Effect of Lozartan on Postischemic Cerebral Blood Flow in Normotensive Rats

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Transient cerebral ischemia considerably impaired autoregulation of cerebral blood flow in rats. Lozartan reliably reduced blood pressure and restored the autoregulatory vascular response to hypotension.

Key Words: *lozartan; cerebral ischemia; cerebral blood flow*

In recent years, clinicians have given numerous positive reference to angiotensin antagonists (lozartan and others) in the treatment of arterial hypertension, ischemic heart diseases, and cardiac failure [2-5]. These diseases are often accompanied by ischemic impairment of cerebral circulation. However, the state of cerebral blood flow (CBF) after the blockade of angiotensin receptors remains little studied.

MATERIALS AND METHODS

Acute experiments were carried out on 20 albino rats (200-300 g) anesthetized with Nembutal (40-50 mg/kg, intraperitoneally) and artificially ventilated. The volume rate of CBF was measured by the hydrogen clearance technique [1]. Systemic blood pressure (BP) was measured by a mercury manometer. Graded hemmorage followed autotransfusion was performed to investigate the autoregulatory response of cerebral vessels to hypotension. Cerebral ischemia was produced by 12-min occlusion of the carotid artery for 12 min until BP dropped to 30-40 mm Hg. The experimental group received intraperitoneal lozartan (3-5 mg/kg in 0.5-0.7 ml), while the control rats were injected with an equal volume of saline. The data were processed using Student's t test at a significance level $p<0.05$.

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RESULTS

Unstable CBF with the predominance of phasic changes and considerable impairment of autoregulation was observed in the control rats for 1.5-2 h after recirculation and postischemic BP recovery.

Postischemic BP in lozartan-treated animals was 20-30% below the initial level. The hypotensive effect appeared 3-5 min postinjection and persisted over 90 min. Lozartan-induced general hypotension was accompanied by an unstable 20-30% decrease in the vas-

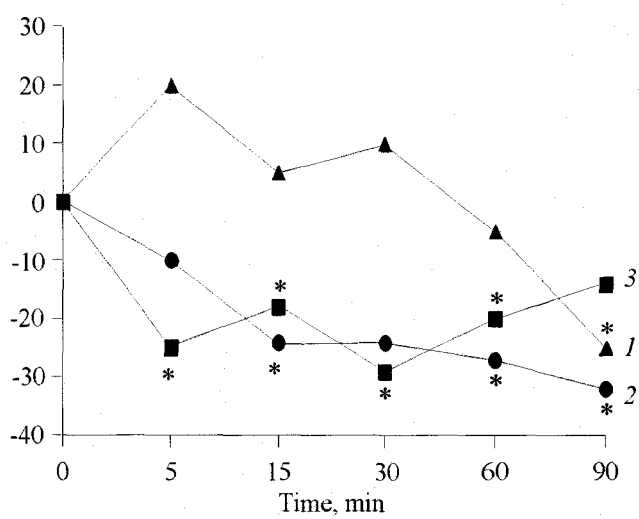

Fig. 1. Effect of lozartan on cerebral blood flow (*1*), arterial pressure (*2*), and vascular resistance (*3*) in the postischemic period. Ordinate: % of initial values. Here and on Fig. 2: *$p<0.05$ in comparison with the baseline.

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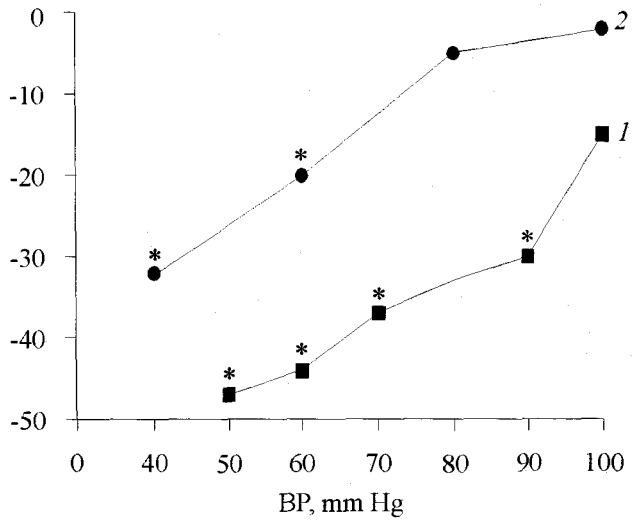

Fig. 2. Autoregulation of cerebral blood flow under conditions of graded reduction of blood pressure (BP) in control (*1*) and lozartan-treated (*2*) animals after cerebral ischemia. Ordinate: changes in blood flow, % of initial value.

cular resistance, as a result, CBF first slightly increased and only 40-60 min later significantly (by 26.9± 5.2%) decreased (Fig. 1). Lozartan improved autoregulatory vascular reactions. Thus, BP drop to 80 mm Hg in the postischemic period caused a 30-40% decrease in CBF in the control animals, but produced no significant changes in CBF of lozartan-treated animals (Fig. 2). It is likely, that angiotensin participates in the autoregulatory vasoconstrictor response of brain vessels to BP increase, and the blockade of angiotensin receptors under conditions of low BP promotes the recovery of CBF autoregulation in the postischemic period.

REFERENCES

1. I. T. Demchenko, *Fiziol. Zh. SSSR*, **61**, No. 1, 178-183 (1981).
2. L. I. Ol'binskaya and Yu. A. Morozov, *Eksp. Klin. Farmakol.*, **59**, No. 5, 76-80 (1996).
3. E. P. Svischenko, *Ukr.Kardiol. Zh.*, Nos. 5-6, 15-22 (1996).
4. C. R. Conti, *Clin. Cardiol.*, No. 6, 1-2 (1995).
5. M. J. Oliverio and T. M. Coffmon, *Ibid.*, **20**, No. 1, 3-6 (1997).