Effects of Enalapril on Cerebral Blood Flow and Its Autoregulation in Hypertensive Rats

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The lower limit of cerebral blood flow autoregulation was shifted to a higher blood pressure in rats with renal and spontaneous hypertension. Enalapril decreased blood pressure and vascular resistance in the brain, stabilized cerebral blood flow, and potentiated autoregulatory response of cerebral vessels to blood pressure drop.

Key Words: *enalapril; hypertension; cerebral blood flow; autoregulation*

Angiotensin-converting enzyme inhibitors are widely used for the treatment of hypertension [4] often accompanied by impairment of cerebral circulation. In light of this, the effects of angiotensin-converting enzyme inhibitors on cerebral blood flow and its autoregulation in arterial hypertension are of considerable interest. However, the data on these effects are discrepant [8-10].

MATERIALS AND METHODS

Experiments were performed on 24 albino rats weighing 200-250 g. The animals were narcotized with Nembutal (40 mg/kg, intraperitoneally) and artificially ventilated [1]. Cerebral blood flow velocity was measured by the hydrogen clearance method [3]. Systemic blood pressure (BP) was measured in the common carotid and femoral arteries by a mercury manometer. Renal hypertension was modeled as described previously [7]. Apart from animals with renal hypertension, spontaneously hypertensive Okamoto-Yamori rats were studied. Enalapril (EP) was administered intraperitoneally in doses of 0.5-1 mg/kg. Results were analyzed statistically [5].

RESULTS

In rats with renal hypertension, the initial BP, cerebral blood flow rate, and cerebrovascular resistance were 170.6±2.2 mm Hg, 66.5±6.3 ml/100 g/min, and 2.7±0.21 mm Hg/ml/100 g/min, respectively. Enalapril significantly decreased BP. This effect appeared within a few minutes postinjection and persisted to the end of the experiment (more than 90 min). Cerebral blood flow increased considerably and 1 h postinjection exceeded the initial level by 20%. Cerebrovascular resistance decreased progressively to 50% below the initial level to the end of the experiment (Fig. 1, *a*).

In spontaneously hypertensive rats, EP led to a stable decrease in BP (Fig. 1, *b*). This effect attained the maximum (a 28.9±2% decrease) 60-70 min postinjection, then decreased, but persisted to the end of observations. In six of seven experiments, cerebral blood flow increased by 12-14% and in only 1 experiment decreased by 18%. Cerebrovascular resistance decreased in all experiments, especially 60-70 min postinjection (by 35%).

Thus, EP reduced BP and increased cerebral blood flow in hypertensive rats irrespective on the nature of hypertension. Hypotensive and cerebrovascular effects of EP were more pronounced in renal than in spontaneous hypertension.

Control studies of cerebral blood flow autoregulation in rats with renal hypertension (without administration of EP) showed that a decrease in BP to 100 mm Hg did not affect significantly the cerebral circulation due to a considerable decrease in cerebrovascular resistance (by 40%) and high coefficient of autoregulation (0.88). A decrease in BP to 60-70 mm

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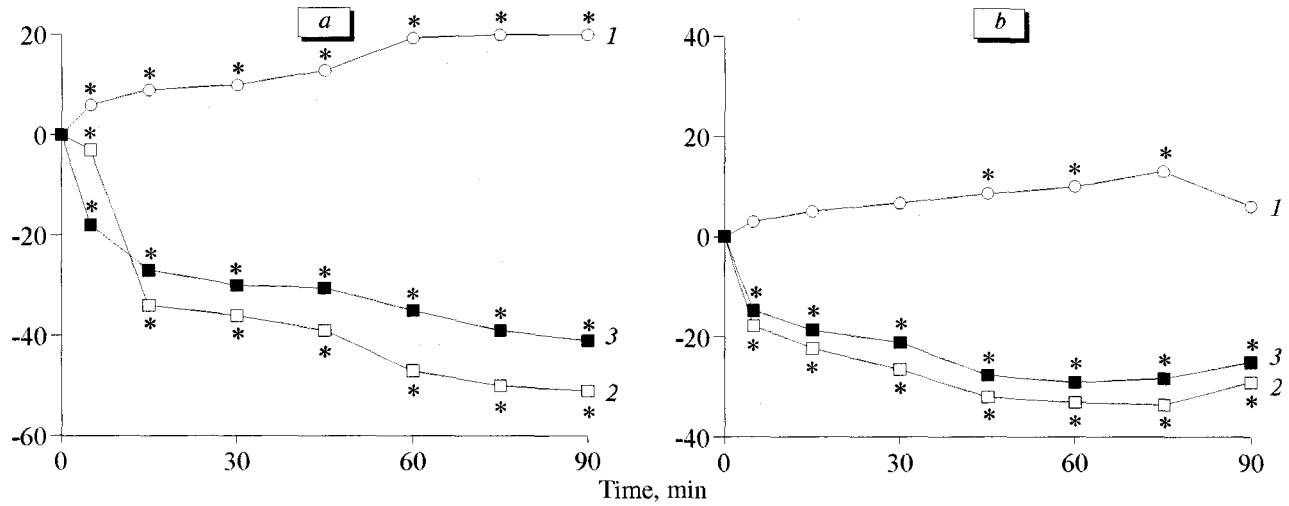

Fig. 1. Cerebral blood flow (*1*), cerebrovascular resistance (*2*), and systemic blood pressure (*3*) in animals with renal hypertension (*a*) and spontaneously hypertensive rats (*b*) administered with enalapril. Ordinate: % of initial level. Here and in Fig. 2: *$p<0.05$ compared with initial level (0%).

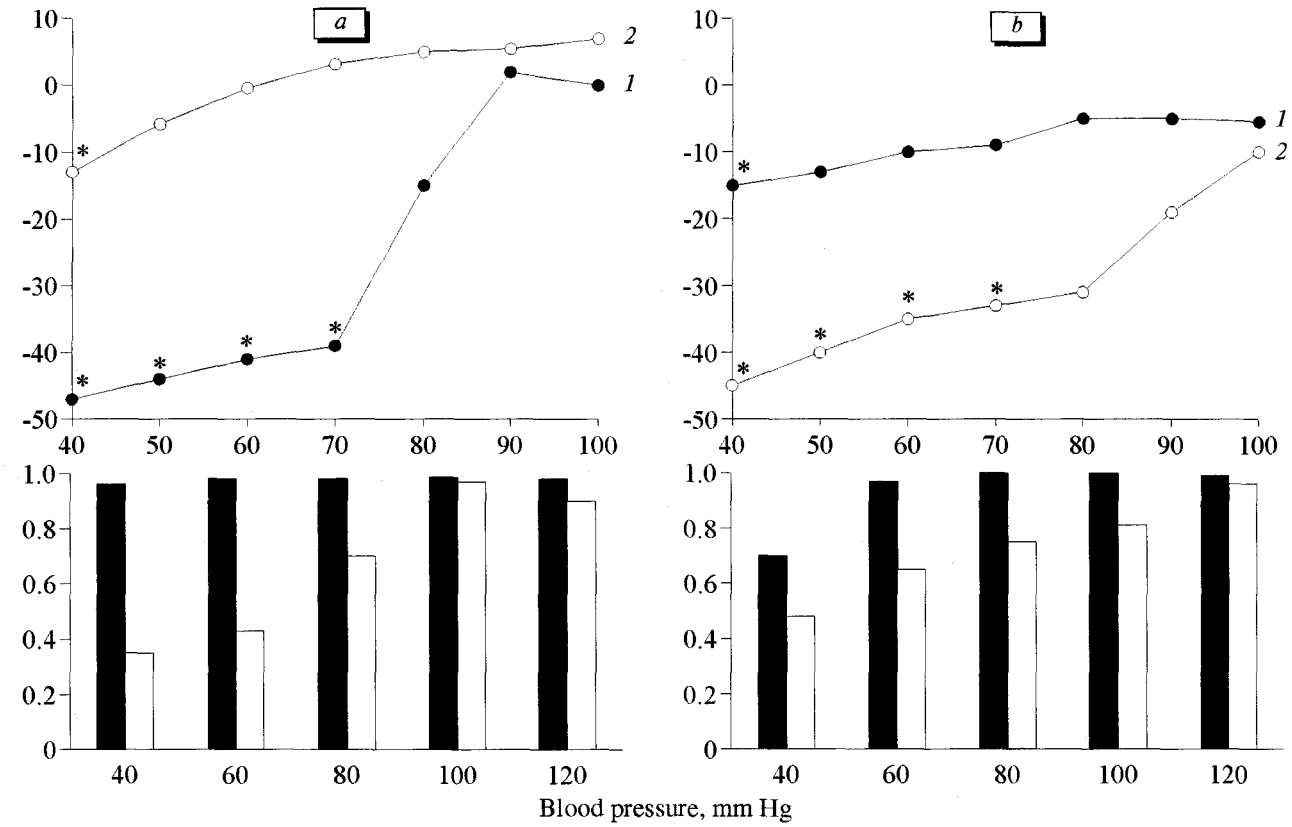

Fig. 2. Cerebral blood flow autoregulation during a decrease in blood pressure in animals with renal hypertension (*a*) and spontaneously hypertensive rats (*b*) under control conditions (*1*, light bars) and after administration of enalapril (*2*, dark bars). Ordinate: cerebral blood flow, % of initial level (upper charts); and coefficient of autoregulation (lower charts).

Hg was accompanied by a 35-40% decrease in cerebral blood flow.

In spontaneously hypertensive rats, a drop of BP to 100 mm Hg was accompanied by a considerable decrease in cerebral blood flow (by 25%). Cerebral blood flow decreased by 30-35% with a decrease in BP to 60-70 mm Hg. Thus, the lower limit of cerebral blood flow autoregulation in hypertensive rats was shifted to higher BP levels, while in normotensive rats this limit corresponded to 50 mm Hg.

In hypertensive rats, EP potentiated autoregulatory reactions of cerebral vessels to BP drop (Fig. 2).

In rats with renal hypertension (Fig. 2, *a*), a decrease in BP to 80 mm Hg was accompanied by a 7-9% increase in cerebral blood flow and a 56% decrease in cerebrovascular resistance, and no significant changes in cerebral blood flow were observed at BP 60 mm Hg. Cerebral blood flow decreased significantly only after BP dropped to 40 mm Hg. The coefficient of autoregulation was high (0.9) at all BP levels studied. Similar autoregulatory reactions to BP drop were observed in spontaneously hypertensive rats (Fig. 2, *b*).

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