscious rats averaged 186·3 mmHg in the post-DOCA group and 127·2 mmHg in the controls in the week before perfusion studies ($P<0·01$).

Tail preparations from the post-DOCA rats showed on average 3-fold greater responses to each dose of noradrenaline and serotonin than controls. Dose-response curves were steeper in the hypertensive group ($P<0·01$ for noradrenaline and $P<0·0005$ for serotonin) and appeared shifted to the left. Maximal response to 2,000 ng noradrenaline averaged 211·1 mmHg in the post-DOCA group compared with 164·4 mmHg in controls ($P<0·0025$). Baseline pressure at a perfusion rate of 0·5 ml/min averaged 18·9 mmHg in the hypertensive group compared with 16·3 mm Hg ($P<0·025$) in controls.

These results indicate that arterioles in post-DOCA hypertensive rats are hypersensitive to noradrenaline, and have undergone structural changes resulting in increased resistance under basal conditions and greater maximal responses. These changes are likely to contribute significantly to a high peripheral resistance. Evidence from other experiments suggests that the kidney must also be involved for hypertension to persist.

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