Experimental Study of Cytoprotective Effect of Melatonin in Radiation Exposure

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The effects of a synthetic analog of melatonin in doses of 10 and 50 mg/kg on the incidence of chromosome aberrations in bone marrow cells was studied in outbred rats exposed to single short-term γ-irradiation in doses of 2 and 4 Gy. Melatonin injected 30 min before the exposure 2-fold reduced the incidence of chromosome aberrations. Possible mechanisms of anticlastogenic effect of melatonin are discussed.

Key Words: *chromosome aberrations; γ-irradiation; melatonin; antimutagenic effect*

DNA is a unique biomacromolecule. Damage to DNA caused by ionizing radiation exposure can have grave consequences for the organism. The search for substances of natural or synthetic origin capable of protecting the genetic system from radiation injuries is therefore a pressing problem of modern radiobiology and radiation medicine. Recent studies have demonstrated a pronounced antimutagenic effect of melatonin (MT) under conditions of exposure to various clastogenic factors [1-5].

We studied the effects of MT on the clastogenic effects of γ-radiation on rat bone marrow (BM) cells.

MATERIALS AND METHODS

Experiments were carried out on 32 outbred female rats (200-280 g). The animals were exposed to short-term whole-body γ-irradiation (Cs^{137}) in doses of 2 or 4 Gy at 1 Gy/min radiation power. Melatonin was injected intraperitoneally in suspension in doses of 10 or 50 mg/kg 30 min before radiation exposure.

Isolation of BM cells, preparation making, and cytogenetic analysis were carried out by standard methods [6,11]. The counts of cells with single and paired fragments of chromosomes, dicentric chromosomes, translocations, with two or more chromosome sets were counted 24 h after the radiation exposure. A total of 100 metaphase plates were analyzed for each animal.

The results were statistically processed by Student's *t* test.

RESULTS

The count of cells with chromosome aberrations (CA) of different types in intact rats was about 1.5%. Exposure to a dose of 2 Gy caused injuries in the genetic apparatus of actively proliferating BM cells and the incidence of CA increased to 15.8±1.7% (Table 1). The mean number of aberrations was 87.0±1.5; the number of paired fragments was 38.0±2.1, single fragments 26.0±1.9, and dicentrics 17.0±1.5. Single translocations and polyploids were found.

The mean incidence of cells with CA 24 h after exposure in a dose of 4 Gy was 13.8±1.7%; the total number of aberrations was 92.0±1.3, the number of paired fragments, polyploids, and single fragments was 50.0±2.5, 32.0±2.5, and 7.0±1.2, respectively. Single dicentrics and translocations were found.

Preventive injection of MT in a dose of 10 mg/kg to rats irradiated in a dose of 2 Gy significantly (2-fold) reduced the incidence of aberrant cells (Table 1). The counts of single and paired fragments and dicentrics also significantly decreased (by 2-3 times).

Melatonin treatment in a dose of 10 mg/kg before exposure in a dose of 4 Gy was ineffective, but in a

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TABLE 1. Effects of MT on the Incidence of CA in BM Cells of Rats Irradiated in Doses of 2 and 4 Gy (*M*±*m*)

Parameter	Group		Irradiation dose, Gy	
			2	4
Incidence of aberrant cells, %	Control	-	15.8±1.7	13.8±1.7
	MT, mg/kg	10	8.0±1.2*	13.3±1.8
		50	-	6.5±1.2*
Total number of aberrations	Control	-	87.0±1.5	79.0±2.0
	MT, mg/kg	10	51.0±2.2	92.0±1.3
		50	-	42.0±2.4*
Single fragments	Control	-	26.0±1.9	7.0±1.2+
	MT, mg/kg	10	9.0±1.2*	12.0±1.6
		50	-	5.0±1.0
Paired fragments	Control	-	38.0±2.1	50.0±2.5
	MT, mg/kg	10	18.0±1.7*	56.0±2.4
		50	-	28.0±2.2*
Dicentric chromosomes	Control	-	17.0±1.6	2.0±0.7+
	MT, mg/kg	10	9.0±1.2*	0
		50	-	0
Translocations	Control	-	2.0±0.6	1.0±0.4
	MT, mg/kg	10	1.0±0.4	3.0±0.8
		50	-	2.0±0.7
Polyploids	Control	-	4.0±0.8	32.0±2.3
	MT, mg/kg	10	0	8.0±1.3
		50	-	4.0±0.8*

Note. $p<0.05$ in comparison with: *control, +exposure dose of 2 Gy.

higher dose (50 mg/kg) it promoted a 2-fold reduction of the incidence of aberrant cells and total number of CA. The counts of paired fragments decreased significantly, particularly of polyploids (8-fold).

Discussing the results, we paid special attention to two aspects. The total number of aberrant cells and CA did not change with increasing the irradiation dose (the incidence of the former remained at the level of 14-16%, the number of CA was 90). On the other hand, the structure of CA changed with increasing the exposure dose: the incidence of dicentrics and single fragments decreased, while the counts of paired fragments and polyploids increased.

Since all the above-listed CA types were unstable (cells containing these CA died after one or several mitoses), the mechanism of this phenomenon can be explained by delayed death of aberrant cells after low dose exposure and hence, by their delayed elimination.

The other aspect seems to be more significant. The results have proven that MT significantly reduces (almost 2-fold) the total number of CA induced by radiation exposure and this was so for in fact all the studied types of unstable CA (fragments, dicentrics, and polyploids).

It is assumed that the protective effect of MT in various modulatory exposures is determined by its antioxidant activity [8,10,12]. However, other mechanisms are also possible, for example, modulation of the functional and proliferative activities of cells and tissues [4].

The anticlastogenic effect of MT, no doubt, contributes to reduction of the intensity of the post-irradiation cell death; this seems to be responsible for the radioprotective effect of MT in total and local radiation injuries [3,13].

The results of our studies in general attest to high antimutagenic effect of MT in clastogenic exposure of not only chemical [7], but also of radiation etiology.

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