EXPERIMENTAL STUDY OF THE MODIFYING ACTION OF DARKNESS ON GROWTH OF MAMMARY GLAND CARCINOMA AND EFFICACY OF HORMONE THERAPY

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The effect of different conditions of illumination on the properties of a transplantable rat mammary-gland carcinoma (RMK-1) and on the efficacy of its hormone therapy was studied. In darkness the percentage of successful takes was reduced, the rate of growth of the RMK-1 tumor was slowed, and the efficacy of estrogen therapy of the mammary-gland carcinoma was increased considerably. It is suggested that the increased efficacy of treatment of the RMK-1 tumor in darkness can be attributed to changes in functional activity of the hypothalamic–pituitary system.

KEY WORDS: conditions of illumination; mammary gland carcinoma; hormone therapy.

The mechanism of the antitumor action of large doses of estrogens and androgens on mammary-gland carcinoma consists essentially of depression of the production of pituitary gonadotropic hormones [2, 7, 8]. The writer showed previously that in darkness the activity of the hypothalamic–pituitary system of rats is reduced, and the reactivity of the pituitary gonadotropic function to the inhibitory action of estrogens and androgens is increased [5, 6]. This suggested that changes in the conditions of illumination could influence the efficacy of hormone therapy of mammary gland carcinoma. However, in the first step it was necessary to find out whether changes in the conditions of illumination are reflected in the course of mammary gland carcinoma itself.

The object of the present investigation was to study the effect of darkness on transplantability and growth of mammary-gland carcinoma in rats and of the efficacy of its hormone therapy.

EXPERIMENTAL METHOD

Experiments were carried out on 123 sexually mature female rats weighing initially 150-200 g. A transplantable strain of rat mammary-gland carcinoma (RMK-1), obtained from the Laboratory of Experimental Endocrinology, Institute of Experimental and Clinical Oncology, Academy of Medical Sciences of the USSR [3, 4, 7], was used as the experimental model of hormone-dependent mammary-gland carcinoma. A

TABLE 1. Percentage of Takes and Size of Developing Tumors in Rats with Transplanted Mammary-Gland Carcinoma and Kept Under Different Conditions of Illumination (M ± m)

Conditions of illumination	Number of rats	Percentage of successful takes of RMK-1	Size of tumor on 10th day (in cm^3)
Ordinary	23	87,0±7,0	0,93±0,25
Darkness	38	50,0±8,0	0,40±0,14
P		<0,05	<0,05

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TABLE 2. Effect of Estrogen Therapy on Growth of Transplantable Rat Mammary-Gland Tumor (RMK-1) under Different Conditions of Illumination

Experimental conditions	Number of rats	Mean weight of tumor (in g)	Inhibition of growth (in %)	Percent absorption
Control (0.5 ml physiological saline)	14	16,0±3,2	—	—
Ordinary illumination + dihydrostilbestrol (5 mg implanted subcutaneously)	15	8,8±1,33	45,0±13,2	6,6±6,6
P_{1-3}		<0,05	—	—
Ordinary illumination + dihydrostilbestrol (5 mg implanted subcutaneously)	15	2,7±0,63	83,0±10,1	46,6±11,9
P_{1-3}		<0,01	—	—
P_{2-3}		<0,01	<0,05	<0,01

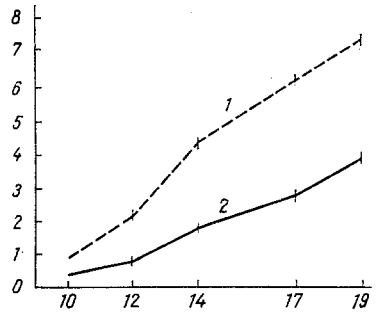

Fig. 1. Dynamics of growth of mammary gland carcinoma (RMK-1) in rats kept in ordinary daylight (1) and in darkness (2). Abscissa – day after transplantation of RMK-1; ordinate – mean volume of tumor (in cm^3; M ± m)

suspension of tumor tissue in physiological saline (1:5) was injected subcutaneously in a dose of 0.5 ml. This volume of tumor suspension contained about 2 million tumor cells. After transplantation of tumor the rats were divided into two groups, one of which was kept in a darkened room, and the other under ordinary conditions of illumination in the animal house. The percentage takes of the RMK-1 tumor, the dimensions of the developing tumros, and the dynamics of growth of the mammary gland carcinoma were investigated. To study the rate of growth of the RMK-1 tumor under different conditions of illumination, the volume of the tumor was measured in the experimental rats on the 10th, 12th, 14th, 17th, and 19th days after transplantation [13].

In special experiments 7 days after transplantation, when tumor nodules measuring 0.3-0.5 cm^3 could already be palpated in most of the rats, 5 mg dihydrostilbestrol was implanted subcutaneously and these animals, as in the previous experiments, were divided into two groups, kept under different conditions of illumination. The experiment lasted 14 days. The animals were killed and the percentage inhibition of growth of the tumors was calculated from their mean weight [10]:

$$\%T = \frac{M_c - M_e}{M_c} \times 100,$$

where M_c is the mean weight of the tumor in the control group and M_e its mean weight in the experimental group.

EXPERIMENTAL RESULTS AND DISCUSSION

The results of the investigation of the effect of darkness on development of the mammary-gland carcinoma in rats are shown in Table 1 and Fig. 1.

In darkness the percentage of successful takes of the tumor was reduced and the tumors grew more slowly.

As Table 2 shows, the efficacy of estrogen therapy given to animals kept in darkness was almost twice as high as under ordinary conditions of daylight. In darkness, moreover, complete absorption of the tumor occurred as a result of estrogen therapy in 7 of the 15 rats, compared with only one of the rats kept in ordinary daylight.

The increase in the efficacy of treatment of the mammary gland carcinoma in darkness can tentatively be explained by changes in the hormonal activity of the pituitary gland [1, 11, 12]. Since strain RMK-1 reacts to hormonal factors, including a change in pituitary gonadotropic activity [7-9], darkness could be a factor increasing the efficacy of hormone therapy of mammary-gland carcinoma in rats.

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