Specific Response to Adrenaline in Arterial Hypertension Induced by Exogenous Calcium Deficiency

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Injection of a synthetic analog of parathyroid hypertensive factor to WKY rats considerably increases and prolongs pressor response to adrenaline. Synthetic analog injected after adrenaline induces a short-term (3-4 min) and potent (to 250%) rise of arterial pressure. Each subsequent injection of the synthetic analog induces a less pronounced in the amplitude and duration pressor response. The α-adrenoblocker phentolamine completely abolishes the effects of the parathyroid hypertensive factor analog.

Key Words: *regulation of blood pressure; arterial hypertension; parathyroid hypertensive factor; catecholamines; α-adrenoblockers*

Parathyroid hypertensive factor (PHF) plays a key role in the pathogenesis of arterial hypertension caused by deficiency of exogenous calcium [1,3,5-7]. Intravenous injection of PHF to normotensive animals induces a pronounced (35-40% above the initial level) and long-term (more than 40 min) rise of arterial pressure (AP) [1]. Taking into account the important role of catecholamines in the regulation of vascular tone and AP, we studied *in vivo* the interaction of adrenaline and a synthetic analog of PHF (APHF) [4].

The present study was aimed at verifying the assumption that catecholamines can mediate physiological effects of PHF. To this end we investigated the effect of α-adrenoblockers on the parameters of pressor response induced by injection of APHF.

MATERIALS AND METHODS

Experiments were carried out on male WKY rats (250-280 g) narcotized with Nembutal (45 mg/kg). Arterial pressure was measured through a catheter inserted into the femoral artery. APHF was synthesized by Dr. S. V. Kulikov (Laboratory of Analytical Biochemistry, Institute of Extrapure Biological Preparations, St. Petersburg). The preparation was injected intravenously in a dose of 40 μg/kg body weight. For evaluation of the modulating effect of the test factor on the pressor response to catecholamines, 60 min after injection of APHF the animals (n=21) received intraperitoneal injection of adrenaline (0.8 mg/kg); 20, 30, and 40 min after that a bolus injection of 40 μg/kg APHF was given to some rats (n=14).

In 7 experiments the α-adrenoblocker phentolamine in a dose of 0.5 mg/kg was intravenously injected prior to PHF.

In the control series (n=7), an equivalent volume of physiological saline was injected instead of APHF; adrenaline was injected in the same doses and according to the same scheme.

The data were processed statistically using nonparametric Mann—Whitney test.

RESULTS

Injection of APHF induced a sharp rise of AP, which attained the maximum by the 40th min postinjection

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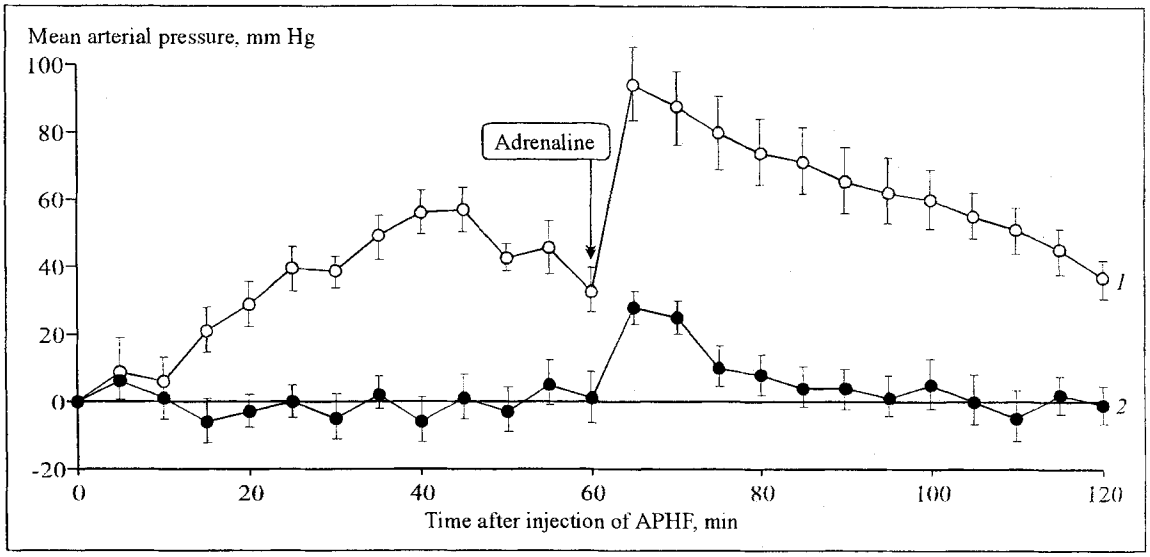

Fig. 1. Changes in arterial pressure in consecutive injection of APHF and adrenaline (*1*, *n*=21) and physiological saline and adrenaline (*2*, *n*=7). Injection of adrenaline is indicated with an arrow.

(Fig. 1, *1*). Adrenaline induced a sustained increase in AP, which exceeded by its amplitude and duration the response to adrenaline injected after physiological saline (Fig. 1, *2*). Repeated injection of APHF caused a transient (3-4 min) and pronounced (to 250%) rise of AP. The amplitude and duration of the pressor

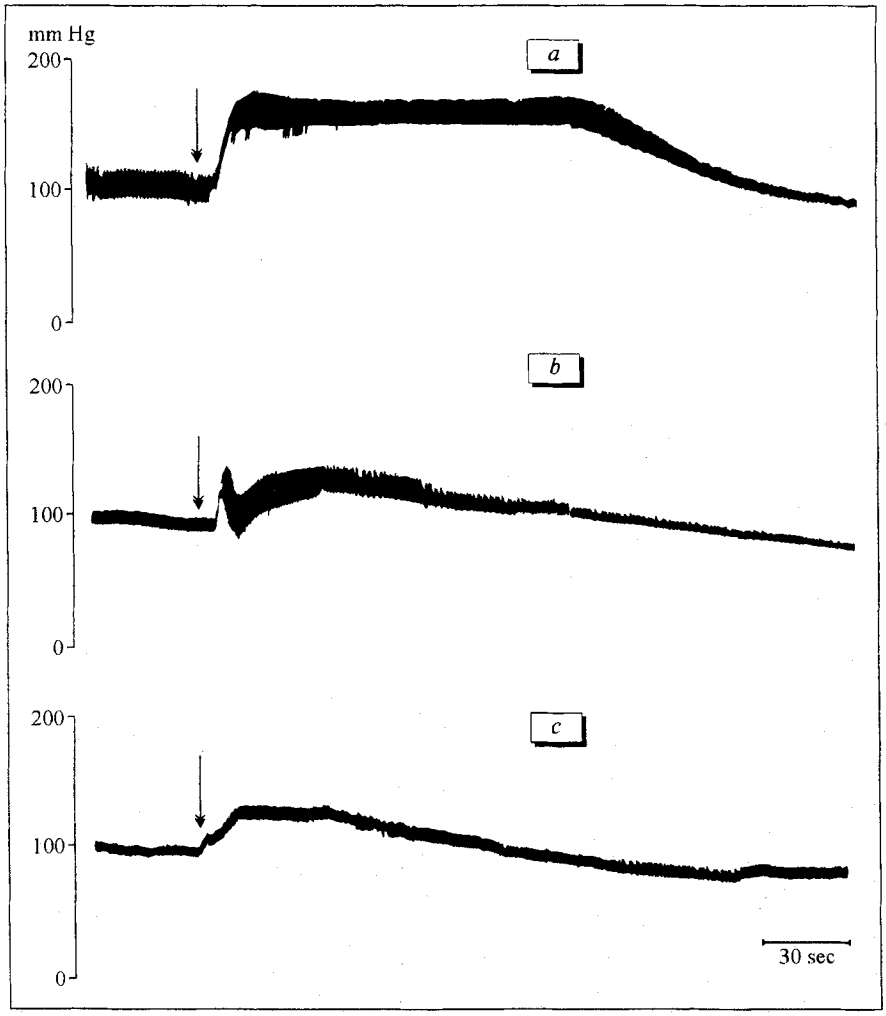

Fig. 2. Effect of repeated injection of APHF on arterial pressure in rat. Injection of APHF is indicated with an arrow.

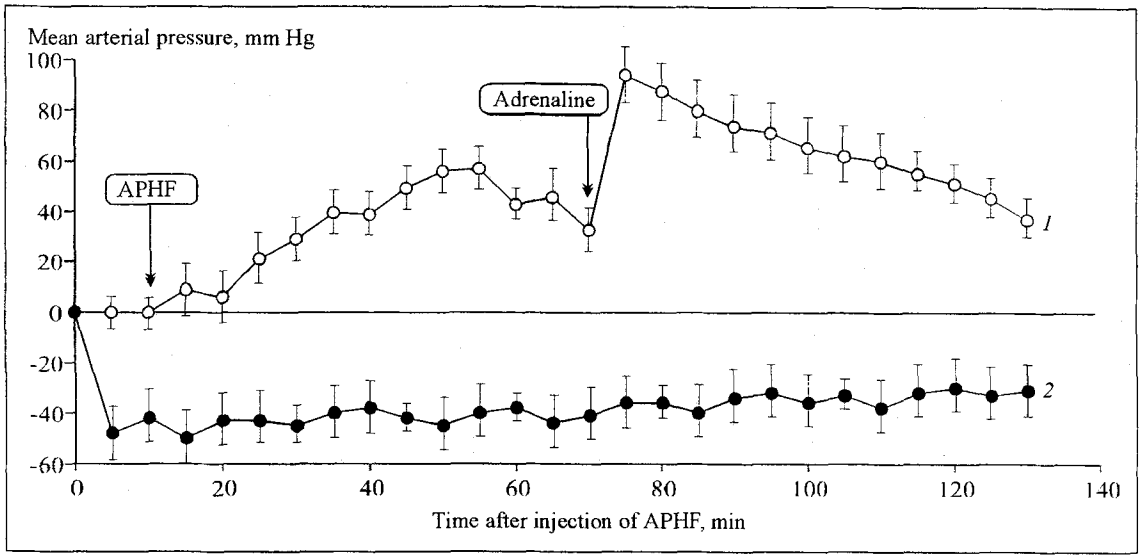

Fig. 3. Changes in arterial pressure after consecutive administration of phentolamine, APHF, and adrenaline (*1*, *n*=7) and physiological saline, APHF, and adrenaline (*2*, *n*=7).

response to each subsequent injection of APHF decayed from injection to injection (Fig. 2).

Preliminary injection of phentolamine completely abolished the pressor effect of both initial and repeated APHF injections (Fig. 3).

Thus, preliminary injection of APHF considerably potentiated and prolonged the pressor response to adrenaline.

The inhibiting effect of α-adrenoblockers suggests that the sympathoadrenal system plays an important role in the development of the pressor response to APHF injection.

From our point of view, marked differences in the reactions to the first and subsequent injections of APHF are very important for understanding the role of the sympathoadrenal system in the pathogenesis of arterial hypertension under conditions of exogenous calcium deficiency.

These data suggest that PHF, on the one hand, can increase sensitivity to exogenous catecholamines, and possibly inhibits their catabolism, which prolongs and potentiates the pressor effect. On the other hand, pressor effect of PHF is to a great extent mediated by its effect on the adrenergic system.

This suggestion is confirmed by the fact that similar disturbances in the functioning of the sympathoadrenal system were observed in spontaneously hypertensive rats (considerably elevated sensitivity to catecholamines) [2]. Rapid tachyphylaxis in repeated administration of APHF against the background of adrenaline suggests that the test factor inhibits reuptake of catecholamines in synapses (probably, via blockade of α_1-adrenoreceptors).

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