SHORT COMMUNICATION

HAEMODYNAMICS AND THE PARTICIPATION OF PRESSOR SYSTEMS IN YOUNG AND ADULT RATS WITH AGE-DEPENDENT DOCA-SALT HYPERTENSION

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Received March 10, 1986
Accepted June 20, 1986

Summary


Increased systemic resistance is the main haemodynamic abnormality in DOCA-salt hypertension which is more pronounced in young than in adult rats. A mild increase of cardiac output also contributes to higher blood pressure in young animals. Arterial compliance is decreased only in young hypertensive rats. The acute blockade of different pressor systems indicates that the role of back-up pressor systems (vasopressin and angiotensin II) is increased in adult DOCA-salt hypertensive animals while the increased activity of adrenergic system and digoxin-like factors contributes to the enhanced hypertensive response of young rats.

Key words: Vasopressin — Angiotensin II — Norepinephrine

The young DOCA-salt treated rats developed more severe hypertension than the adult animals (Musilová et al. 1966). Yamamoto et al. (1983) found that the mean arterial pressure of adult DOCA-salt treated rats was elevated due to the rise of systemic resistance. In these hypertensive animals, the activity of the renin-angiotensin system (RAS) was suppressed (Gavras et al. 1975), while the contribution of pressor effects of vasopressin (VP) (Möhring et al. 1977) and the sympathetic nervous system (Rascher et al. 1981) was augmented. The participation of individual pressor systems in the maintenance of high blood pressure (BP) of adult DOCA-salt hypertensive rats was demonstrated by the acute blockade of circulating pressor agents with specific antibodies (vasopressin — Möhring et al. 1977), by the administration of competitive antagonists (angiotensin II — Gavras et al. 1975, vasopressin — Mento et al. 1984), adrenoceptor blocking agents (Burnier et al. 1984) or converting enzyme inhibitors (Miyauchi et al. 1980). Similar data are very scarce in young DOCA-salt hypertensive animals in which an important pressor role of a digoxin-like factor was disclosed (Kojima 1984). In order to elucidate the haemodynamic mechanisms of the age-dependent hypertensive response, we studied BP effects of the acute blockade of the above mentioned pressor systems in conscious young and adult rats with DOCA-salt hypertension.

Uninephrectomized young [4-week-old] and adult [12-week-old] Wistar male rats were treated with DOCA [20 mg/kg, twice a week] and drank 1 % saline. Unoperated age-matched water-drinking animals served as controls. After 6 weeks of DOCA-salt treatment polyethylene cannulas were inserted into the carotid artery and jugular vein under light ether anaesthesia. Four hours later, the mean arterial pressure (MAP) and cardiac output (CO) were measured in 6—10 conscious rats using the dye dilution technique (Zicha et al. 1982). In other subgroups of conscious normotensive or hypertensive animals we studied MAP decrease after single intravenous doses of a converting
enzyme blocker (captopril, 10 mg/kg), α1-adrenoceptor blocker (prazosin, 0.5 mg/kg), competitive antagonist of vasopressin pressor action (Simek et al. 1983) [(Pen²Tyr-(Me)²]LVP, 0.4 mg/kg) or rabbit anti-digoxin serum (0.5 ml/kg). The MAP changes were recorded 30 min before and 60 min after drug administration and expressed in % of initial MAP values. The data were evaluated by Student's t-test and Hotelling's t-test.

Blood pressure was increased in both age groups of DOCA-salt treated rats but hypertension was more pronounced in the young animals (Fig. 1). MAP of both young and adult DOCA-salt hypertensive rats was elevated due to the rise of systemic resistance (TPR). The difference in MAP between young and adult hypertensive rats could be attributed to a mild elevation of both CO and TPR in the younger group (Hotelling $T^2 = 15.6, F = 7.22, df 2/13, p<0.01$). The pulse pressure of young DOCA-salt hypertensive rats ($3.8±0.29$ kPa) was increased as compared to the controls ($4.5±0.36$ kPa) as well as to adult hypertensive rats ($4.3±0.78$ kPa). This was due to increased arterial rigidity (estimated from the pulse pressure/stroke volume ratio) in young but not in adult rats with DOCA-salt hypertension (Fig. 1). In agreement with the observation of Yamamoto et al. (1983) we also demonstrated the importance of systemic resistance elevation for the BP rise in adult DOCA-salt treated rats. On the other hand, the more

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**Fig. 1.** Haemodynamics of conscious normotensive [control], young and adult DOCA-salt hypertensive rats — blood pressure, cardiac output, systemic resistance and pulse pressure/stroke volume ratio (PP/SV). Data are means ± S.E.M. Asterisks indicate values significantly different ($p<0.05$) from the control value. Significant differences between young and adult rats are indicated above both corresponding columns.
pronounced hypertension of young animals was due to a mild increase of cardiac output and raised systemic resistance. A significant decrease of arterial compliance was found only in young but not in adult DOCA-salt hypertensive rats. This contrasts with the findings of Yamamoto et al. (1983), but Cox (1979) also reported decreased arterial compliance only in younger DOCA-salt hypertensive rats. Thus the haemodynamic pattern of age-dependent DOCA-salt hypertension resembled that of salt hypertension induced in homozygous Brattleboro rats (Zicha et al. 1982).

Fig. 2. The changes of mean arterial pressure (MAP) after acute blockade of the principal pressor systems in conscious control, young and adult DOCA-salt hypertensive rats. Full circles indicate significant MAP decrease in comparison with initial MAP value (p<0.05). For further explanation see text to Fig. 1.

The BP of control rats was decreased only by the administration of prazosin and captopril (Fig. 2). In young hypertensive animals, the BP fall was greatest after prazosin and antidiogoxin serum while the antagonist of VP pressor action lowered BP mildly and captopril was without effect. On the other hand, in adult hypertensive rats, both VP antagonist and captopril induced a moderate BP decrease but antidiogoxin serum had no effect (Fig. 2). Our findings confirm that RAS is less involved in the maintenance of BP in DOCA-salt hypertensive than in normotensive rats (Gavras et al. 1975, Mento et al. 1984). A moderate BP decrease was induced by captopril only in adult DOCA-salt hypertensive rats in which similar BP changes had already been reported (Miyamori et al. 1980). Different BP responses to captopril in young and adult DOCA-salt treated rats might reflect a different degree of RAS suppression (Karen et al. 1978), even if the role of other vasoactive systems (kinins, prostaglandins) cannot be fully excluded. The role of VP in the maintenance of DOCA-salt hypertension was recently reexamined by Mento et al. (1984) and Yamamoto et al. (1984). They concluded that the VP functions as an important back-up pressor system if plasma VP was sufficiently elevated. Our data indicate that VP participation depends on the age at which DOCA-salt treatment started. It remains to be determined whether greater BP response to VP blockade in adult rats was due to increased plasma VP level or due to abnormal cardiovascular reactivity to this hormone. α1-adrenoceptor blockade lowered BP in all groups. BP changes were most prominent in young DOCA-salt hypertensive rats in which BP was also dependent on the increased activity of a digoxin-like factor (Zicha et al. 1984). The acute blockade of principal pressor systems disclosed a different pattern of their participation in the maintenance of elevated BP in young and adult rats with DOCA-salt hypertension.
References


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