BIOPHYSICS AND BIOCHEMISTRY

Mechanism of Arterial Pressure Elevation in Calcium Deficiency

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UDC 612.14+616.12-008.331.1+470.23

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 117, № 5, pp. 476-477, May, 1994
Original article submitted August 3, 1993

We compared the effects of intravenous administration of the calcium-dependent hypertensive factor from the plasma of patients with essential hypertension and of a synthetic heptapeptide with hypertensive activity. Both substances prove to induce prolonged and pronounced elevation of arterial blood pressure.

Key Words: *arterial hypertension; exogenous calcium; parathyroid hypertensive factor; catecholamines*

Previously we showed that in WKY rats deficiency of exogenous calcium induces the development of sustained arterial hypertension (AH), pronounced alterations in the function of the erythrocyte ion transport systems, and expression of the hypertensive factor [1]. This factor is similar to the parathyroid hypertensive factor (PHF) discovered by Pang *et al.* in the plasma of spontaneously hypertensive rats and some patients with essential hypertension [2,3].

A peptide simulating *in vitro* all hemodynamic effects of PHF was synthesized at the Institute of High-Purity Preparations by Drs. S. V. Kulikov and A. P. Eryukhina.

In this study we compared the hypertensive activity of this peptide and the plasma of patients with essential hypertension.

MATERIALS AND METHODS

Experiments were performed on male WKY rats weighing 258-280 g narcotized with nembutal (45 mg/kg). Arterial pressure (AP) was monitored with the aid of a catheter inserted via the femoral artery. Plasma was injected intravenously in a dose of 5 ml/kg body weight. For removal of the known vasopressors (catecholamine, vasopressin, and angiotensin) plasma was dialyzed via a membrane nonpermeable to molecules with a molecular weight of more than 1000 D.

The minimal effective dose of the peptide was 20 μg/kg body weight. The peptide was administered in a dose of 40 μg/kg.

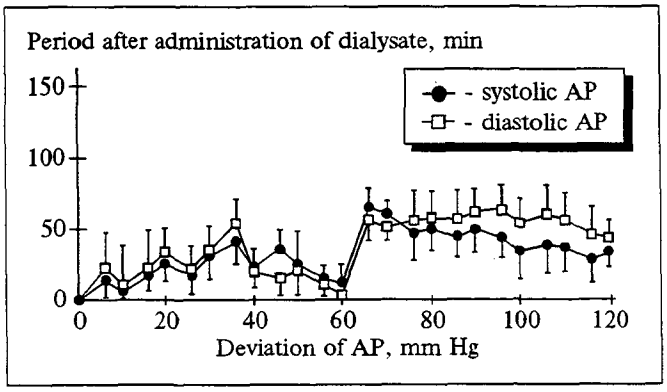

Fig. 1. Dynamics of AP after administration of dialysate of plasma from patients with essential hypertension and epinephrine to WKY rats ($n = 15$)

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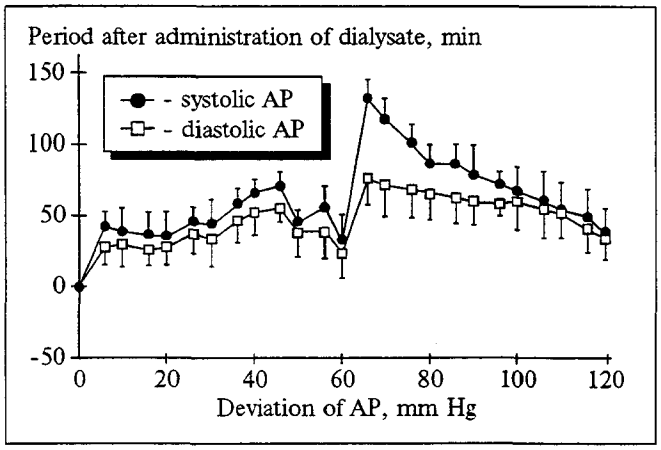

Fig. 2. Dynamics of AP after administration of peptide and epinephrine to WKY rats ($n = 12$)

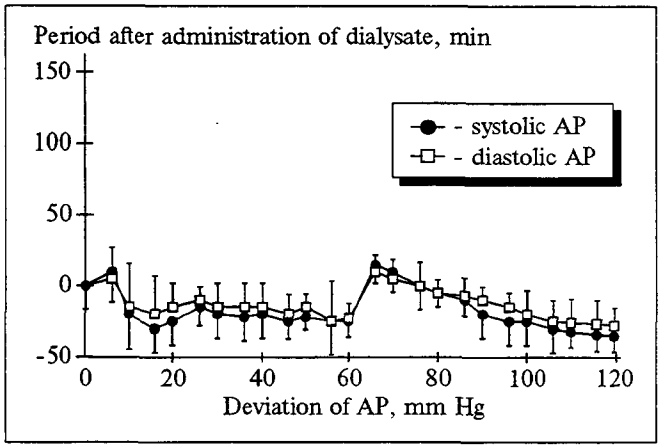

Fig. 3. Dynamics of AP after administration of physiological saline and epinephrine to WKY rats ($n = 12$)

For a study of the interaction of this peptide with catecholamine epinephrine (0.8 mg/kg) was injected intraperitoneally to all the animals at the 60th min of the experiment.

For evaluation of the hemodynamic effect elicited by injection of a considerable volume of fluid (8-10% of the circulating blood volume) in some animals dialysate or peptide solution was replaced by physiological saline (the control series).

The data were statistically analyzed with the use of the nonparametric Wilcoxon-Mann-Whitney test.

RESULTS

Administration of the dialysate and peptide induced a pronounced (40% of the initial level) and prolonged (up to 60 min) elevation of AP, and potentiated and prolonged the pressor effect of epinephrine. The elevation of AP was 100-150% of the initial level and lasted for 40-45 min (Figs. 1 and 2).

In control series (Fig. 3) the pressor effect was weak (not more than 10% of the initial level) and short (less than 10 min). It was followed by a moderate lowering of AP. Under these experimental conditions epinephrine produced a short-term (not more than 15 min) and moderate (15-20% of the initial) elevation of AP. Thus, intravenous administration of the synthetic peptide simulated the hemodynamic effects of PHF.

The results obtained suggest that the calcium-dependent hypertensive factor has an important role in the pathogenesis of primary AH. This factor, as well as that of the synthetic peptide, may exert its effect both via a direct influence on vascular tone and by increasing the sensitivity of the vascular wall to the influence of other vasopressors, specifically catecholamines.

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