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EFFECT OF INTERLEUKIN-2 ON EXPERIMENTAL EMOTIONAL HYPERTENSION

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KEY WORDS: arterial hypertension; interleukin-2; immune system

The role of immune disturbances in the development of various forms of experimental hypertension has been discussed in recent years. For instance, underdevelopment of the thymus, a deficiency of T lymphocytes, and the presence of thymocytotoxic autoantibodies have been discovered in spontaneously hypertensive rats [10, 11]. The use of immunocorrective procedures (injection of thymus tissue extracts, of antithymic serum, or of immunosuppressive preparations) in this model of hypertension has been shown to have an antihypertensive action [5-7]. A hypotensive effect of immunosuppressive therapy has been found in New Zealand Black mice with spontaneous hypertension [9]. It has been shown that the development of hypertension in hypertensive Lyon rats can be prevented by neonatal thymectomy [4]. There is also evidence of changes taking place in the immune system in human subjects with essential arterial hypertension: raised blood levels of immunoglobulins, autoantibodies to vessel walls and to smooth muscle cells, and deposition of immunoglobulins in the renal arteries [3, 6]. In connection with the facts described above, and also since in experimental models of hypertension the clearest manifestation is weakening of T-cell functions, the study of the role of the T-cell growth factor interleukin-2 (IL-2), a powerful mediator of the immune system, in the development of hypertension is particularly interesting.

The aim of this investigation was to study the effect of human recombinant IL-2 on the course of experimental arterial hypertension.

EXPERIMENTAL METHOD

Chronic experiments were carried out on 20 noninbred male and female albino rats aged 5-7 months and weighing 200-260 g. A model of emotional hypertension was created in a "conflict situation" by daily (for 1 month) exposure to a physical stress factor, namely electrodermal stimulation of the limbs for 1 h by a pulsed current (10-100 V) on stochastic mode, and allowing for individual reactivity of the animals [1]. The systolic blood pressure (BP) was recorded by an electroplethysmographic method in the caudal artery of the rats, using a mercury manometer, an

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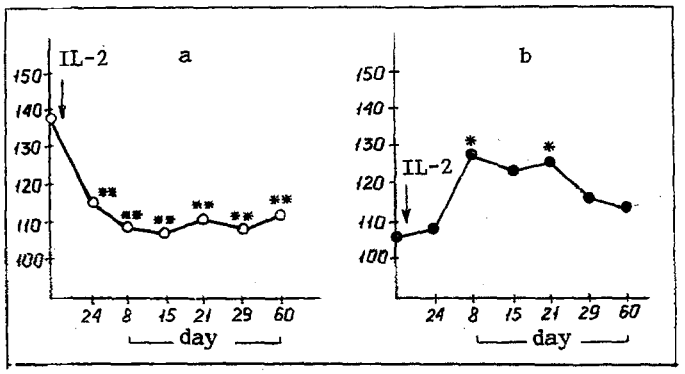

Fig. 1. Effect of injection of IL-2 on systolic BP of rats with emotional hypertension (a) and normotensive rats (b). Abscissa, time after injection of IL-2 (in hours and days); ordinate, systolic BP (in mm Hg). *p < 0.05, **p < 0.01. Significance of differences in systolic BP levels compared with initial level.

"IM-789" indicator, and a rubber occlusion cuff [2]. The group of animals with experimental emotional hypertension consisted of 15 rats whose systolic BP was 139.7 ± 2.8 mm Hg. The control group consisted of five normotensive rats with systolic BP of 105.0 ± 3.5 mm Hg. A single subcutaneous injection of human recombinant IL-2 (from L'vov Research Institute of Hematology and Blood Transfusion) was given in the region of the hind limb in a dose of $5 \cdot 10^3$ U/kg body weight. The volume injected did not exceed 0.3 ml. The systolic BP was recorded 2 h after injection of the preparation and weekly thereafter for 3 months.

EXPERIMENTAL RESULTS

Analysis of the results indicates a fall of systolic BP in the group of hypertensive rats under the influence of human recombinant IL-2 (Fig. 1).

For instance, only 2 h after injection of the preparation the systolic BP was significantly lower in 12 of the 15 rats (80%) of that group. In one rat BP was unchanged, and in two rats it rose a little. For the group as a whole, 2 h after injection of IL-2 a highly significant ($p < 0.01$) fall of the systolic BP was observed to 115.7 ± 3.7 mm Hg. During the following week BP continued to fall, and by the 8th day of observation the mean BP for the group was 109.4 ± 3.4 mm Hg ($p < 0.01$) compared with the initial level. By the 15th day, the systolic BP in all 15 rats had fallen below its initial values, and its mean level for the group was 107.9 ± 2.8 mm Hg ($p < 0.01$). Subsequent observations showed that the systolic BP of the hypertensive rats remained at a consistently low level for 2.5 months after administration of IL-2.

It is a noteworthy fact that the higher the initial BP in rats with hypertension, the greater its decrease after IL-2 administration.

In the group of normotensive animals injection of IL-2 (after minor fluctuations of BP in different directions during the first hours after injection of IL-2) caused a significant rise of BP, which reached its peak level toward the 8th day (Fig. 1). Later BP fell gradually, and by the 29th day after injection of IL-2 and for the next 2 months thereafter it did not differ significantly from the mean BP of rats of the same group before IL-2 injection.

The results indicate a marked and prolonged antihypertensive action of IL-2 in rats with emotional hypertension. This may indicate a substantial disturbance of IL-2 production in this model of hypertension.

The results of this investigation agree with previous data [12] on the antihypertensive effect of IL-2 in spontaneously hypertensive rats. Meanwhile, in the previous study [8], a hypotensive action of IL-2 was not found in spontaneously hypertensive rats. This difference in the results of experiments conducted by different workers on the same model of hypertension may be attributed, in our opinion, to the considerable difference in the doses of IL-2 used in the two studies.

There are reports that IL-2 is effective not in all models of hypertension. For instance, no hypotensive action of IL-2 could be found on a model of renal hypertension [12]. In this case it is admissible to postulate a specific effect of IL-2 in the essential form of arterial hypertension.

Thus further proof has been obtained of the role of the immune system in the development of experimental hypertension and also, perhaps, of essential hypertension in man.

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IMMUNOCORRECTION IN DESTRUCTIVE PANCREATITIS

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A factor in the pathogenesis of acute pancreatitis [8-10] is a marked disturbance of hemostasis, caused initially by enzymic and later by suppurative toxicosis. For that reason methods of detoxication used in the combined treatment of acute pancreatitis must be regarded as pathogenetically justified. In recent years interest of research workers in the study of the possible role of immunocorrective mechanisms in the pathogenesis of acute pancreatitis has increased. The aim of this investigation is a comparative study of the immunocorrective influence of modern methods of detoxication in acute destructive pancreatitis.

EXPERIMENTAL METHOD

Experiments were carried out on 40 male mongrel dogs weighing 13-15 kg. The model of destructive pancreatitis followed that described in [1]. Acute pancreatitis was treated by hemoperfusion (HP), plasmapheresis (PPH),

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