Plasma Antioxidant Activity and Chromosome Aberrations in Humans Exposed to Long-Term Low-Dose γ-Irradiation

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Plasma antioxidant activity was evaluated in the lecithin-Fe^{2+} model system and cytogenetic studies were carried out in 16 men. A relationship between elevated antioxidant activity of the plasma and increased level of chromatid aberrations and with percentage of aberrant cells was detected in the experimental group, but no correlation was found between antioxidant activity and the integral dose of γ-irradiation and rate of its accumulation. An assumption was made about exhaustion of the "buffer capacity" of the antioxidant defense system resulting from long-term exposure to unidentified factors of technogenic nature increasing plasma antioxidant activity and level of chromosome aberrations. In subjects with high level of antioxidant defense, naturally low antioxidant activity and low percentage of chromatid aberrations were probably maintained.

Key Words: *antioxidant activity; chromosome aberrations; γ-irradiation*

Multicomponent antioxidant defense system (AOS) prevents excessive generation of AOF and negative aftereffects of uncontrolled free radical oxidation reactions in humans [12,14]. Obviously, the efficiency of AOS and the fate of primary injuries to biomolecules are genetically determined by individual features of this system [7]; functional status of this system determines the adaptation potentialities and the life span. It was hypothesized that blood plasma is a limiting component of AOS playing the key role in the transport and distribution of antioxidants in the whole body [14]. The level of chromosome aberrations increased in peripheral blood lymphocyte culture obtained from irradiated subjects in delayed periods after exposure [2,3].

We evaluated the relationship between AOS and level of chromosome aberrations in subjects exposed to low-dose ionizing radiation.

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MATERIALS AND METHODS

Cytogenetic studies and evaluation of antioxidant activity (AOA) were carried out in two groups of healthy subjects. Group 1 consisted of 16 men aged 43-65 years working at a large nuclear chemistry plant (Siberian Chemical Plant — SCP) for 22-37 years; the integral doses of γ-exposure varied from 17 to 122 rem, the mean rate of dose accumulation was 2.60±0.33 rem/year. The control group consisted of 23 subjects aged 12-47 years living in ecologically clean region 65 km from Tomsk. Peripheral blood lymphocytes were routinely cultured with phytohemagglutinin for 52 h. Two hours before fixation colchicine (0.5 μg/ml) was added. The cells were fixed with a methanol:acetic 3:1 acid mixture. The preparations were stained by the method of Giemsa. A total of 100-600 metaphase plates from each individual were examined (a total of 11,218 cells). Paired fragments, dicentric and annular chromosomes (chromosome aberrations), solitary fragments and chromatid exchanges (chromatid aberra-

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tions) were counted, and the percentage of aberrant cells was estimated. AOA was measured by spectrophotometric evaluation of products reacting with thiobarbituric acid. The reaction was carried out in a lecithin-Fe^{2+} ion model system with analyzed blood plasma sample [6]. The data were processed using nonparametric ranked tests: Mann—Whitney *U* test and Spearman's correlation (*R*) test. The relationship between AOA variability and age, length of service at SCP, integral dose of γ-irradiation, and rate of its accumulation was analyzed by common analysis of correlations after Pearson (Statistica 5.5).

RESULTS

The groups did not differ by the number of dicentric and annular chromosomes (markers of radiation injury) (Table 1) [1,3], which indicates a negligible effect of radiation on chromosome variability in SCP workers. The groups did not differ by the levels of chromosome aberrations and paired fragments per 100 cells. The level and incidence of chromosome aberrations in SCP workers did not surpass the values in liquidators of the Chernobyl power plant accident [9] and in residents of polluted regions [1,3]. High level of solitary fragments and chromatide aberrations and high percentage of aberrant cells were detected in SCP workers in comparison with rural residents. This was presumably due to age (SCP workers were 1.5 times older), effects of chemical and biological mutagens, or effects of factors of unknown origin.

No relationship between AOA and age was detected. This is in line with published data indicating that the integral AOA is resistant to age-associated changes [7,15], while activity and content of antioxidant enzymes and low-molecular-weight antioxidants decrease alter the age of 75 years [11,13]. We revealed seasonal variability of AOA [7,8]; presumably, this can explain the differences in AOA in different populations (Table 1). Effects of genetic, other external or stochastic causes cannot be ruled out. In group 1 AOA values increased with the increase in the number of chromatid exchanges (R=0.446, p=0.083), and a significant relationship between increased AOA and increase in the number of solitary fragments (R=0.639, p=0.008) was revealed. AOA increased with the increase in the number of chromatid aberrations (R=0.636, p=0.008; Fig. 1).

No relationship between AOA variability and number of chromosome aberrations, paired fragments, dicentric and annular chromosomes was detected. AOA increased with the increase in the percentage of aberrant cells (R=0.605, p=0.013). No changes of this kind were detected in AOA values of the rural population. Fragments of values in two individuals with multiaberrant cells (6 and more aberrations per cell) were situated near the AOA-level of chromatid aberrations regression line (Fig. 1).

No relationship between AOA variability and integral dose of γ-irradiation and rate of its accumulation was detected [2]. However, AOA increased in subjects with longer service at the plant (Pearson's coefficient of correlation 0.388±0.246, p=0.137). This indicates a greater effect of chemical and biological factors on individual AOS status in comparison with the radiation factor.

Increased AOA in subjects with greater number of chromatid aberrations, percentage of aberrant cells, and length of service at SCP can be a result of interrelated causes: prolonged exposure to anthropogenic and/or biological mutagens results in exhaustion of the "buffer capacity" of antioxidant defense, paralleled by increase a plasma AOA, or individuals with high "buffer capacity" of AOS retain the natural low level of AOA and low level of chromatid aberrations for a longer time during similar exposure to various factors. Increased antioxidant status in Ehrlich tumor in mice exposed to γ-radiation [10] supports the first hypothesis, as well as high level of AOS defense in tumor tissues *in vivo*, which are characterized by high level

TABLE 1. Results of Cytogenetic Examinations and Plasma AOA Levels in Different Groups (M±m, per 100 cells)

Parameter	Control (n=23)	Chronic exposure (n=16)	U	p
AOA	4.813±0.766	3.950±0.921	76.0	0.002
Chromosome aberrations	0.64±0.54	1.71±2.03	140.0	0.209
Paired fragments	0.48±0.43	1.45±1.67	131.0	0.130
Dicentric and annular chromosomes	0.18±0.29	0.23±0.74	160.0	0.493
Chromatid aberrations	0.89±1.05	2.06±2.09	100.5	0.017
Solitary fragments	0.79±1.06	1.71±1.64	92.0	0.009
Chromatid exchanges	0.10±0.21	0.35±0.62	140.5	0.214
% of aberrant cells	1.36±1.13	2.78±2.19	104.0	0.021

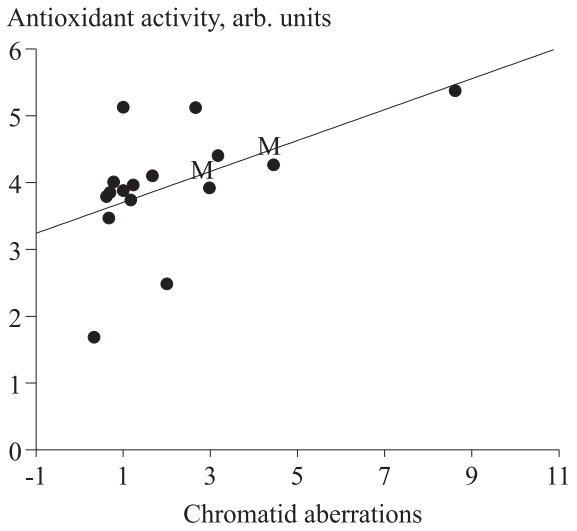

Fig. 1. Linear regression between antioxidant activity and level of chromatid aberrations. Abscissa: number of chromatid aberrations per 100 cells. M: individuals with multiaberrant cells.

of aberrations [4]. In our model system lecithin—Fe^{2+} ions total AOA is mainly determined by the effects of iron-binding and iron-oxidizing components of AOA (ceruloplasmin, transferrin, bilirubin). The effects of other components of plasma AOA (ascorbate, urate, α-tocopherol, carotenoids) on the characteristics of this system are negligible [5].

We cannot rule out the effect of rare-ionizing γ-irradiation on plasma AOA. We previously showed that AOA decreased in individuals aged over 55 years exposed to a dose of over 107.8 rem at the dose accumulation rate of 3.58±0.12 rem/year [6].

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