Serotonin Metabolism in Immunocompetent Organs of Tumor Rats after Autohemochemotherapy

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Administration of cyclophosphamide by the method of autohemochemotherapy produced a greater serotonin-potentiating effect in immune organs compared to that observed during systemic chemotherapy.

Key Words: *serotonin; immune organs; autohemochemotherapy*

Chemotherapy is an important modern method of antitumor treatment. The disadvantage of this method is a negative effect of cytostatic drugs on the organism (*e.g.*, organs of the immune system). Administration of chemotherapeutics by means of autohemochemotherapy (AHCT) potentiates antitumor activity and abolishes the toxic effect on organs and tissues.

The monoamine system is involved in neurohormonal regulation of immune process in the organism [3].

Here we studied the effect of AHCT on serotoninergic activity of immune organs.

MATERIALS AND METHODS

Experiments were performed on 56 male outbred albino rats weighing 180-200 g. The animals were divided into 4 groups (14 rats per group). Group 1 rats were intact. Group 2 included rats with sarcoma-45. Group 3 consisted of tumor rats that received systemic chemotherapy (SCT) with cyclophosphamide (CP). Group 4 consisted of tumor rats receiving AHCT with CP.

CP was administered on days 1 and 4 of study. SCT was performed by infusion of CP in a single dose of 50 mg/kg. For AHCT, the blood (1 ml) was preincubated with a single dose of CP at 37°C for 45 min and reinfused into the jugular vein.

The concentrations of serotonin and 5-hydroxyindoleacetic acid in the hypothalamus, thymus, and spleen of rats were measured by the spectrofluorometric micromethod 2 weeks after repeated administration of CP. Fluorescence of treated and reference samples was measured on a MPF-4 spectrofluorometer (Hitachi).

The results were analyzed by nonparametric Wilcoxon—Mann—Whitney test. The differences were significant at $p \leq 0.05$.

RESULTS

CP produced a potent effect on hydroxyindole metabolism in the hypothalamus, thymus, and spleen of rats (Table 1). Serotoninergic modulation increased in the hypothalamus. The basal serotonin level in rats decreased after SCT, but increased to the control level in animals of the AHCT group. Increased synthesis of serotonin compensated for its accelerated inactivation in the thymus under both regimens of therapy, but the changes were most pronounced after administration of serotonin by the method of AHCT (Table 1). Independently on the route of administration, CP contributed to an increase in serotonin inactivation in the spleen. This effect was most significant after SCT. Serotonin accumulation in tissues was significant only after administration of the cytostatic by means of AHCT (Table 1).

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TABLE 1. Concentrations of Serotonin and 5-Hydroxyindoleacetic Acid in the Hypothalamus, Thymus, and Spleen of Rats with Sarcoma-45 after SCT and AHCT (*M*±*m*)

Organ, parameter	Group			
	1	2	3	4
Hypothalamus				
serotonin	2.15±0.20	1.38±0.24*	1.23±0.28*	2.08±0.31°
5-hydroxyindoleacetic acid	0.50±0.13	0.65±0.07	0.87±0.13	0.93±0.10*+
Thymus				
serotonin	0.63±0.04	0.91±0.19	0.86±0.09*	1.13±0.14*+°
5-hydroxyindoleacetic acid	0.170±0.014	0.32±0.06	0.33±0.02*	0.46±0.06*+°
Spleen				
serotonin	0.90±0.15	1.10±0.21	1.40±0.17*	1.81±0.18*+
5-hydroxyindoleacetic acid	0.20±0.03	0.35±0.04	0.65±0.05*+	0.47±0.08*°

Note. $p<0.05$: *compared to group 1; +compared to group 2; °compared to group 3.

The mechanism of the activating effect of CP on serotoninergic structures in these organs is unknown. Our results do not explain whether CP produces a direct effect or its influence is mediated by endogenous humoral factors. It cannot be excluded that the effect of CP is a trace response to cytotoxic stress.

Serotonin concentration in organs increased most significantly after administration of CP by means of AHCT. These changes contribute to mobilization of defense reserves, since serotonin is the key transmitter of the stress-limiting system. The increase in serotoninergic activity in the hypothalamic-pituitary complex potentiates neuroendocrine functions and contributes to mobilization of major adaptive systems in the organism. The increase in serotonin concentration in tissues (*e.g.*, lymphatic tissue) reflects the adaptive response, which abolishes the effect of stress factors [1].

Our data on the sparing effect of AHCT with CP on immune organs are consistent with published data on better preservation of lymphoid structures in the thymus and spleen, absence of serious toxic damage to immune organs, and increase in extremely low membrane potential of immunocompetent cells [2]. These factors determine the adequate immune response of an organism to cytostatic therapy.

REFERENCES

1. N. A. Zlobina and S. B. Lur'e, *Uspekhi Fiziol. Nauk*, **25**, No. 3, 19 (1994).
2. T. V. Zubkova and O. V. Tarnopol'skaya, *New Methods of Intensive Therapy for Cancer Patients* [in Russian], Moscow (2000).
3. G. Yu. Struchko, L. M. Merkulova, V. E. Sergeeva, *et al.*, *Immunologiya*, No. 1, 15-19 (2001).