ROLE OF THE THYMUS IN REALIZATION OF THE IMMONUMODULATING ACTION OF HYDROCORTISONE

É. V. Gyulling, M. B. Sambur, and V. N. Pisanko

UDC 612.017.1.014.46:615.357.453]-06:612.438

KEY WORDS: thymus; hydrocortisone; immunomodulation.

Experimental and clinical immunologic studies have shown that under certain conditions hydrocortisone (HC) has a marked dose-dependent action on reactions of cellular and humoral immunity [1, 9, 10]. HC, as a stress-realizing hormone, also causes significant changes in the thymus, manifested by destruction, differentiation, and intra- and extrathymic redistribution of thymocytes [2, 3, 12]. On the basis of modern views regarding close functional interconnection between the various formations of the immune system, it can be tentatively suggested that modulation of immune responses of peripheral lymphocytes due to HC is largely effected by cellular and humoral mechanisms of the thymus, the central regulatory organ of immunity.

The aim of this investigation was to determine the role of the thymus in realization of the immunomodulating action of HC.

EXPERIMENTAL METHOD

Experiments were carried out on adult female CBA mice weighing 18-20 g obtained from the Stolbovaya nursery, Academy of Medical Sciences of the USSR. Some of the mice underwent thymectomy [8] 4-5 weeks before the experiment. Water-soluble HC (Solu-Cortef from Upjohn, Belgium) was injected intramuscularly into the mice in a single dose of 10 mg/kg, which gives rise to marked changes in the lymphatic organs [2]. Control animals received a 0.9% solution of sodium chloride.

The role of the thymus in the realization of the modulating action of HC on cellular immunity was determined by comparing data on the effect of this hormone on development of delayed-type hypersensitivity (DTH) to foreign thymocytes and erythrocytes, and also on the rejection time of allografts in normal thymectomized animals. DTH was induced by injection of 10^4 rat thymocytes (RT), heated for 20 min to 56°C, or sheep's red blood cells (SRBC) into the hind footpads of the mice. The intensity of the reaction was assessed by measuring the

TABLE 1. Effect of HC on DTH in Normal and Thymectomized Mice (mean data)

Group of animals	Substance injected	Antigen	No. of expts.	Weight of popliteal lymph nodes, mg		Differences in weight relative to control, in %	P
				expt.	control		
Normal mice	0,9% NaCl	RT	8	3,6 (3—4)	2,3 (2—3)	56,5	<0,01
		SRBC	5	4,3 (3—7)	2,9 (2—5)	48,3	<0,05
	HC I	RT	11	3,0 (2—4)	2,6 (2—3,5)	15,4	>0,05
		SRBC	5	3,1 (2—4)	2,9 (2,4)	6,9	>0,05
	HC II	RT	12	3,4 (1—5)	3,0 (1—4)	13,3	>0,05
		SRBC	8	3,9 (3—5)	3,8 (2,5—5)	2,6	>0,05
Thymectomized mice	0,9% NaCl	RT	5	5,8 (5—7)	4,4 (3,5—5)	31,8	<0,05
		SRBC	5	4,4 (4—5)	3,3 (2—4)	33,3	<0,05
	HC I	RT	5	4,5 (3,5—5)	3,4 (2—4)	32,4	<0,05
		SRBC	7	4,9 (4—6)	3,7 (3—4)	32,4	<0,01
	HC II	RT	5	6,0 (5—7)	4,2 (4—5)	42,9	0,01
		SRBC	6	4,9 (4—5,5)	3,3 (2—4)	48,5	<0,01

Legend. HC I injected 24 h before sensitization, HC II 24 h before reacting injection of antigen. Limits of variations shown in parentheses.

Professor A. I. Kolomiichenko Research Institute of Otolaryology, Ministry of Health of the Ukrainian SSR, Kiev. (Presented by Academician of the Academy of Medical Sciences of the USSR N. N. Gorev.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 99, No. 1, pp. 78-80, January, 1985. Original article submitted November 19, 1983.

0007-4888/85/9901-0096$09.50

increase in weight of the popliteal lymph node after repeated injection of the corresponding cells into the footpads in a dose of 10^6 in 0.05 ml of 0.9% sodium chloride solution [6].

A skin allograft was transplanted from C57BL mice into CBA mice by the method in [13].

The results were subjected to statistical analysis by the Wilcoxon–Mann–Whitney nonparametric U test [5].

EXPERIMENTAL RESULTS

Two injections of foreign thymocytes or SRBC into the hind footpads of the mice induced marked DTH (Table 1) in both normal and thymectomized animals. Injection of HC into normal mice 1 day before sensitization or the reacting dose of antigen significantly inhibited the development of this reaction, as shown by a marked decrease in the difference in weight of the popliteal lymph nodes of the experimental and control limbs of the mice. Meanwhile, injection of HC into thymectomized mice did not affect the development of DTH in these animals.

Similar results also were obtained in experiments with transplantation of a skin allograft, whose rejection was largely due to the DTH reaction [11]. For instance, the mean length of survival of the skin graft in normal CBA mice of the control group ($n = 9$) was 12.8 days. A single injection of HC 6 days after the operation significantly prolonged the survival of the graft to 19.4 days ($P < 0.05$). Injection of HC into mice after preliminary thymectomy, at the same time after allografting, had no significant effect on the mean length of survival of the grafted skin, which was 1.5 and 13.7 days in animals of the control ($n = 7$) and experimental ($n = 7$) groups, respectively.

Since in the thymectomized mice HC does not inhibit the development of DTH, it is most probable that the suppressor action of this hormone on increased sensitivity of cellular type in normal animals is realized under certain conditions mainly through the thymus. We know that the central organ of the immune system is extremely sensitive to hydrocortisone, under the influence of which mass destruction of cortical thymocytes and their increased emigration take place, and the secretory activity of the thymus is modified [4, 7]. It can be postulated on the basis of data obtained previously [3] that with the dose of HC used in the present investigation, the DTH reaction is inhibited by nonspecific suppressor cells emigrating from the thymus.

LITERATURE CITED

1. A. D. Ado, General Allergology [in Russian], Moscow (1978).
2. V. M. Glushkov, V. V. Ivanov, V. M. Yanenko, et al., Modeling of Adaptive Redistribution and Restored Accumulation of Thymus Lymphocytes [in Russian], Kiev (1982).
3. V. M. Glushkov, V. V. Ivanov, V. M. Yanenko (V. M. Janenko), et al., in: Working Conference on Mathematical Modeling in Immunology and Medicine, New York (1982), pp. 131-140.
4. P. D. Gorizontov, Fiziol. Zh. (Kiev), No. 3, 317 (1981).
5. É. V. Gubler and A. A. Genkin, The Use of Nonparametric Statistical Criteria in Medical and Biological Research [in Russian], Leningrad (1973).
6. É. V. Gyulling and M. B. Sambur, Fiziol. Zh. SSSR, No. 2, 237 (1981).
7. R. V. Petrov, R. M. Khaitov, V. I. Man'ko, et al., Control and Regulation of the Immune Response [in Russian], Moscow (1981).
8. A. Barbul, D. A. Sisto, and G. Efron, Transplantation, 28, 427 (1979).
9. A. S. Fauci, in: Glucocorticoid Hormone Action, Berlin (1979), p. 449.
10. J. S. Goodwin, Cell. Immunol. Immunopathol., 25, 243 (1982).
11. G. D. Snell, J. Sausset, and S. G. Nathanson, Tissue Compatibility [Russian translation], Moscow (1979).
12. L. Rozenszain, J. Kalechman, J. Danziger, et al., in: Experimental Hematology Today, Basel (1982), p. 71.
13. H. Kaunat, Immunologische Arbeitsmethoden, Jena (1976).