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IMMUNOCORRECTIVE THERAPY OF THE TRAUMATIC SYNDROME

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Mechanical trauma leads to marked changes in the immune system which can be interpreted as inhibition of immunobiological defense [1, 5, 9, 10, 13]. This has provided the basis for the inclusion of immunostimulators of the thymalin type in the combined treatment of such patients, with good therapeutic effects [4]. Detailed studies in experiments on animals have shown that the functional activity of the immune system changes in phases during the course of traumatic shock and the post-traumatic period [2], and this must be taken into account when different immunomodulators are prescribed. In turn, estimation of the effectiveness of immunomodulators can provide definite information for the elucidation of the mechanisms of immunologic changes in the traumatic syndrome.

The aim of this investigation was to study the effectiveness of the combined use of thymalin and interferon for the prevention and treatment of the traumatic syndrome in rats. The survival rate was chosen as the criterion of efficacy, and the mechanisms of this phenomenon were assessed at the level of immunobiological defense factors.

EXPERIMENTAL METHOD

Traumatic shock was produced by Cannon's method in male Wistar rats weighing 200-250 g [3]. The development of a post-traumatic syndrome in the course of traumatic shock was studied until the 7th day. The survival rate, in per cent, was determined from the number of surviving animals on the 7th day. The animals as a whole were divided into four groups with six or seven rats in each group: 1 (basic) — traumatized animals treated with thymalin combined with interferon; 2, control — traumatized, untreated animals; 3) control — uninjured animals receiving thymalin and interferon; 4) traumatized animals receiving thymalin alone. The scheme of administration of the immunomodulators was as follows: 1 h after trauma thymalin was injected intramuscularly in a dose of 0.02 mg/100 g body weight, after which thymalin was given in the same dose together with interferon (10 U/100 g intramuscularly) for 6 days. On the 7th day the animals were decapitated. The functional state of the immune system was estimated by means of the following parameters: the percentage of T lymphocytes in the rosette-forming test with sheep's red blood cells, the number of theophylline-sensitive T lymphocytes (TS-lymphocytes) in the test with treatment of T-RFC with theophylline, the level of circulating immune complexes (CIC) by precipitation in a 3.76% solution of polyethylene-glycol, and the serum lysozyme activity, by a nephelometric method [6].

EXPERIMENTAL RESULTS

Combined administration of thymalin and interferon to the injured animals give a marked increase of survival rate during the first 7 days of the traumatic syndrome. Among injured animals of group 1 receiving the immunomodulators (55 rats) the mortality was 13.3%, compared

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TABLE 1. Parameters of Immunologic Reactivity in Rats on 7th Day of Post-traumatic Period

Group of animals	Leukocytes (• 10^9/liter)	T-RFC, %	Suppressor T cells, %	CIC, units	Lysozyme, units
Intact rats	8,3±0,42	50,0±2,9	13,2±3,46	50,0±7,2	7,4±0,4
1	7,5±0,3	38,0±2,8	9,0±2,36	100,0±6,0	4,0±0,72
p		0,02		0,002	0,01
2	9,2±0,5	25,0±2,0	0	35,0±5,0	2,0±0,2
p		0,03	0,01		0,002
3	8,1±0,96	41,0±2,6	3,0±1,2	38,0±3,8	3,0±0,9
p			0,03		0,007

with 27.2% among the animals (45 rats) of group 2. Analysis of the separate immunologic parameters revealed changes which could lie at the basis of the mechanisms of increased resistance of the animals receiving combined treatment with thymalin and interferon. On the 7th day of the post-traumatic syndrome the untreated rats (Table 1) had no marked changes in their total peripheral blood leukocyte count, but showed a sharp decrease (to 25%) in the number of T lymphocytes, loss of sensitivity of the T lymphocytes in vitro to theophylline (TS lymphocytes 0%), a considerable decrease in serum lysozyme activity, and a tendency for the CIC level to fall. Despite depression of the T-cell component recorded in the early phases of development of the traumatic syndrome [2], and persisting on the 7th day of its development, treatment of these animals with thymalin alone had no marked effect on the survival rate of the animals (group 4). This may be evidence of the complex genesis of the fall in the T lymphocyte level in the traumatic syndrome, connected both with a stress-induced redistribution of the immune cells and with a change in their functional properties.

Combined treatment of the injured rats with thymalin and interferon led to an increase in the survival rate, accompanied by changes in virtually all the immunologic parameters studied, as reflected in the absence of any marked fall of the T lymphocyte level (their number fell only to 38%), preservation of sensitivity of the T lymphocytes to theophylline in vitro (TS lymphocytes 9%), a less marked fall of the serum lysozyme activity (4 units), and a twofold increase in the CIC level. The use of a combination of thymalin and interferon with intact animals was reflected only in the number of TS lymphocytes and the serum lysozyme activity (Table 1).

Infliction of severe mechanical trauma on the animal thus led to marked changes in its immune status, manifested on the 7th day of the post-traumatic syndrome by considerable depression of the T-cell component of immunologic reactivity. Considering the difficulty of interpretation of the theophylline test under pathological conditions [14], the possibility of a considerable fall in the content of suppressor T cell fraction of the lymphocytes together with changes in the functional properties of the T lymphocytes connected with a change in the intracellular cAMP concentration, which depends on the mediator–hormonal balance, that is sharply disturbed in traumatic shock, cannot be ruled out.

The therapeutic effect of the combination of the immunomodulators thymalin and interferon may perhaps be due to a combination of effects connected with potentiation of functional activity and the process of differentiation of T lymphocytes induced by thymalin [8], and the effect of interferon, manifested as weakening of toxic manifestations, stimulation of phagocytosis [16], increased lysozyme production [11], and its effect on normal killer cells [17], and, probably, on the suppressor activity of T lymphocytes. Administration of interferon, especially in the early stages of development of the traumatic syndrome, can also be regarded as replacement therapy. for under the influence of stress the endogenous interferon level falls considerably [12, 17].

The fact described above may be evidence of a pathogenetic role of disturbances of the immunobiological defense system in the dynamics of the traumatic syndrome, and they indicate the need for the use of immunomodulators in the combined treatment of the traumatic syndrome.

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