EFFECT OF HEPARIN ON THE GENERAL ADAPTATION SYNDROME

B. P. Lukashin, Ya. V. Agapov,
O. D. Bakhtybaev, and A. S. Goidenko

UDC 616.45-001.1/.3-092:612.115.35

The alarm response of the general adaptation syndrome in rats was inhibited by administration of heparin. The results may be associated with increased resistance of the tissues to stressors because of reversible inhibition of enzymes of the respiratory-energy cycle in the cells.

KEY WORDS: heparin; general adaptation syndrome; alarm response.

Besides its anticoagulant function, heparin also plays a no less important role as a regulator of enzyme activity [1, 2, 7]. Heparin inhibits many of the effects of ACTH and glucocorticoids [8, 11, 13]. Evidence has also been obtained that heparin binds ACTH and adrenocortical hormones in vivo and in vitro [7, 10, 12].

It was accordingly decided to study the effect of heparin on the development of the general adaptation syndrome (GAS).

EXPERIMENTAL METHOD

Experiments were carried out on 216 noninbred albino rats weighing 170-230 g. The GAS was induced by immobilizing the animals for 24 h [4], or by subcutaneous injection of 1-2 ml of 1% atropine solution or 4% formalin solution (0.1 ml/100 g body weight twice a day for 2 days). During immobilization of the rats of the experimental group, heparin (Richter) was injected in a dose of 750 units/kg 15 min before and 4 h after fixation. Animals receiving injections of atropine and formalin were given an injection of heparin once a day in doses of 250-1000 units/kg. The animals of the control group received intraperitoneal injections of physiological saline at the same times. The effect of heparin was judged from changes in the typical triad of the alarm response [4].

EXPERIMENTAL RESULTS AND DISCUSSION

Atrophy of the thymus, an increase in weight of the adrenals, and hemorrhages into the stomach were found after 24 h in the immobilized animals. Injection of heparin reduced the severity of the alarm response (Table 1). After injection of 2 ml atropine, heparin (750 units/kg) had no significant effect on the first phase of the GAS. If a smaller dose of atropine was given heparin had a significant effect on the change in weight of the thymus and adrenals (Fig. 1). The results explain the absence of effect of heparin on the weight of the thymus in results published previously [5, 6] on the grounds that the action of the stressor was evidently too strong. The experiments in which formalin was injected showed that the decrease in weight of the thymus diminished progressively as the dose of heparin was increased from 250 to 1000 units/kg (Fig. 2). Hence, whatever method was used to produce stress in the rats, heparin diminished the alarm response in them.

The tissue mast cells (heparinocytes) and basophilic leukocytes of the peripheral blood are known to be sources of heparin in the body. Under the influence of various unfavorable factors the pituitary-adrenal

Department of Normal Physiology, S. M. Kirov Military Medical Academy, Leningrad. (Presented by Academician V. N. Chernigovskii.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 80, No. 9, pp. 16-18, September, 1975. Original article submitted October 21, 1974.

TABLE 1. Effect of Heparin on Alarm Response in Rats Immobilized for 24 h

Type of experiment	Number of animals	Number of animals with hemorrhage into stomach	Weight of organs (in mg/100 g body weight)	
			thymus	adrenals
Intact animals	20	—	272±9	24,0±0,8
Immobilization + physiological saline	30	18	171±10	40,2±1,1
Immobilization + heparin	30	10*	217±15*	31,5±0,8*

*Differences significant when $P < 0.05$.

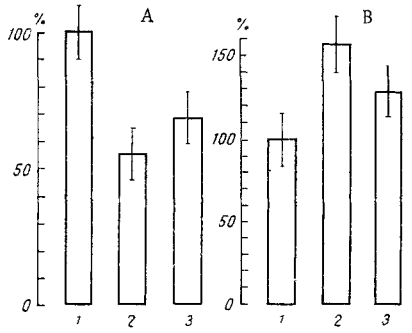

Fig. 1

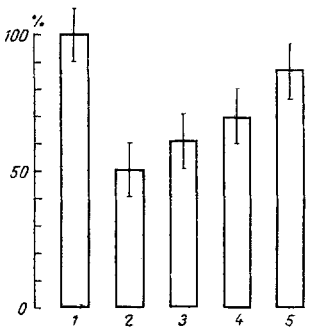

Fig. 2

Fig. 1. Effect of heparin on changes in weight of the thymus (A) and adrenals (B) in rats receiving atropine daily for 2 days: 1) intact animals; 2) atropine (1 ml) + physiological saline; 3) atropine (1 ml) + heparin (750 units/kg).

Fig. 2. Effect of heparin on changes in weight of the thymus in rats receiving formalin daily for 2 days: 1) intact animals; 2) formalin + physiological saline; 3) formalin + heparin (250 units/kg); 4) formalin + heparin (740 units/kg); 5) formalin + heparin (1000 units/kg).

system is activated; this, in turn, causes disintegration of the mast cells [1, 9]. Through the feedback principle, this latter factor evidently helps the body to control the intensity of the GAS.

These results can be regarded as a consequence of inhibition of the adrenal cortex or binding of glucocorticoids by heparin. However, it must be remembered that heparin increases the resistance of cells of the parenchymatous organs to the action of extremal factors, by inducing "preventive inhibition" in them as a result of reversible blocking of the enzymes of the respiratory-energy cycle [3]. In that case, inhibition of the alarm response could arise through weakening of the degree of injury, i.e., through an appropriate decrease in the dose of the stressor. Summation of the two mechanisms of heparin action is a possibility that cannot be ruled out.

These results indicate fresh perspectives in the study of adaptation and the role of the mast cells in the maintenance of homeostasis.

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